Voice of the Patient Report

Externally Led Patient-Focused Drug Development Meeting on:

Membranous Nephropathy

Public Meeting: August 27, 2021

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Submitted as patient experience data for consideration pursuant to section 569C of the Federal Food, Drug and Cosmetic Act to: Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration (FDA).

This report reflects the National Kidney Foundation's and NephCure®'s accounts of the perspectives of patients and care partners who participated in an Externally Led Patient-Focused Drug Development Meeting, an effort to support the FDA's Patient-Focused Drug Development Initiative.

VOICE OF THE PATIENT REPORT

Report on the Externally Led Patient-focused Drug Development (EL-PFDD) Meeting on Membranous Nephropathy

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STATEMENT OF USE

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INTRODUCTION

On August 27, 2021, the National Kidney Foundation (NKF) and NephCure® held an Externally Led Patient-focused Drug Development (EL-PFDD) meeting on membranous nephropathy (MN). The goal of the meeting was to provide the U.S. Food and Drug Administration (FDA), product developers, clinicians, and academic researchers a forum in which to learn directly from MN patients and their care partners about their experiences and perspectives on living with the disease. This meeting was conducted as a parallel effort to the FDA's PFDD initiative, a commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) to more systematically gather patient perspectives on their conditions and the available therapies to treat their conditions. Recently, the agency passed the PFDD mantle to patient advocacy groups to organize and conduct EL-PFDD meetings.

More information on this initiative can be found at ***https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings***

Note: This EL-PFDD meeting was held before NephCure Kidney International® changed its name to NephCure®. In this report, we refer to the organization as NephCure®.

OVERVIEW OF MEMBRANOUS NEPHROPATHY

Definition and Etiology of Membranous Nephropathy

Membranous nephropathy is an autoimmune disease of the kidney's filters (glomeruli). It is one of the most common causes of idiopathic nephrotic syndrome in Caucasian non-diabetic adults.[1]

Membranous nephropathy is caused by the binding of autoantibodies, mainly directed against the phospholipase A2 receptor (PLA2R)[2] on podocytes, the cells that line the outer surface of the glomerular capillary wall. This binding leads to a build-up of immune complexes along the glomerular basement membrane (GBM), compromising the integrity of the filtration barrier and thereby permitting leakage of protein into the urine. Continued kidney damage from MN can eventually lead to kidney failure.

Classification of Membranous Nephropathy

Membranous nephropathy is considered as either primary or secondary. Primary MN comprises about 80% of cases[3] and is caused by circulating autoantibodies against specific podocyte proteins. In secondary MN (about 20% of MN cases), an underlying cause is identified, such as systemic autoimmune disease (e.g., lupus), malignancies, hepatitis B and C antigenemia, and certain drug toxicities.

Primary MN is the more common form of MN and therefore was the focus of this EL-PFDD meeting. Hereafter, MN refers to primary MN unless otherwise specified.

Epidemiology of Membranous Nephropathy

Membranous nephropathy is a rare disease; the prevalence is estimated at less than 5,000.[4] The annual incidence of MN in North America is estimated at about 12 per million.[5] The average age of onset of the disease is between 50 – 60 years.[1] The incidence of end stage kidney disease (ESKD, the need for dialysis or kidney transplant) due to MN is about 1.9 per million/year in the US.[6]

Diagnosis of Membranous Nephropathy

Membranous nephropathy has typically been diagnosed on a kidney biopsy through the presence of specific light microscopic features and the presence of immune complexes containing IgG and target antigens such as PLA2R in the GBM seen by immunofluorescence microscopy. Currently, a diagnosis of MN is supported by the presence of proteinuria and anti-PLA2R autoantibodies in the blood.[7]

Clinical Course of Membranous Nephropathy

The onset of MN is often heralded by proteinuria and edema. It is commonly believed that without intervention, spontaneous complete remission of proteinuria occurs in about 30% of patients, with about 30% experiencing partial remission (sub-nephrotic proteinuria) and having a good prognosis, and a final about 30% showing persistent nephrotic-range proteinuria, who often progress to ESKD.[8] Recurrence of MN after renal transplantation may occur in up to 50% of patients, with a higher risk of recurrence in patients with high levels of circulating anti-PLA2R autoantibodies.[9]

Treatments for Membranous Nephropathy

There are no FDA-approved treatments for MN. At the time of this report, ClinicalTrials.gov[10] cites 15 U.S. interventional clinical trials for MN (Phases 1 – 4; not all are new chemical entities) in various stages of completion. One trial is in Phase 3.

Upon a diagnosis of MN, the levels of circulating autoantibodies are often monitored to assess whether disease remission will eventuate without the use of strong drugs. Supportive, non-specific care is provided, aimed predominantly at managing proteinuria and the nephrotic syndrome. Such treatments include 1) angiotensin-converting enzyme (ACE) inhibitors or 2) angiotensin-receptor blockers (ARBs) to address high blood pressure and proteinuria; 3) diuretics, 4) a low-sodium diet to combat edema and fluid retention; and 5) anti-coagulants to prevent clotting. Statins may be prescribed for cardiovascular protection.

Clinical practice guidelines[7] recommend risk-based treatment of MN. Risk is based primarily on blood levels of autoantibodies and/or nephrotic range proteinuria. Low risk patients are watched for progression of the disease, while patients at moderate risk for disease progression may be treated with rituximab or a calcineurin inhibitor with or without glucocorticoids. Patients at high risk for disease progression may be treated with rituximab or cyclophosphamide with glucocorticoids (modified Ponticelli protocol[11]) or a calcineurin inhibitor with rituximab.

Although these regimens have been shown to achieve a good clinical response in some patients, the side effects and toxicities associated with their off-label use frequently make them unacceptable treatment options for many patients.

MEETING OVERVIEW

This EL-PFDD Meeting on MN provided the FDA, product developers, clinicians, and academic researchers the opportunity to hear directly from patients and their care partners about their experiences living with MN and their views on disease-related topics. Specifically, the goals of this meeting were to afford the FDA an overall understanding of:

- Patient experiences and perspectives on living with MN, especially daily disease burdens
- Factors that influence patient willingness to enter clinical trials, including patient and care partner perspectives on how to minimize the burden of participation in such trials and the benefits and risks for their participation
- Patient experiences with, and views on, the limitations of current therapies; patient insights into desirable characteristics of potential new therapies; and benefits and risks that influence patient willingness to try new therapies

Meeting Format

This meeting was held in a virtual format. The proceedings were livestreamed and orchestrated by a moderator. Patient and care partner input was gathered through patient testimonies, dialogue with patient Discussion Panelists, and the virtual audience via email and phone calls. Only patients and care partners were asked to participate in the dialogue.

Discussions during the meeting focused on three broad topics: 1) the day-to-day effects of living with MN, 2) patient and care partner experiences and perspectives on clinical trials for MN, and 3) current challenges associated with treatment of MN. An overview of the meeting is seen in the Meeting Agenda (Appendix 2). The Discussion Questions used to guide the audience discussions are found in Appendix 3.

Patient Testimony Panels

Two patient Testimony Panels were heard in which five patients per panel gave five-minute pre-recorded presentations on their experiences regarding the symptoms and daily burdens and impacts of MN (Topic 1) and current challenges for treating MN (Topic 3). Full testimony texts are presented in Appendix 4. Testimony panels were not used for Topic 2 on clinical trials. Panelists were selected by NKF and NephCure representatives from their respective memberships and the MN community at large. Criteria for selecting panelists were set to maximize clinical and demographic diversity on each panel.

Patient Discussion Panels and Moderated Audience Discussion

Each Testimony Panel was followed by a four- or five-member Discussion Panel of patients and care partners and a parallel moderated audience discussion. Discussion panelists disclosed their experiences and preferences regarding clinical trials for MN. During the moderated audience discussions, the moderator interacted directly with the Discussion Panelists. Between these discussions, phone calls and written comments from the virtual audience were broadcast and read, respectively.

Polling Questions

Polling Questions (Appendix 5) were posed to the participants to reveal the demographics of the attendees and their perspectives on the different discussion topics. Polling Questions were based on a pre-meeting survey of prospective participants, input from the meeting co-chairs, and the literature. Care partners were asked to respond on behalf of the patients for whom they provide care (not on behalf of themselves), even if the patients also responded.

Polling was conducted via an online platform through which participants responded. Responses were projected instantly for audience viewing and described simultaneously by the moderator. The results are described in the text and depicted graphically in Appendix 6.

