

# Treatment Options for Nephrotic Syndrome

## Los Angeles Family Wellness Day

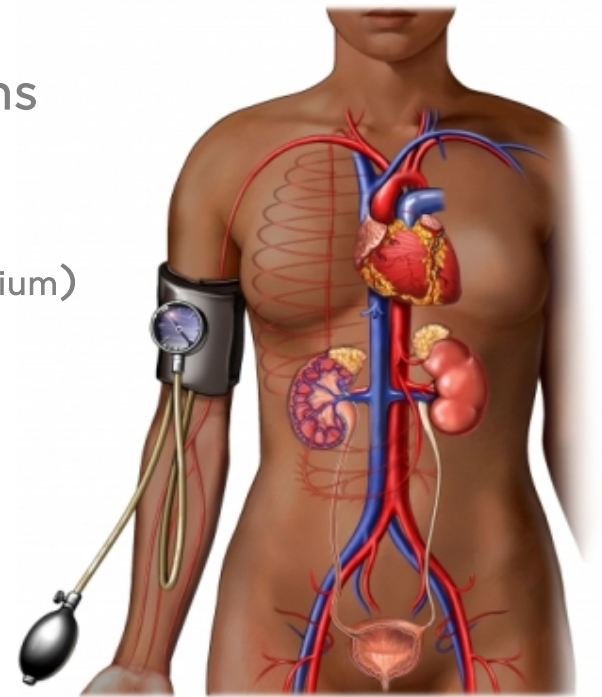
### January 20, 2019



# What Do The Kidneys Do?

Healthy, functioning kidneys are important because they:

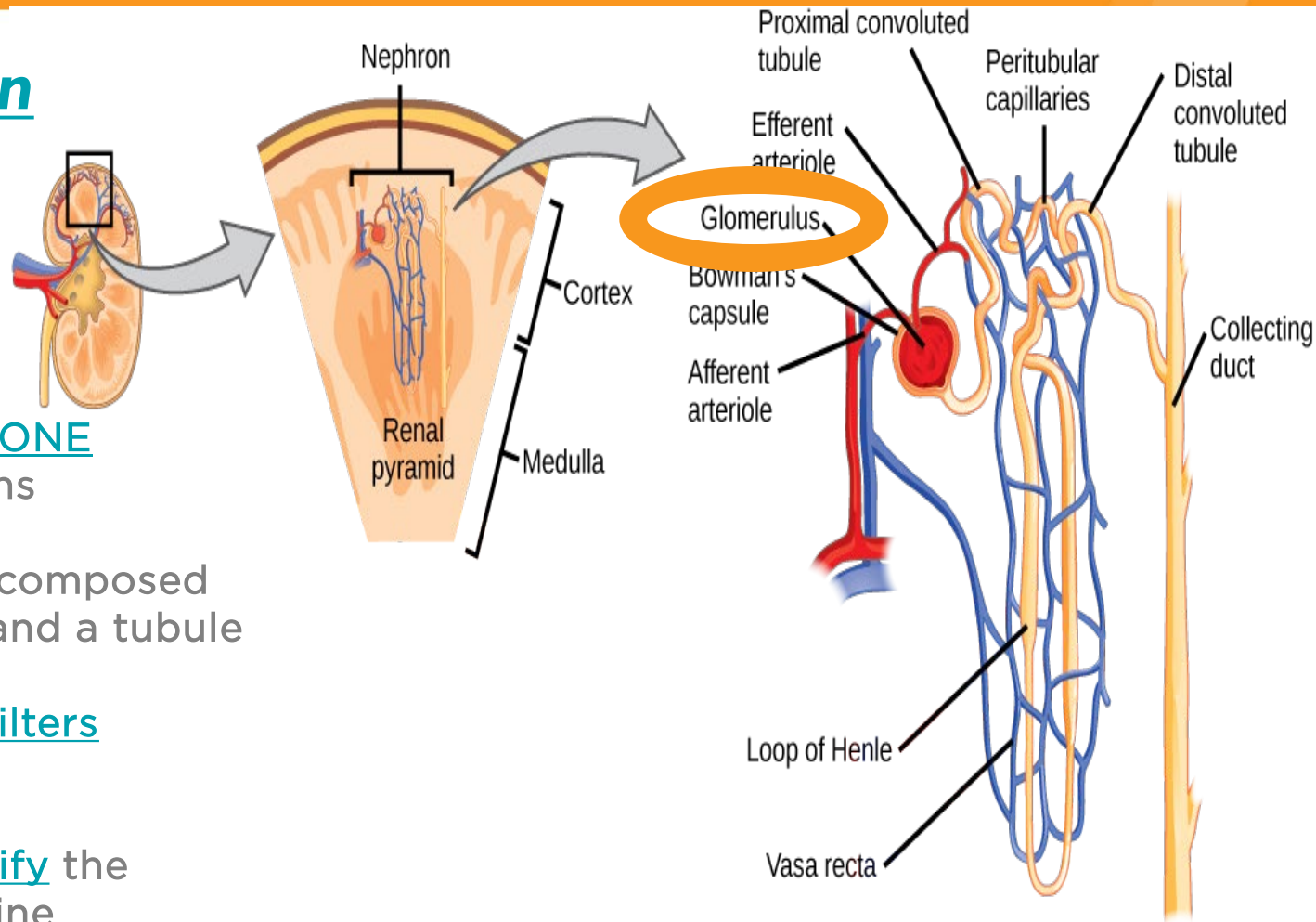
- Eliminate waste products, drugs and toxins from the blood
- Regulate:
  - electrolyte concentrations (like salt, potassium)
  - amount of fluid within the body
  - blood pressure
- Help maintain acid base balance
- Produce hormones that affect blood and bones