Post-meeting Comments

To expand on the perspectives gathered at the meeting, patients and care partners were encouraged to submit comments to NKF and NephCure after the meeting. Comments were accepted until September 27, 2021.

Enduring Documentation of Meeting

The archived meeting recording, this meeting report, and the meeting transcript are available on the following websites:

National Kidney Foundation https://*kidney.org*

NephCure *https://nephcure.org/*

Key Themes

The input from the meeting emphasized the challenges of living with MN, its impact on day-to-day life, patient views of clinical trials, and their perspectives on currently available therapies. Several key themes emerged from this meeting:

- Fatigue: Patients described how the fatigue associated with MN and its treatment significantly affected their daily lives. Patients expressed that this loss of energy, often coupled with "brain fog," which made it difficult to concentrate or focus, affected their ability to function at their jobs or at school and impeded their abilities to participate in physical or social activities.
- Edema: Patients described the burdens of carrying extra fluid weight from edema (e.g., increasing by up to 24 pounds in 24 hours) and the pain of skin that stretches to accommodate the fluid accumulation. The swelling and weight gain from edema was reported as a source of shame for younger patients.
- Psychosocial issues: Participants described how the invisible nature of MN and a lack of understanding of the disease among their friends, coworkers, and peers caused strained relationships and led to social isolation. This often added to the existing anxiety and depression participants described, which was frequently attributed to the many unknowns associated with their disease and treatment. Patients discussed their fears of progressing to dialysis or a kidney transplant, and their concerns about how these procedures would affect their families and their quality of life.
- Plans/future: Participants described frustration with the inability to make short- and long-term plans for their or their loved ones' futures amidst worries about disease recurrence and treatment failure. Female participants noted that the incompatibility of their treatment options with pregnancy was a significant concern as they considered starting families.
- Clinical trials: Participants voiced their general willingness to enroll in clinical trials for MN. They felt meaningful outcomes were slowing, stopping, or reversing decline of kidney function. Patients were willing to enroll in a clinical trial for a product for which they understood the evidence of safety and efficacy. Overall, patients felt clinical trials are necessary for the development of MN-specific treatments and some expressed willingness to tolerate discomfort in the pursuit of safe and effective therapies.
- Treatments: Patients expressed their frustrations with the current trial and error approach to treatment that they often experienced, as well as the multitude of side effects and toxicities often associated with these therapies. Many participants noted that the side effects from currently available treatment options for MN were often worse than the disease itself.
- Ideal treatment(s): Patients emphasized that an ideal treatment for MN would specifically target their disease without the side effects associated with current therapies.

Participants

A total of 267 people attended the livestreamed meeting, including 112 MN patients and care partners.

The demographic composition of the patient and care partner participants was revealed by demographic Polling Questions (Appendix 5.1). Most respondents (88%) were patients living with MN and 12% were care partners of someone with MN (Appendix 6; Figure 1). The majority (37%) of respondents resided on the East Coast, followed

by 26% in the Mid-west and West Coast. Five percent each were from the U.S. West and Mexico or Caribbean Islands. (Appendix 6; Figure 2).

Most respondents (44%) were between 50-59 years of age, while 12% were 70 years or older. None of the respondents were between the ages of 60-69 years. Twenty-five percent of the respondents were 30-39 years old. Approximately 6% of the respondents were either between 40-49 or 18-29, or under 18 years old. (Appendix 6; Figure 3).

Respondents predominantly identified as female (65%), while 35% identified as male. No respondents identified as non-binary or non-gender conforming (Appendix 6; Figure 4). Most respondents were Caucasian (82%), 12% were Latinx, 6% were Asian American, and no respondents were African American or American Indian (Appendix 6; Figure 5).

Most patients received their diagnosis between 3-5 (47%) or more than ten (29%) years ago. Eighteen percent of respondents reported receiving their diagnosis 6-10 years ago, with 6% being diagnosed in the last 1-2 years. None of the respondents had received a diagnosis of MN less than one year ago (Appendix 6; Figure 6).

None of the respondents were on dialysis, nor had any respondents received a kidney transplant (Appendix 6; Figure 7).

REPORT OVERVIEW

This report summarizes the perspectives shared by MN patients and care partners at the EL-PFDD Meeting, including patient testimonies, audience discussions, and responses to Polling Questions posed during the meeting.

This Voice of the Patient Report intends to increase the understanding by the FDA, product developers, clinicians, and academic researchers of the patient experience of MN, including symptom burdens, views on clinical trials, and perspectives on current and future treatments. Through this patient input, this document also highlights the unmet needs of MN patients. Thus, this report may aid the FDA in considering the patient voice as the agency fulfills its roles in the drug development process, which include advising sponsors on their drug development programs, such as clinical trial design, evaluating products for marketing approval, and assessing benefit-risk for products under review.

Patient input from this report may also be valuable to the drug development process more broadly. For example, it may guide pharmaceutical companies in their development process by uncovering previously unappreciated and unmet burdens of living with MN and may direct research decisions toward targeting disease mechanisms that underly such issues.

In addition, this report may describe barriers to clinical trial participation by patients with MN and may inform the determination of clinical trial endpoints that are inherently meaningful to patients.

In this report, patients and care partners are collectively referred to as “patients and/or care partners,” “participants,” or “respondents.” When responses to Polling Questions are reported, the responses are from patients and care partners in the virtual audience. “Care partner” refers to a family member, partner, or friend who provides direct care for and support to the patient.

Percentages from Polling Questions reported in the text and as numerals in the Appendix figures are rounded-off from the original data. Consequently, the sum of percentages for a given graph may not total 100% and the bar heights may not always precisely reflect the percentages within.

We note that, while the participants at this meeting represented a clinically and demographically diverse group, the extent to which this group reflected the MN patient population at large is unknown, in part due to the lack of quality epidemiology and natural history information on MN. Moreover, there may be symptoms, impacts, treatments, or other aspects of the disease that are not included in the narrative. Therefore, this report is not meant to represent comprehensive views and experiences of any specific group of individuals or entities.

De-identified quotes from patients and care partners in this report were taken from patient testimonies, remarks from Discussion Panelists, email comments, statements transcribed from phone calls, and email comments received after the meeting.

PERSPECTIVES FROM PATIENTS

TOPIC 1. LIVING WITH MEMBRANOUS NEPHROPATHY: DISEASE SYMPTOMS AND DAILY IMPACTS

Quotes have been edited for grammar and punctuation and condensed.

The first discussion topic focused on MN symptoms and their impacts on the daily lives of patients and their families. The session began with video presentations from five Testimony Panelists currently living with MN (Appendix 4.1; Topic 1). The patients described their symptoms and the daily burdens of living with MN. Noteworthy excerpts from these presentations are below. Full testimonies are found in Appendix 4.2.

Marge *(adult patient)*

> *"*[I] *had to … move to … be near my son and daughter-in-law …* ***I felt my life was slipping away*** *and I wanted to have family close by …"*
>
> *"****An ambulance was called for me twice in Kroger's grocery*** *because I fainted and fell to the floor. Those were certainly the most embarrassing times of my life."*
>
> *"****My biggest fear in life is that the MN will come back and destroy the rest of my kidney function****."*

Taylor *(adult patient)*

> *"****My doctors were hopeful*** *that, since I was young, my disease would be easier to control.* ***They were wrong****."*

Alma *(parent of child patient, Lauren)*

> *"*[*My daughter*] *would cry some days saying that* ***she was thirsty but had already had her limit of liquid*** *for the day."*
>
> *"…on multiple occasions,* **[my daughter]** ***would cry from the pain and frustration of being poked multiple times*** *to get blood from her swollen arms."*
>
> *"****Every day I wake up hoping today won't be the day that*** **[my daughter's]** ***condition takes a turn for the worse****."*

Dean *(adult patient)*

> *"In a span of twenty-four hours I had* ***gained 24 pounds in water weight*** *…"*
>
> *"Looking back at my medical charts recently* ***I was shocked as to how sick I actually was*** *during those early years."*

Name withheld *(Teen patient)*

*"… after my diagnosis**, I withdrew from everyone. I became depressed spending most of my time alone or crying** … I wasn't able to get out of bed and missed school."*

*".. I would always be sad and angry … I needed someone to understand because **all these fears were eating away at me."***

*"**I was devastated when I was told*** **[fasting during Ramadan]** ***was out of the question** with all my meds. …* [Not fasting] *robs me of the joy of Ramadan. For an entire month, I feel separated from my family because instead of focusing on what Ramadan symbolizes, I'm preoccupied with concerns."*

After the patient testimonies, Discussion Panelists and audience participants described daily challenges with symptoms and the impact of these challenges on their lives and families.