# What Do The Kidneys Do?

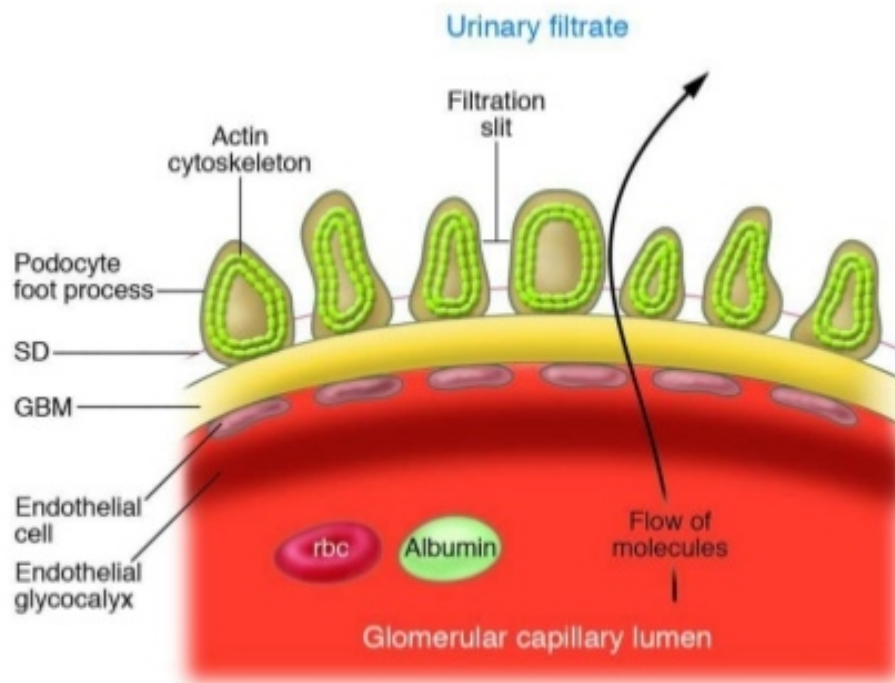
## The Nephron

- Each kidney has ONE MILLION nephrons
- Each nephron is composed of a glomerulus and a tubule
- The glomerulus filters wastes and fluid
- The tubules modify the waste to form urine