Polling Questions, Discussion Panel, and Audience Discussion

After the testimony presentations, Polling Questions (Appendix 5.2; Topic 1) were posed to the audience to gather broader patient input on the symptoms and daily impacts of MN. This was followed by a moderated audience discussion structured around the Discussion Questions (Appendix 3; Topic 1), which were shared with the audience. This dialogue included a discussion with five Discussion Panelists (Appendix 4.1; Topic 1). During the moderated discussion, patients and care partners in the audience provided verbal (phoned-in) and written (emailed) comments on their perspectives on the physical, emotional, and social effects of MN on their daily lives. Participants also discussed their worries about MN, what it means for their futures or their loved ones' futures, and the social isolation associated with having an "invisible disease."

Described below are the results of the Polling Questions, portions of the Panel Discussion, quotes from testimonies, and relevant phoned-in and emailed comments during the discussion.

Effect of Most Significant Symptoms on Daily Life

Patients were asked to select from a panel of symptoms that they may have experienced (Appendix 5.2; Topic 1; Question 1). The six most frequently cited symptoms were swelling (edema, 18%), fatigue (17%), anxiety and/or depression (16%), "brain fog" (forgetfulness, poor concentration, losing track of time, etc.) (13%), high blood pressure (12%), and muscle and joint aches and pains, including gout (9%). Ophthalmic (6%) and gastrointestinal problems (e.g., nausea, 4%), high blood sugar/diabetes (2%), and recurrent infections (1%) were also cited. One percent of respondents indicated they experienced "other" issues that were not listed. None of the patients reported experiencing symptoms related to bones or teeth (Appendix 6; Figure 8).

When participants were presented with the same panel of symptoms or conditions and asked to select the three that most negatively affect their daily life (Appendix 5.2; Topic 1; Question 2), they identified fatigue (being tired or exhausted; 23%), swelling (edema) and anxiety or depression (both 17%), and "brain fog" (13%) as the most bothersome symptoms, followed closely by high blood pressure (11%) (Appendix 6; Figure 9).

When asked about the daily impact of MN (Appendix 5.2; Topic 1; Question 3), half of those who responded indicated that MN moderately impacts their daily lives while nearly a third (28%) reported that it affects their lives minimally and 22% indicated that MN affects their lives significantly. None of the patients reported that MN does not affect their lives at all (Appendix 6; Figure 10).

The daily impact of MN varied from patient to patient (and care partner to care partner) and from day to day. Some patients reported that, on good days, they could accomplish their goals and interact normally with friends, co-workers, and loved ones. However, many participants noted that, on bad days, even the most basic tasks became too challenging to attempt or complete, due to fatigue, swelling, and pain. Daily activities were planned cautiously with consideration as to how patients might be affected by the occurrence of symptoms, with many patients and care partners noting that they limited their plans toward minimizing risks and impacts. This affected several aspects of patients' lives, including their jobs and social lives.

The discussion with the Discussion Panelists and audience members further explored the impact of the major and additional symptoms in greater detail. Patients' experiences and the effects of these symptoms uncovered by these discussions are detailed below.

Fatigue

Participants described how fatigue impeded their abilities to participate in an active lifestyle and also in keeping up with the physical demands of daily life. While participants indicated their energy levels may fluctuate throughout the week, most patients indicated that they experience more "bad" days than "good" days.

> *"On my best days, I have more energy, I can dance, chase the grands* [grandchildren] *and swim. But* ***I have to crash and sleep the day after****."*
>
> *"…* ***I can't stand long enough to cook or clean up afterwards*** *… Once, after walking the dog, I lay down on a neighbor's lawn.* ***I was so dizzy and exhausted*** **[that]** ***I couldn't make it home …****"*
>
> *"I enjoyed walking in the fall when it wasn't too hot, but with membranous* [nephropathy]*,* ***I cannot walk more than a few blocks without feeling completely wiped out*** *…"*

> *"It depends on where I'm at with the* [protein] *spill … **at least twice a month, the 'freight train' days come**. Most days, I would say are at least 'car' days—you're dragging, dragging ... **After three o'clock in the afternoon comes, I can't think. It's over**."*

> *"Before I got sick, I biked 10 miles a day, kayaked, as well as a bit of running and a lot of yoga. Now, most of that is not possible. **Holding down my job is hard, given my fatigue levels, and my anxiety levels have been rather high**."*

Edema (swelling)

A significant portion of patients reported experiencing edema, which many reported as having a considerably negative impact on their daily lives. Many patients reported that edema is often associated with severe pain, making it difficult to do basic activities, such as walking and standing.

> *"… another month it* [edema] *went back up into my feet and then just **overnight it went up into my face and around my eyes**."*

> *"On most days that I did go to school, **I didn't participate in PE*** [physical education class] ***because the edema in my legs and pain in my ankles made it too difficult**."*

> *"**I was in a tremendous amount of pain daily**, mostly from feeling **like my skin was going to burst open from swelling and the pressure that the swelling was putting on my joints**."*

> *"**MN causes me to swell so greatly that I cannot walk. I also cannot write, cook, play with my child or do anything that requires dexterity.**"*

> *"The swelling came on very quickly. **I gained 30 pounds** …"*

> *"**Swelling was so severe it hurt to walk and putting my feet up did nothing to help**. I finally sought help when my face started swelling."*

> *"Staying hydrated outside when it's 95 degrees out with a 100 percent humidity, **having to pound water, but yet limit the amount of water you can drink** because* [of] *the amount of water you store. **It's this vicious cycle** of water pills and **trying to stay hydrated while the water pills are dehydrating you at the same time**."*

"Brain fog" (forgetfulness, poor concentration, losing track of time)

Participants reported "brain fog" as a symptom that negatively affected their daily lives. Patients indicated that forgetfulness and lack of concentration, along with fatigue, made their school and work challenging and affected their job performance.

*"… **every day was a struggle to get through …** and just a foggy feeling."*

*"**I was constantly exhausted, having difficulty concentrating** …"*

*"**The majority of the time, I felt like I was in a fog and was going about my daily routine only because I had no other choice**."*

Effect of Additional Physical Symptoms

Although not as extensively discussed or universally experienced, pain, nausea, gout, recurrent infections, and the inability to tolerate hot weather were noted by both Testimony Panelists and audience members as having significant impacts on their daily lives. Participants described how the impact of these complications affected their home, work, school, and social lives.

Pain

*"**I experience intermittent aches and pains**, which come and go without warning, including **severe muscle cramps**."*

*"**Some of those early symptoms were extreme pain in my back around my kidneys**. This caused me to miss school many times …"*

*"**I also experienced times when I was bedridden due to back pain**, and I could not participate in physical sports and miss*[ed] *time with family and friends."*

Nausea (gastrointestinal problems)

"When I was first getting diagnosed, I guess the level of toxicity in my blood was high enough that it was causing me to feel nauseous a lot."

*"**It** **[nausea]** **would just come and go … throughout the day**. So, it wasn't any time of day that it happened more than others. It was just constantly like, 'Oh, I have to stop. Got to take a breather, cause I'm feeling a little sick right now.'"*

"It **[nausea]** ***was pretty consistent for the first couple months*** *that I was diagnosed, and then, once I started treatment, it was **hard to tell if it was the actual disease that made me nauseous or the drugs that made me nauseous**. So, **I pretty much had nausea for a full year**."*

Gout

"[It] *just knocks you out. Even with medications you can't do literally anything for three or four days at a time because **you're just completely immobile**."*

*"**You didn't even want a sheet touching** [you]**, it's so painful**."*

*"**I just found out I have gout, three days ago**. So, I'm dealing with the **pain** of that severe flare- up, which **I've never experienced before a day in my life**. And it's not fun."*

*"**Gout has been a recurring issue** for me throughout my disease."*

Recurrent Infections

***"… I could not travel, socialize with friends, or collaborate in person with work colleagues** for fear of being exposed to common illnesses."*

Heat Intolerance

*"The heat in Houston affected me greatly. If I became overheated, **I would pass out wherever I was, followed by throwing up and defecating**."*

*"I find myself **struggling to do things that a 25-year-old would have done in normal circumstances**, like going to outdoor concerts, going on hikes with friends, because **it was going to be too hot for me and I wouldn't be able to keep up with everybody** … "*

*"**Once it gets past 85** [degrees]**, maybe 90, it's an indoor day for me**. Just being out in the heat will drain me much quicker than the average person. And, you know, **I get nauseated with the heat exposure too**, and just really need to take it easy."*

Social and Emotional Effects

During the discussion on social and emotional effects of MN, patients were questioned on which, if any, of a set of seven experiences they had encountered (Appendix 5.2; Topic 1; Question 4). Respondents most frequently (31%) noted that others do not understand what it is like to live with MN. This was followed by the stress that having this disease places on families (18%) and limitations in daily function and feelings of social isolation (both 12%). Respondents also reported not being able to participate in hobbies (10%), missing work or school (8%), and not being able to participate in sports or other physical activities (6%). In contrast, some respondents reported none of the above limitations (4%) (Appendix 6, Figure 11).

Social isolation, limitations on daily function, family stress, and participation in activities

During the audience discussion, participants noted that the cumulative effects of having MN, experiencing its symptoms and treatment lead to a sense of social isolation, with most respondents confirming the polling results that others do not understand what it is like to live with MN. This affects their relationships with family and friends and prevents them from participating in normal social activities.

Several participants described how their symptoms affected their ability to work at their job or at school. Many of the symptoms discussed above, such as fatigue, inability to concentrate, forgetfulness, pain, and fear of infections, were noted as inhibiting participation in work, school, and social activities.

> *"*[My daughter] *also resisted scheduling 24-hour urine tests because they were* ***awkward and disruptive to her schedule****."*
>
> *"… the* ***biggest disappointment in having MN was having to give up my passion*** *for pet therapy work with children at Arkansas Children's Hospital."*
>
> *"****Because of my pain, my family had to cut down on our outings****. We couldn't go out on hikes, visit downtown San Francisco, or tour lighthouses."*
>
> *"I had recently attempted to enlist in the U.S. Army. Even though I had a letter from my nephrologist endorsing the enlistment,* ***the U.S. Army turned me down due to my kidney disease ….****"*
>
> *"…* ***the headaches would be so severe that it made it impossible to work or spend time with family****."*
>
> *"****On doctor's orders, I have to leave work by three o'clock in the afternoon*** *…* ***So, every day I'm charged three hours of vacation just to leave work early****, so I can have the energy to carry on everything else* ***that I have to do****."*

Participants reported that social isolation was frequently caused by the "invisible" nature of their disease, which made it difficult for others to understand or empathize with what life with MN is like. This caused sometimes unreconcilable strains on friendships and workplace relationships.

> *"Just the fact that others don't know, and* ***how do you explain when it's not visible*** *… you can't really see it—and so* ***how do you talk about it?****"*
>
> *"*[It is] ***hard to explain to the people*** *that you work with because* ***they look at you and you look fine and you sound fine****, and you know,* [it seems like] *'oh, you're just trying to leave work early' type of thing … They don't understand … the* ***water pills that you have to take just to get to work****, and* ***the 10 pounds you gained last night*** *while you drank all that water yesterday, like they just don't get any of that."*
>
> *"… I was usually always home where my parents could keep an eye on me.* ***This chipped at the close relationship I had with my cousin, and we began to grow apart****."*
>
> *"Fighting MN for the most part—****we look fine, but we hurt mentally and physically****."*
>
> *"*[While] *my close friends knew about my diagnosis and while they were supportive****, others would make hurtful comments implying I was lying about my pain*** *to get out of class."*

> *"I* [keep it] *to myself, it just means that **I'm not fully being honest with my loved ones**."*
>
> *"I can only imagine if I was trying to find a job right now, **how I would explain that to a new employer**, as a condition of employment, that I need to be able to leave work at a certain amount of time because my energy level expires."*

In addition to the social isolation already mentioned that comes with MN, several participants noted how the COVID-19 pandemic has further compounded their feelings of stress, anxiety, and isolation.

> *"With COVID, **my life is stressful and anxiety ridden**.*
>
> *"I'm **secluded socially** because of COVID and the drugs that I take.* **[It's] *very lonely***."
>
> *"**I have to take extra precautions that a lot of folks that I know don't** … **I've been on immunosuppressive therapy, so it brings all kinds of risks**."*

Anxiety, Depression, and Anger

Participants commonly reported experiencing anxiety and/or depression, and anger while coping with MN, and that these symptoms significantly affected their daily lives. For many patients, anxiety and/or depression and anger were related to the uncertainty surrounding their prognosis, including the unpredictability of recurrence of symptoms and the risk for recurrence after transplant. Patients indicated that, even on "good days," they experienced anxiety about when symptoms would appear. They also discussed difficulties in planning for the future and the negative outlook for their quality of life. Although hopelessness was not specifically mentioned during discussions, a sense of depression and bleakness was evident among many participants.

> *"**I had to seek psychological help, because it started to have an effect on my family, and I just had a baby** … It was supposed to be one of those times where it's happy and you're supposed to be connecting with your family and your new newborn,* [instead, I was] ***just trying to keep up and keep going for my family**."*
>
> *"My symptoms through nursing school were severe. **I felt worthless**."*
>
> *"**It's like a rollercoaster** … and that contributes to the anxiety and the feelings that you struggle with internally, because I can … have really good labs today and … next month … they'll be just all over the place. **There's no predictability and that's very hard**."*
>
> *"I was angry at everyone for saying I'd get better because **there just wasn't a guarantee**."*

> *"The first couple of years with **MN I wasn't myself**. My dad says I was the loudest, most outspoken, and happy kid in the family. But after my diagnosis, **I withdrew from everyone. I became depressed**, spending most of my time alone or crying, and being comforted by my dad…"*
>
> *"**At least once a week** because of depression, **I wasn't able to get out of bed and missed school**."*
>
> *"I feel stressed. A **stress of potential relapse**."*
>
> *"… **when my friends were worried about what they were getting for Christmas, I was trying to figure out how we can afford medications or whether or not I was on my way to kidney failure and, ultimately, death**."*

One patient emphasized the lack of perceived importance of mental health relative to physical symptoms.

> *"Being diagnosed with such a serious and rare illness at a young age* [15] ***forced me to confront my mortality before my brain was ready**. **My mental health suffered enormously** … I really wish the patient's mental health played a larger role in treatment because **it's just as important as treating the physical symptoms of membranous nephropathy**."*

Care partners of patients reported worrying about how to care for their children with MN and how to recognize and respond to daily and urgent symptoms.

> *"So, **it's that fear of what do I have to look for**? What am I looking for to see that she's swelling? Is it going to go down? Do we need to call the nephrologist? What steps do we need to take?"*
>
> *"As a parent, **the diagnosis brought on feelings of guilt**. What did I miss? What could I have done differently?"*
>
> *"I asked her* [daughter] *to check her urine for foamy pee. She told me this morning, 'Mom, my urine was foamy.' **I secretly started to freak out** … Mornings like this make my mind start to wonder, how much damage is this disease causing her kidneys?"*

Anxiety related to the future

A common theme among participants' remarks was the constant sense of worry that they felt with their disease and the inability to plan for the future. Patients noted that they frequently worry about future recurrence or progression of the disease. Some worried whether treatment options would be available to them in the future; many patients expressed frustration and concern about whether these treatments would be available to their families to administer to them as their disease progressed.

> *"I saw a PCP* [primary care physician] *and then a nephrologist who ordered a kidney biopsy. The diagnosis was MN … I was in shock. I left her office* ***very unsure of my future and very scared****."*
>
> *"Medicare would not cover ritux* [rituximab] *because it's off label for MN…. **How will I treat it if rituximab is not an option? Will I need dialysis? Will I need a kidney transplant?**"*
>
> *"I didn't know what was going to happen, how long I'd have MN or what it would mean in the future. **I was just so scared of having to live with MN for the rest of my life.**"*
>
> *"Today, **I have the same fears as six years ago**: I'm scared of being on meds forever, of never being in full remission ... Every so often, these thoughts plague my mind, and **I am fearful of what my life could become**."*
>
> *"**I'm worried I won't recognize the symptoms** before the MN gets out of hand."*

In addition to interfering with long-term planning, these worries affect short-term planning and may limit the daily activities of patients.

> *"**You can't make plans,** because you can think 'I'm going to have a good day today,' or you just don't know; **sometimes it comes out of nowhere**."*

Psychosocial effects of edema

In addition to the physical toll of edema, participants indicated that swelling contributes to significant social problems. A substantial proportion of patients reported experiencing low self-esteem while coping with edema, in part because the extra weight associated with edema negatively affects their appearance. Even for participants who felt their edema was not noticeable to others, they reported social isolation from having "invisible" pain.