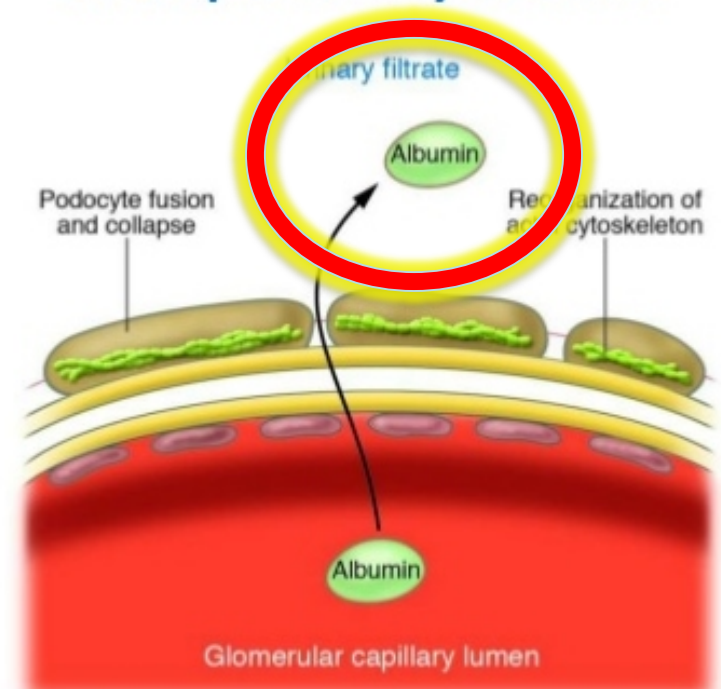


# Disruption of the Glomerular Structure Leads to Nephrotic Syndrome

## The Glomerular Filtration Barrier



## Failure of the Filtration Barrier in Nephrotic Syndrome



# The Kidney is like a Strainer



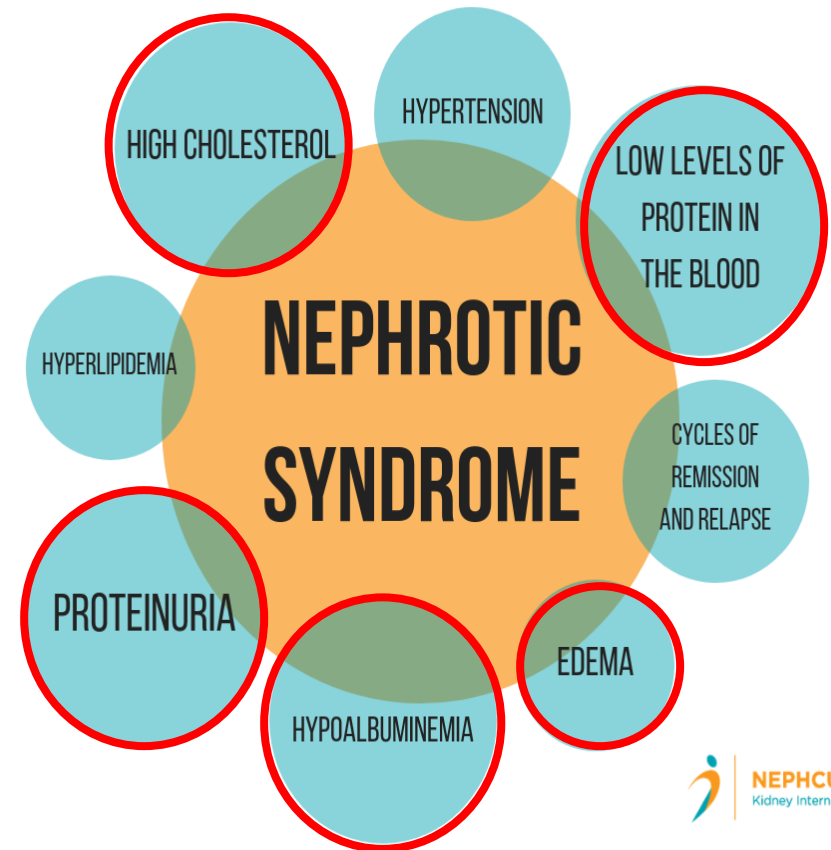
Think of the kidney as a strainer - it keeps the good stuff in and drains the water.

When you have Nephrotic Syndrome, the strainer holes are too big and the good stuff gets out.



# Nephrotic Syndrome

- Nephrotic Syndrome (NS) is a collection of symptoms that are due to loss of good proteins from the body
- We measure this by looking for:
  - Higher protein in urine
  - Lower protein in the blood
- NS is a [sign of kidney damage](#)
- Damage can be from a disease that affects the kidney and other organs
  - Examples: Lupus, Rheumatoid arthritis, HIV, Hepatitis B and C
- Damage can also be from a [kidney disease](#)
  - This is called *Primary, or Idiopathic*



# Primary Nephrotic Syndrome: Many kidney disorders

## “NEPHROTIC WHAT?!”...

*Understanding Primary Nephrotic Syndrome*

**TIP:** Don't be intimidated by the disease names; they are just *descriptions* of how the kidney tissue looks under a microscope.



**Nephrotic Syndrome (NS) is not a disease, but an umbrella term for the collection of signs and symptoms that occur when the kidney filters (glomeruli) leak protein into the urine.**

**Some symptoms of NS include:**

- Proteinuria ('leaking' protein into the urine)
- Edema (swelling)
- Hypertension (increased blood pressure)
- Hypoproteinemia (low blood protein)
- Hypercholesterolemia (high cholesterol)

Someone who is experiencing these symptoms but has *not* had a kidney biopsy is diagnosed with **Nephrotic Syndrome.**

To learn more about what is causing a patient's Nephrotic Syndrome, doctors may choose to perform a kidney biopsy. After a biopsy, a patient is usually diagnosed more specifically, based on what can be seen under the microscope. The most common diagnoses are:

**Focal Segmental Glomerulosclerosis (FSGS)**

Some sections of kidney filters show scarring.

**Minimal Change Disease**

Kidney tissue shows very little change from normal kidney tissue.

**Membranous Nephropathy**

Kidney tissue has a thicker than normal filtering barrier or glomerular basement membrane.



# Kidney biopsies make specific diagnosis

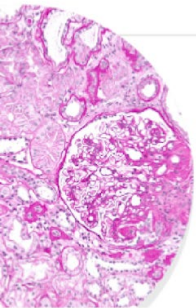
## BIOPSY PROCEDURE



- 1. Biopsies are typically performed by a nephrologist or interventional radiologist.
- 2. Biopsies are often done after light sedation or local anesthesia.
- 3. A small piece of tissue from one kidney is taken by a specialized needle for examination under a microscope by a kidney pathologist.
- 4. After a biopsy, limited activity or bed rest will be recommended for a period of time.

### THE LOW-DOWN ON

## Kidney Biopsies



Kidney biopsies are important because they can help your doctor learn what is causing your nephrotic syndrome and how severe it is. This will help them form your treatment plan. Additional biopsies may be done later on to see how your treatment is working.



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# Biopsies for Kids and Adults

## FOR KIDS

**Nephrologists will usually recommend a child have a biopsy if:**

- They have certain findings when they are first diagnosed (such as abnormal kidney function or a family history of nephrotic syndrome.)
- They do not respond to their very first course of prednisone ("steroid resistant")
- They initially responded to steroids but have gradually become less responsive or have frequent relapses or cannot be weaned off steroids ("steroid dependent")
- They have unusual findings such as abnormal kidney function.



## FOR ADULTS

**Kidney doctors are more likely to recommend a biopsy for adult patients when they are first diagnosed.**

**The results of a biopsy will help determine what is causing a patient's Nephrotic Syndrome and can help guide treatment.**



# Treatment Goals

## Short Term

- Reduce / eliminate protein spillage into the urine
- Improve clinical symptoms (swelling, edema, fatigue)
- Correct abnormalities of the blood levels (cholesterol, albumin)

## Long Term

- Prevent recurrences of protein spillage into the urine
- Preserve kidney function
- Avoid treatment-related complications



# Treatment Options: First Line

1

Usually, patients  
are treated with  
**corticosteroids**  
first.

Corticosteroids  
(Prednisone)

# Treatment Options: Second and Third Line and Rescue therapies

2

If steroids **fail to cause remission** (usually within 8-12 weeks), or if a patient becomes “**steroid dependent**,” one or more of the following treatments may be tried.

Cyclophosphamide  
(Cytosan)

ARBs

Cyclosporine (Neoral)

Methylprednisolone  
(Solu Medrol)

Mycophenolate  
(MMF, Cellcept, Myortec)

Plasmapheresis  
(Liposorber)

Adrenocorticotropin  
(ACTH Acthar Gel)

Prograf (Tacrolimus)

ACE  
Inhibitors

Rituxan  
(Rituximab)

# Additional Options: Experimental treatments (clinical trials)

3

There are a number of other potential treatments that may reduce proteinuria in Nephrotic Syndrome patients. Ask your doctor about **clinical trials** for these.