> *"My face would swell, and I worried if my patients would question my ability to care for them ... **It was obvious that I was sick myself. How could I possibly care for someone else**?"*
>
> *"**Living with MN has been hard on my self-esteem due to edema and fatigue.**"*
>
> *"Prior to my diagnosis, I had easily put on 30 pounds ... I even had people reaching out to me about weight loss plans and fitness classes when they noticed my weight gain.* [This was] *also **very humiliating**."*
>
> *"**It's not just physical, it is mental** … You end up feeling like the Stay-Puft guy* [The Stay-Puft Marshmallow Man] *and **it's hard to physically get moving to try to correct it**."*

Children and Family

MN patients with children and grandchildren noted the frustration associated with the inability to care for and interact with their loved ones.

> *"I have a four-year-old child and, because of my MN,* ***I'm only able to fully take care of her two [to] three days per week****."*
>
> *"The grands* [grandchildren] *know when grammy must lie down;* ***they see it on my face*** *…"*
>
> *"With my family,* ***I've tried to explain it to them****. Every day I'm tired … And* ***when it's really bad, it's*** [I've been hit by] ***a 'freight train' day and I need to sleep****."*
>
> *"…* ***there's always that worry … maybe one day I won't be able to do this. Will I have to coach from a wheelchair?****"*
>
> *"With a four-year-old daughter,* ***it's really hard to keep up when you have this condition****. You're constantly sick because of your medication."*

Female participants noted difficulties regarding family planning while living with MN and the toll such uncertainty adds to their already stressed mental health.

> *"At this very moment, I'm weighing my options. I could do nothing* [but] *wait and see if my proteinuria continues to lower on losartan or move forward and prolong starting a family. As a 35-year-old woman, I feel like* ***there's no viable treatment for me that does not risk my fertility****."*
>
> "***I worry about my ability to have children in the future and if my children will have the disease, too."***

One patient emphasized the need for women-centered research and approaches to managing and treating the disease.

In addition, parents of children and teenagers with MN expressed the frustration and hopelessness associated with the unknowns about their children's future quality of life, what kinds of lives their children would be able to lead with MN, and how to share the seriousness of the disease with their children while still giving them hope for their futures.

> *"My daughter's 15 today and* ***she has a whole life ahead of her. What is that going to look like****? Will she … go to college? … be able to have kids? Will her condition progress and will she have to go into dialysis?*
>
> *"For me, as a caregiver and as a parent,* ***it sits in the back of my mind constantly****. When are things going to develop?* ***Is the shoe going to drop?*** *Is she going to get worse … And what does that mean?"*

"As a mother, I worry. You know, ***the constant worrying about 'what if?' and trying to balance all of that is very tough.****"*

*"****…how will a change in her condition impact her future****?"*

"Teenagers think they're invincible and that nothing that happens will affect them, but that's not the reality ... And ***trying to get that message across to her is tough****."*

TOPIC 2. CLINICAL TRIALS IN MEMBRANOUS NEPHROPATHY

Following the discussion about symptoms, burdens, and impacts of MN on patients' lives, Polling Questions and audience discussion disclosed patients' experiences with and preferences for participating in clinical trials (Appendix 5.2; Topic 2; Questions 1, 2), their concerns about participation in these studies and what factors were important to them when deciding whether to participate in a clinical trial.

During the audience discussion, patients with experience in clinical trials voiced their support for these studies and many indicated that they would be willing to participate in another trial, citing superior care, gaining a better understanding of their disease, and a willingness to endure discomfort, such as side effects and repeat biopsies, for the "greater good." Nevertheless, participants expressed some caution, noting as concerns the importance of designing a trial for which the study logistics are not burdensome and access to the evidence for the efficacy and safety of the product under investigation.

Polling Questions and Audience Discussion

Experiences with and/or willingness to enter clinical trials

Patients who had participated in a clinical trial and patients who had not had the opportunity to participate expressed their interest in enrolling in (another) trial. Patients shared their positive experiences in trials in which they had participated and also expressed their willingness to endure discomfort if they thought they were contributing to the development of an MN-specific drug that could help all MN patients.

"I would definitely sign up for a trial. In fact, ***as soon as I was diagnosed, I went looking for a trial*** *after being told about it."*

"I just feel that ***the more people who actually do participate who have this disease, the better they can narrow down a drug*** *that will actually work for everybody."*

"I've never been offered to get on a plane, to go fly anywhere, to go test, to do anything or talk to anybody, but yeah. ***Would I? Absolutely. I absolutely would****."*

Factors influencing a decision to enroll in a clinical trial

When asked in a Polling Question (Appendix 5.2; Topic 2; Question 1) about the top three factors that would influence their decision to participate in a clinical trial, respondents were most concerned about potential side effects from the drug being tested (19%), followed by whether they might receive a placebo (15%) (Appendix 6; Figure 12). Patients also expressed concerns regarding needing to stop their current treatment (11%), whether their nephrologist recommended participation, and whether there was evidence for the efficacy of the study drug (both 10%), Also noted as important factors for enrollment were the distance to the trial site (9%), route of drug delivery (8%), need for a kidney biopsy (6%), frequency of exam appointments (5%), and length of the trial (5%). One percent of respondents chose other factors, while none of the respondents were concerned about their ability to commit to the trial or about hearing negative things about clinical trials.

Kidney biopsies

Patients' preferences regarding kidney biopsies were disclosed by polling. The majority of respondents indicated their willingness to enter a clinical trial if biopsies were required (Appendix 5.2; Topic 2; Question 2; Appendix 6; Figure 13), with 50% preferring one biopsy in one year and 19% and 6% of patients willing to participate in a trial requiring two or three biopsies in one year, respectively. A quarter of respondents reported that they would enroll in a clinical trial only if it did not require any kidney biopsies.

> *"The kidney biopsy was the easiest part of the MN experience for me.* ***I would take monthly biopsies if it meant we had a good shot at getting rid of this disease****."*
>
> *"I even picked up to three kidney biopsies a year because in all of my disease,* ***the kidney biopsies were one of the easier things that I did*** *during those years that I was in active disease."*
>
> *"… you want to do a* ***kidney biopsy three times a year? Let's get it done****."*
>
> *"I've only had one biopsy. It was not a pleasant experience, but if it's going to make life easier for myself or anyone else, sure."*
>
> *"After* [daughter's] *kidney biopsy, she could not do physical education class for three weeks."*

Symptoms, accessibility and logistics, side effects, trial endpoints and purpose

When considering whether to enter a clinical trial, patients shared thoughts on symptom reduction, treatment accessibility as related to a low logistical burden, and potential side effects.

> *"I think the important key points of a clinical trial for me would be: (a)* ***reducing the symptoms,*** *because they are so intense; (b) the* ***accessibility of the medication****—I had to travel a couple of hours away for my rituximab*

infusions when we tried those the first time—I would like that to be closer to home because I do have a life here …; (c) **[fewer]** ***side effects from the drug***.*"*

"I would think the ***side effects would be the one for me****; that would be the downfall …There's usually a point that you're like, 'I can't do this anymore.' You would* ***try to tolerate it as much as you could****. Then,* ***once it's affecting your everyday life, then*** **I** ***would have to stop***.*"*

"The current medication that's out there right now, you have to deal with every side effect on that list. I wouldn't really care about the side effects, because ***if it's going to be for the greater good, if there's going to be some positive coming out of it, I'm good with that***.*"*

TOPIC 3. CURRENT CHALLENGES TO TREATING MEMBRANOUS NEPHROPATHY

The third discussion topic focused on patient experiences with MN treatments, including pharmaceutical treatments, medical procedures, and non-pharmaceutical strategies. The session began with video presentations from five MN patient Testimony Panelists, who described their experiences with MN treatments. After the presentations, four Discussion Panelists provided further insights into the challenges of treating MN. This conversation was structured around Discussion Questions (Appendix 3; Topic 2) to initiate dialogue. Audience members echoed many of the points made by Testimony and Discussion Panelists and offered additional perspectives on what is needed in the MN treatment spectrum. The discussion emphasized the frustration and discontent of patients regarding their treatment options.

Noteworthy excerpts from the patient testimonies are below.