Sparsentan

Losmapimod (p38MAPKi)

Abatacept  
(Orencia)



# Treatment of Nephrotic Syndrome

Widely accepted initial therapy  
for both children and adults :

## Prednisone



Prednisone is an immunosuppressant, but it may function in more than one way. This may help reduce swelling, and, hopefully, help the kidneys function properly

- If there are frequent relapses, or the patient is non-responsive,
  - Talk to your doctor about adding other medications to the prednisone
  - Talk to your doctor about trying a different therapy plan
  - Be prepared for the “laundry list” of side effects that may occur
  - Talk to your doctor about clinical trials

# Personalized Treatment of Nephrotic Syndrome

Primary Nephrotic Syndrome  
is difficult to treat because of the  
variable causes and clinical courses

- Steroid Responsive vs. Steroid Resistant
- An “off-label” medication is one that is approved by FDA for a disease that is not Nephrotic Syndrome, but used to treat it anyway by a doctor’s recommendation
- Clinical trials are always an option
  - For both children and adults
- Some patients have found alternative therapies useful for some of the symptoms
  - Acupuncture, vitamin therapies, diet and lifestyle changes

Second-line for some of the symptoms  
Therapies

Abatacept  
Acthar  
Cyclophosphamide  
Cyclosporine  
Mycophenolate mofetil  
(Cellcept or Myfortic)  
Rapamycin  
Rituxan  
(Rituximab)  
Tacrolimus (Prograf)

\*Talk to your doctor about the appropriate therapy for you-based on symptoms, age, side-effects, delivery methods, etc.



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# Current Treatment Options

- **None** of them:
  - Are **specifically designed** to treat Nephrotic Syndrome
- **Sometimes traditional treatments:**
  - Have some short and long-term **side effects**
  - Are classified as ‘off label’ and therefore may bring **insurance headaches**
  - May become **ineffective** over time



# Common Questions about Nephrotic Syndrome Treatments

Are there established guidelines  
for how to treat  
Nephrotic Syndrome?



# Common Questions about Nephrotic Syndrome Treatments

I was labeled “steroid resistant”

My doctor still has me taking  
prednisone with my second line  
medication.

Why?





# Common Questions about Nephrotic Syndrome Treatments

Why do different doctors  
prescribe different second line  
medications for people with the  
same diagnoses?



# Common Questions about Nephrotic Syndrome Treatments

I want to participate in a clinical trial,  
but my doctor wants to try  
other medications first.  
Does this make sense?



# Common Questions about Nephrotic Syndrome Treatments

Should I get a genetic test?  
Will the results impact my treatment  
plan?



# DUPLEX is an example of an available clinical trial

## Why would I want to join a clinical trial? How do I know which clinical trial is right for me?

### About the DUPLEX Study



The aims of the study are to learn how safe the investigational medication is and to see how well it works to slow the decline of kidney function in patients with FSGS.



Approximately 300 people will participate in about 150 study sites worldwide.



The study will last up to 27 months.



Participants receive either sparsentan or a comparator medication, which are taken by mouth.

### You may be eligible to participate in the DUPLEX Study if you:

- Are 8–75 years of age living in the US (18–75 years of age in other countries)
- Have been diagnosed with FSGS without a known or obvious cause

Talk with your doctor and family members about joining the DUPLEX Study. Sites are open and currently recruiting.

To find a site near you,  
visit **FSGSDUPLEX.com**,  
**clinicaltrials.gov**  
**NCT03493685**, or contact  
**medinfo@retrophin.com**

# The Gateway Initiative: Helping Clinical Trials Succeed and Addressing Gaps in Treatment






# Solution 1

## Clinical Trials are not well publicized

### Gateway to find patients & expand the clinical trial-ready community



**Question 1**

Please answer the next 4 questions on behalf of the person with kidney disease.

QUESTIONS 1 OF 4

What is your diagnosis?

PLEASE ASSUME THAT THE CONDITIONS LISTED ARE "PRIMARY" OR "IDIOPATHIC". IF YOU HAVE A GENETIC MUTATION, WE WILL CONSIDER IT TO BE "PRIMARY" FOR THE PURPOSES OF THIS QUESTION.

- ☐ FSGS
- ☐ MINIMAL CHANGE DISEASE
- ☐ IGA NEPHROPATHY
- ☐ MEMBRANOUS NEPHROPATHY
- ☐ C3 GLOMERULOPATHY
- ☐ NEPHROTIC SYNDROME

- User friendly clinical trials.gov digital tool
- [www.kidneyhealthgateway.com](http://www.kidneyhealthgateway.com)

Global expansion

- NephCure Canada
- NephCure European partnerships

# KidneyHealthGateway.com Digital Tool



## Am I Eligible?

What is your current eGFR ?

WHY ARE WE ASKING THIS QUESTION?