Mark *(adult patient)*

*"****I felt confused and stressed, especially when I tried to explain my extremely limited*** **[treatment]** ***choices to friends and family***.*"*

Eric H. *(adult patient)*

*"****I have occasional lightheadedness from the blood pressure meds and decreased endurance*** *when I'm speaking for prolonged periods of time. This is a byproduct of lower blood pressure and what is perhaps* ***a good sign for my kidneys but a blow to my ego***.*"*

Seferiana *(adult patient)*

*"… at times****, I felt like I'm in a dead end with no viable treatment or remission in sight****. It is frustrating to feel like I've plateaued, and* ***the lack of a viable option has made it impossible to plan for my life***.*"*

Nina *(adult patient)*

*"**I … resigned from my dream job** a few years ago as a preschool teacher **because of my MN and the immunosuppressive drugs** that I was on."*

*"I work very hard to keep my body in shape, and I'm proud of my legs, but because of the prednisone, if I bump up against something or seriously cut myself, **the scarring is so bad and embarrassing. It makes me sad when I look at the scars, and I remember that this is my reality**."*

*"**I can remember the feeling of victory weaning off these drugs in 2019, and I could remember the defeat I felt to jump right back into the protocol**."*

Eric R. *(adult patient)*

*"**The first month was terrible** starting these medications. **I had bouts of stomach pain and nausea very frequently that I never had before**."*

*"I began a serious diet …after losing about 60 pounds, my labs showed signs of remission. **I had to follow a low potassium diet, which was extremely difficult to follow because most of the foods I ate to help with weight loss, were high in potassium**."*

In the discussions that followed the patient testimonies, Discussion Panelists and audience participants described their journeys across the MN treatment spectrum by recounting the successes, limitations, and effects of their current treatment regimens. Many patients indicated that they endured multiple drug regimens, ranging from one to 20 different daily medications.

Polling Questions, Discussion Panel, and Audience Discussion

Polling of the participants revealed that, among the drugs patients were receiving or had taken, the most commonly reported medications used to treat MN were ACE inhibitors, ARBs, beta-blockers, diuretics (water pills), other blood pressure medications (27% of respondents), statins or other cholesterol-lowering agents (23%), and immunosuppressive or anti-inflammatory agents (22%). Fourteen percent reported taking an anti-depressant or anti-anxiety medication. One percent of respondents reported using allopurinol for gout or high uric acid and 12% said they used other or non-pharmacological remedies not included in the survey. None of the respondents reported taking drugs to reduce potassium or phosphate and none reported not taking medications (Appendix 5.2; Topic 3; Question 1; Appendix 6; Figure 14).

In response to another polling question (Appendix 5.2; Topic 3; Question 2), 75% of respondents indicated that their current treatment regimen reduced their most significant symptoms moderately well, while 10% considered their symptoms somewhat or very well reduced. No respondents felt that their current treatment regimens had no

effects. Five percent of respondents reported that they were not currently receiving any treatment for their MN. None of the patients reported that their treatments had no effect (Appendix 6; Figure 15).

Perspectives on Current Treatments

In discussions, patients described the difficulties of finding effective treatments to manage their MN symptoms. Participants discussed their experiences with corticosteroids, immunosuppressive agents, such as calcineurin inhibitors, alkylating agents, and B-cell depleting therapies, and other treatments, such as antihypertensive medications, statins, and diuretics.

Participants almost universally voiced frustration with finding effective treatments and the way treatments affected their daily lives, even when the treatments were helping.

> *"After two infusions* [of Rituximab]*, I was a little better but* ***was no longer able to function as a program manager for five surgeons and had to retire from my job*** *…"*
>
> *"Taking time off of work to seek treatment for IV therapy—it was never a couple of hours, it was* [always] *a day.* [Or] *I* [would have] *to come in late because I got labs done in the mornings or … doctor appointments* [or] *treatment sessions.* ***It's just very taxing on your day-to-day time constraints, and the work-life balance there****. It's really hard with a nine-to-five job."*

Participants also expressed frustration with needing to try numerous types of treatments and not knowing which would be effective. Patients shared their hopelessness and frustration from when they were unable to avoid treatments with serious side effects, as well as from trying multiple treatments and enduring side effects but not achieving relief or remission.

> *"****We tried just about everything to avoid cyclophosphamide*** *because I'm so young and we didn't know necessarily how that was going to affect me in the future. So, we tried to take some ARBs … immunosuppressants … diuretics,* and symptom management *…"*
>
> *"I was on … cyclophosphamide, first with the prednisone and then to tacrolimus after, because there was a side effect to the cyclophosphamide that* [meant]**] *I had to get off of it, but I* [still]** ***lost my hair****."*
>
> *"MN is something I can never escape from because of* ***all the drugs I take every morning and evening*** *... **the drugs I will take*** **[to]** ***have remission cause other symptoms that are serious*** *as well. It's not just about the kidneys."*

> *"I had gained 35 pounds and I lost it very quickly with the Lasix®, but I was constantly going to the bathroom. I had to take breaks, and I just feel like* ***everything that I tried to help me also hurt me in a way."***
>
> *"I had a few treatments that made things a bit better but* [I] ***never went into remission****."*
>
> *"****My body is so tense and nervous the week before labs****. Will the doctor have to increase the dosages and will my body respond with worsening side effects? Will I have muscle spasms where the feeling of two hands inside my legs twisting in opposite directions have me limping around the house in pain? Will I have increased night sweats where I wake up literally drenched from head to toe? … Or if he decreases my meds, will the disease rev up again?"*

A common theme expressed by participants was that the options for treating MN are often as debilitating, if not more so, than the disease itself (e.g., with prednisone, see "Pharmacological Treatments"). Dissatisfaction with this aspect of MN treatment leads to frustration and fear that, if current treatments fail, patients are out of options.

> *"For the next 12 years,* ***I was prescribed and endured the existing standard of treatment*** *for my MN …* ***I suffered debilitating side effects****, such as severe headache, nausea, vomiting, extreme high blood pressure, muscle cramps, joint pain, episodes of painful gout, and excessive weight gain."*
>
> *"*[The treatment for edema] *really caused* ***a lot of mental and physical drain*** *on me in such a short amount of time …"*
>
> *"I remember being* ***overwhelmed with fear and anxiety*** *after researching each drug and their side effect profile."*
>
> *"I was not working during my treatment, and* ***I don't think I could have with all the side effects of the drugs and the disease itself****."*
>
> *"****I have almost abandoned all of my treatment programs because of the side effects that they entail."***
>
> *"*[Right now] *… my family* [and I have] *some satisfaction, but there's always '****how long is it going to last? What's next?****'"*

Finally, patients reported the need to take medications to offset side effects of drugs they took for their MN.

> *"****You take something, and it causes something else*** *…* ***I found myself taking pills to take pills*** *which made no sense to me."*

Pharmacological treatments

Prednisone

In discussions, audience members expressed their frustrations most frequently with the side effects of prednisone. Participants described a wide range of physical and psychological side effects, including weight gain, difficulty sleeping, sweating, mood swings, bruising, joint pains, brain fog, shakiness, muscle weakness, nausea, depression, and excessive hunger.

The effects of drug treatments on clinical signs and symptoms of MN varied, with some patients reporting that they responded well clinically to treatment with prednisone and others reporting that it had no positive effect on their disease. Frequently, though, even when prednisone was an effective treatment, participants felt it was not worth the side effects that they experienced, even on doses as low as 10 mg.

> *"**I had anger issues because of prednisone**."*
>
> *"At the time* [that I was taking prednisone], *I worked for the city council, and **I found myself impatient and short with constituents** calling in for help."*
>
> *"**Prednisone caused some sleep issues**, so I started taking it early in the morning, which helped."*
>
> *"**Sweating, just, you know, any time of day**."*
>
> *"Prednisone also causes **easy bruising, cuts, bleeding, scarring** and contributes to the **lengthy healing time** of those cuts and bruises."*
>
> *"What* [prednisone] *does to your memory and your cognition and your mood—**it's just a very difficult drug to function on**."*
>
> *"I had many side effects to all the meds, **the most from prednisone**."*
>
> *"I am slowly weaning off prednisone after four years and **the joint pain is excruciating**."*
>
> *"Prednisone* [is a] ***very intense drug**. It allows you to get very little sleep* [and] *the sleep is not quality. When you do sleep, it's like having 20 cups of coffee ... So, naturally, **if you're trying to hold down a job** … **it's virtually impossible because you're not sleeping**."*
>
> *"The prednisone caused me to be **hungry all the time and never full. I was moody at work, and my colleagues noticed that I was always on edge**."*

Patients with longstanding disease also noted that taking prednisone was associated with long-lasting side effects, including tremors, weight gain, high cholesterol, chronic pain, amenorrhea and/or irregular menstruation, liver

scarring, ruptured tendons, diabetes, and osteoporosis. Patients voiced concerns that past treatment decisions were creating more consequences now.

> *"**I still suffer from the long-term effects of prednisone**."*
>
> *"I'm **diabetic now,** **[with]** **scarring on my liver, ruptured tendons, weakened muscle definition and usability** ... the list goes on."*
>
> *"While I was on steroids, **my hands shook so much that I would hide my right hand with my left** to avoid having others see*[ing] *and ask*[ing] *questions. Even though I was weaned off steroids a couple years ago, **the hand tremors have never gone away. I still struggle with simple tasks** because the tremors prevent my hands from ever being still."*
>
> *"I also have to take Prolia® shots every six months in my stomach **because of the osteoporosis caused by the long-term use of prednisone**."*
>
> *"To be able to get out of bed, have energy, and be present in life is not something now that I take for granted. And yes,* **[prednisone and cyclosporine]** ***have helped me to do this, but at a big price**."*
>
> *"**Prednisone made me gain a hundred pounds**. Because I was on the max dose for so long, **it caused a tendon to rupture. They've had to completely reconstruct my foot** … It's horrible that prednisone is the first line of defense."*
>
> *"I was on prednisone and cyclophosphamide, and as a female, **they messed up my period and I'm still not over those** **two and a half** **years later**. I lost it for six months and when it came back it was so irregular and abnormal, **I thought I had gone into early menopause**."*
>
> *"*[I came] *off of the prednisone and I dealt with **about six months of significant body pain** because the prednisone I was taking at such a high dosage had masked so many different things."*
>
> *"I got myself onto gabapentin because of the chronic pain that you deal with when you come off of a steroid, but I have to go to work … and I have to coach football and I have to do these different things that **you can't just be on a narcotic pain med forever**."*
>
> *"*[Prednisone and cyclosporine have] *helped my MN, but* **[they're]** ***causing permanent damage to my bones**."*

Immunosuppressants

Immunosuppressive agents were a commonly reported treatment currently used by patients (Appendix 5.2; Topic 3; Question 1; Appendix 6; Figure 14). Calcineurin inhibitors, such as cyclosporine and tacrolimus, and the alkylating agent cyclophosphamide had milder symptoms associated with their use compared with prednisone, but audience members still noted a host of undesirable side effects while taking these drugs, including burning and tingling sensations in the extremities, puffy gums, both hair loss and excessive hair growth, bladder problems, sun toxicity, stress, nausea, brain fog, migraines, night sweats, and bruising.

> *"I had to stop taking cyclophosphamide because I had **a rare bladder reaction** to it about three months into it."*
>
> *"**What impacted me most emotionally was when I took the cyclophosphamide, my hair** [started] **falling out.** That impacted me so emotionally because **I had no control over that and I knew that I had to take the medication if I wanted to get better** … I was constantly trying to cover up the spots in my hair that were missing."*
>
> *"I've been on a regimen of cyclosporine, which says you can't really be in the sun very long. That kind of stuff really affects your daily activities and what you want to do. I work in the* [sic] *outdoor environment, so **it really impacts what I can do at work**."*
>
> *"**Cyclosporine also typically caused nausea** within an hour of taking the dose, even when I took it with food."*
>
> *"I did **cyclosporine** and that was **very high maintenance** in terms of monitoring to make sure it didn't get over certain levels.* **[It]** ***took a lot of time and energy*** *and even when it wasn't* [at] *toxic levels, **I was getting very bad migraines**."*
>
> *"*[With cyclosporine,] ***I was having night sweats …**"*
>
> *"*[Cyclosporine] *also **caused my skin to bruise at the slightest contact**."*
>
> *"When I was on the cyclosporine, the main side effect that I had was **hair growth on my face**. Being a female, that was **very, very embarrassing**. **Swollen gums** were another side effect that I had … Every day looking in the mirror, **it had an impact on my life**."*
>
> *"*[With cyclosporine and prednisone,] *the nerves in my fingers* [will] *be* [so] *sensitive to hot water in the shower* [that] ***I have to take a cold shower because my fingers tingle so much and I can't hold on*** **[to]** ***a soap or wash my own hair** …"*
>
> *"*[With cyclosporine,] ***I couldn't stand out in the sun for more than 10 minute**s. You would throw up and you would feel dizzy, and you get these weird stomach cramps."*

> *"**All of the issues I mentioned previously*** [vomiting, passing out during treatment with cyclosporine, blood pressure medications] ***were worth it**, though, as within a year or so, **my disease was under control**,* [although] *not quite what we would call remission."*

Frequent infections related to immunosuppression were reported as treatment-related events.

> *"The cyclosporine diminished my immune system, and I was sick multiple times in the course of treatment. **I caught every cold and bug that went around**."*

While most participants noted that immunosuppressants at least somewhat successfully managed their MN symptoms, they expressed concerns about the long-term effects of using these drugs.

> *"One of the major concerns I have with* [cyclosporine] *is the risk of cancer, which can occur years after taking the drug. Based on my family history, the **use of this drug would substantially increase the likelihood of me having cancer** in the future."*

> *"I … know someone … taking cyclosporine who got lymphoma ... that could be … anecdotal, but … it is* [in] *the label, so just **taking this stuff is very scary because, what with the toxicity of this drug** and what it can do, **I'd much rather go with something like a prednisone** where you at least know what you're getting."*

Multiple patients described their experiences with rituximab. For those who were able to receive rituximab, many reported that the treatment helped them to achieve remission but, for some, it did not eliminate all of their symptoms. Although patients reported only minimal, if any, side effects, one patient mentioned "chemo brain" as a side effect, similar to brain fog, that is most severe during and immediately after infusion and that may improve over several months but will sometimes last up until the next infusion. One patient reported an allergic reaction to rituximab, while another experienced a reaction to prophylactic antihistamine treatment. Post-infusion fatigue was also mentioned as a side effect. Because rituximab is administered intravenously, the treatment was also considered time-consuming and uncomfortable.

> *"Although the rituximab treatment was successful and I am technically 'in remission,' **I still have reduced kidney function** … which was stable but has started to drop recently."*

> *"*[Rituximab] *infusions **left me physically exhausted**, and I would have to take a full day off work to accommodate the treatments. **The treatment itself is physically uncomfortable and anxiety producing**, having an IV inserted each time and not knowing if my body would have an allergic reaction."*

> "**[After an infusion,]** ***I can have something in my hand; it'll be a glass of milk and I'll call it a couch***. *I'll be driving to my parents' house and all of a sudden, I'm like, 'How did I get here?' I forget plans.* ***I used to have a memory where I could remember everything. Now I'll look at someone and I know their name, but I can't get it out***."

> *"I did not have many side effects that I could point to from* [rituximab] *other than to say I was given high doses of Benadryl® to try to ward off any allergic reaction.* ***The Benadryl made me very tired*** *and, unfortunately, we didn't achieve remission, but* ***we were able to reduce my cyclosporine from 250 milligrams every 12 hours to over 150***."

> *"With the rituximab infusion, I did have a* ***pretty severe allergic reaction*** *in the chair while getting my infusion, hives all* [over] *my face.* ***I would like for that to not happen again***."

> *"They give me 50 milligrams of prednisone and then they give me Benadryl and Tylenol. Then, I get the Rituxan infusion."*

ACE inhibitors, ARB, beta-blockers, statins, and diuretics

The two most frequently reported classes of drugs patients cited as treatments for their MN were ACE inhibitors, ARB, beta-blockers, and diuretics for reducing high blood pressure and swelling, and statins for controlling cholesterol (Appendix 6; Figure 14). Multiple patients noted that some of the side effects from these drugs, while not debilitating, contributed to the burden of their disease.

> *"My daughter takes an ACE inhibitor, and* ***she gets dizzy at times with the medicine***. ***She also gets nausea*** *with the medicine while at school and has to run to the bathroom because she feels like throwing up."*

> *"Valsartan has to be adjusted at least twice a year because* ***my blood vessels will burst in my eyes if my blood pressure gets too high***. ***This feels like someone took a knife and stabbed me in the eyeball***."

> *"I tried several statins for cholesterol. However,* [the] *myalgia—****muscle pain—was so severe I could not tolerate them*** [sic]."

> *"My BP* [blood pressure] *hasn't been affected by this disease, so I had to stop taking* [the blood pressure medication] *because* ***I was getting dizzy and fainting spells***."