Not Sure Of Your eGFR? Copy And Paste This Link Into A New Browser Tab To Calculate Your Estimated Value -  
<https://www.questdiagnostics.com/Home/Physicians/Egfr-Calculator>

- ☒ > 60
- ☐ 45-60
- ☐ 30-44
- ☐ 15-29
- ☐ <15
- ☐ NOT SURE

< BACK

Patient friendly website  
with log-in feature for  
customized trial connector

TRIALS

CURRENTLY ENROLLING

INTERVENTIONAL

Birmingham, AL

### DUPLEX FSGS Study Birmingham, AL

This clinical trial will determine the effectiveness of Sparsentan at reducing proteinuria in patients with primary FSGS.

LEARN MORE

AM I A FIT?

TRIALS

CURRENTLY ENROLLING

INTERVENTIONAL

Boston, MA

### DUPLEX FSGS Study Boston, MA

This clinical trial will determine the effectiveness of Sparsentan at reducing proteinuria in patients with primary FSGS.

LEARN MORE

AM I A FIT?

TRIALS

CURRENTLY ENROLLING

INTERVENTIONAL

Chapel Hill, NC

### DUPLEX FSGS Study Chapel Hill, NC

This clinical trial will determine the effectiveness of Sparsentan at reducing proteinuria in patients with primary FSGS.

LEARN MORE

AM I A FIT?

TRIALS

CURRENTLY ENROLLING

INTERVENTIONAL

Chicago, IL

### DUPLEX FSGS Study Chicago, IL

This clinical trial will determine the effectiveness of Sparsentan at reducing proteinuria in patients with primary FSGS.

LEARN MORE

AM I A FIT?

TRIALS

CURRENTLY ENROLLING

INTERVENTIONAL

Columbia, SC

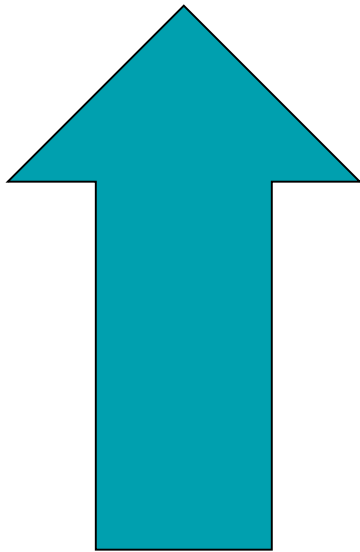
### DUPLEX FSGS Study Columbia, SC

# Solution 2

## Top Docs Directory

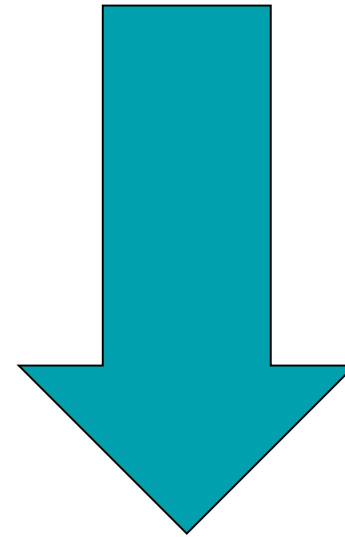
### NEPHROTIC SYNDROME SPECIALISTS PROGRAM

#### Timely treatment and prognosis



Patients who receive expert care **earlier** are more likely to access **appropriate treatments** (including clinical trials) **sooner** and experience **better outcomes**

*\*Some nephrologists see only a handful of primary nephrotic patients throughout their career!*



Patients who experience a **delay** in finding expert care are **at risk** for irreversible kidney (podocyte) damage



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# NEPHROTIC SYNDROME SPECIALISTS

## Pilot Phase

- 100 Nominated Pediatric & Adult Clinicians
- Selection Criteria
- Continuing Medical Education Program
- List of designated specialists

## 2019 & Beyond

- Growing list to 300 specialists
- Expanding to countries beyond the US
- Leveraging influence around trials



NEPHROTIC SYNDROME  
SPECIALISTS



# SUMMARY

- Goals of Treatment:
  - Reduce proteinuria
  - Lower blood pressure
  - Reserve kidney function
- Each therapy has its own risks and side effects - have an open and honest conversation with your doctor
- Clinical Trials are therapeutic options too. Ask your doctor
- The importance of clinical trials and the Gateway program to help you find the right trial for you
- Lifestyle changes help reach treatment goals