> *"Soon after beginning lisinopril,* ***I came down with a persistent cough and face swelling that sent me to the emergency room***."

> *"You deal with the water pill side effects of* ***cramping, the significant charley horses*** *that you get, when you take water pills."*

"This [Repatha®] *shot is painful.* ***It feels like a wasp sting****. As I push the button to administer the drug into my leg,* ***it brings tears to my eyes every time****."*

"On the prescribed 75 milligrams [of losartan] *per day,* ***I experienced tingling in my arms and hands****, so my dose was limited to 50 milligrams."*

"Many of my symptoms have been controlled using statins, an ACE inhibitor, and an SSRI [selective serotonin reuptake inhibitor]*. However,* ***these drugs are hard on the body****, and the ACE inhibitor causes* ***some dizziness and low blood pressure*** *for me."*

*"****I passed out in Walmart® one day and had to be taken to the ER*** [emergency room]*. My nephrologist attributed it to a blood pressure drop. And, even today, I still become lightheaded from the blood pressure medicine if I happen to bend over and stand up too quickly."*

Medical procedures

Participants also described their experiences with the medical procedures used to treat MN, such as dialysis.

Dialysis

Dialysis is one form of renal replacement therapy available to MN patients. Throughout the program, many participants expressed anxiety about the prospect of going on dialysis as their disease progressed and they ran out of pharmacological treatment options. These worries were attributed to the need for machine support to live and the hopelessness of reaching this stage of the disease. In discussions, participants expressed that dialysis was uncomfortable and time consuming. Additionally, it made day-to-day life difficult.

*"****I'm scared*** *… that my kidneys will fail to the point of needing dialysis."*

*"****Dialysis is a burden*** *and it does not fully replace the function of your kidneys."*

"I'm scared of … needing dialysis … ***these thoughts plague my mind*** *and I am fearful of what my life could become."*

Kidney transplantation

None of the patient panelists or audience respondents reported receiving a kidney transplant (Appendix 5.1; Question 7; Appendix 6; Figure 7), but patients did express their concerns about reaching this stage of the disease.

*"****I think about my loved ones who will have to care for me*** *if I need dialysis or a transplant if I progress to the end stages of my disease* ***and the financial burden that it could cause****. Since this disease has no treatment or cure,* ***these are the things I think about daily****."*

"…my daughter's 15 today … Will she have to have, you know, a transplant?"

"… **who will have to care for me if I need dialysis or a transplant** … and the financial burden that it could cause."

Non-pharmacological treatment

Panelists and audience members, particularly those with longstanding disease, shared their experiences with trying non-pharmacological treatments to alleviate symptoms that were not addressed by traditional therapies.

Diet, exercise, weight management, and other approaches

Throughout the program, participants noted that a change in diet played a key role in managing their MN and symptoms, including starting low-sodium diets and plant-based protein diets. Participants noted that these diet changes can be challenging and socially isolating, particularly for children, and that keeping track of their diet restrictions can affect their daily enjoyment of food as well as social activities that involve meals and eating. Participants also noted that exercise helped with their weight management and, in some cases, changes in diet and/or weight allowed them to participate in exercise and activities their disease formerly prohibited them from enjoying.

"I have tried weight management, diet management, and holistic approaches. My weight would go up and down. Recently, we took a fairly drastic step. ***I just had a gastric sleeve done****. I have had to really increase my protein intake, but* ***the swelling and edema is*** [sic] ***dramatically reduced****. So, right now, along with exercise and diet, I would say that was one of the more beneficial things that I've done."*

"… ***it was impossible to eat out*** *while also trying to stick to my low-sodium diet."*

"After four to six months of these [healthy] ***dietary changes, my energy levels increased****. I lost weight. The* ***swelling in my ankles disappeared****, and* ***my muscle and joint pain subsided****."*

"When [my daughter] *had strict dietary restrictions and was invited to a friend's house for pizza and movie night,* ***it made her feel uncomfortable that she couldn't eat****."*

"[Although I gained] *control of my blood pressure…with my lowered weight and* ***the increased vegetable intake caused my potassium to spike.*** *As a result,* ***I had to follow a low-potassium diet, which was extremely difficult to follow****, because most of the foods I ate to help with weight loss were high in potassium."*

*"****My mom had made everything she cooked from scratch****."*

"[One time] *my family bought tubs* [of seasoned fries], *but* ***I wasn't allowed to taste even one and*** **[I]** ***felt angry at being left out****."*

*"**I am careful to eat sufficient protein*** [but] *not to exceed 50g/day. **If I don't, my serum protein and albumin reduce**. I … work with a dietitian ..."*

*"…even now, when grabbing anything … **the first thing we do is check the sodium**."*

*"**I made vast dietary changes after learning that I was now a kidney patient** … I have been on a **plant-based diet for four years, which has improved my overall health**."*

Alternative treatment options

In addition to diet and exercise, patients reported willingness to try other, non-pharmacological approaches to treating their disease, such as giving up alcohol or protein. One patient reported how the use of CBD in conjunction with steroid and immunosuppressive treatments has helped to alleviate minor symptoms.

"I have been taking CBD [cannabidiol] *oil, which has helped **decrease the muscle cramps, tingly fingers, and night sweats** from happening three to four times a week to maybe one or two times a month. Very thankful for that."*

Treatment Successes: Remission

Along with their fears, patients also shared successes that they have had with their treatments, specifically, reaching remission. Patients were aware that their time in remission or partial remission was not predictable and many expressed a "one day at a time" attitude and strategy for appreciating the periods when they could have relief from their symptoms.

*"**I had minimal side effects from the rituximab** … After enduring 13 years of treatment using the existing standard of care for MN, **my MN was officially declared in remission** after only 12 months of the rituximab infusions."*

"[Once I was put on the combination of prednisone and cyclosporine,] ***I very quickly moved towards remission to where I was eventually taken off*** [both drugs], *which is awesome, given the long-term side effects. You worry about that. **I've been in remission for a year now** and I've never been in remission for longer than a couple months max."*

*"I am about five years in, in partial remission, and **I am fortunately off some medication that most impacted my daily life**, such as blood thinning medication."*

"[Tacrolimus] *is the treatment that worked for me. I reached remission about six months after diagnosis, and **I have stayed in remission for** **two and a half** **years**."*

> *"… I was on cyclosporine previously, which put me in a partial remission, but* [it was not] *until I did the rituximab—that's the one that actually put me through to remission."*
>
> *"A few months after* [my third and fourth rituximab infusions], *I'm happy to say that it brought my levels down to the point where I am now considered to be fully in remission."*
>
> *"Soon after starting prednisone, I began moving towards remission. The PLA2R* [phospholipase A2 receptor] *tests and related labs were within normal limits, so I was weaned off the prednisone and then the cyclosporine. That was almost a year ago and* ***this is the longest I've ever been in remission****."*

While patients universally sought complete remission, the path to this outcome was often viewed as difficult, and even when remission was reached, it was not always described as a panacea. Patients described their lives in remission and the toll that reaching remission has taken.

> *"Currently my disease is in remission ... but* ***just because I remain in remission does not mean I can live my life as anyone without the disease****. I still take medications, weigh myself daily and have periods of exhaustion …* ***I live fearful about if or when my disease will relapse.****"*
>
> *"****I reached remission pretty*** *quickly, about six months after [treatment started], and I've been in remission,* ***but the treatment … really caused a lot of mental and physical drain on me*** *... I'm glad that I'm in remission, but I think,* ***quality of life is something that you have to think about too****."*
>
> *"After four years of taking prednisone and cyclosporine every day …* [*I am*] *in remission. My nephrologist wants me to stay on this protocol for another nine months, but I brought to his attention that, yes,* ***this combo has helped my MN, but it's causing permanent damage to my bones.****"*
>
> *"I did resort to cyclophosphamide, which essentially did put me into remission but* ***the side effects of that were absolutely terrible*** *– with the nausea, I lost a bunch of my hair, just not being able to do what a normal 20 year old should be able to do."*
>
> *"…every two years I would be coming out of remission …* ***each time I came out of remission, there was more damage being done to my kidney*** *... Now I'm on a maintenance type protocol* [*of* rituximab] *… that I get every nine months."*
>
> *"…* ***I know this thing is going to come and*** *go … There's going to be ups and downs and partial remissions."*

One patient disclosed feelings of uncertainty about repeating the protocol that achieved remission for her.

> *"Looking back, **I'm not sure I would have chosen to take the medications** that my doctor gave me because of all the side effects, **even though I reached remission very quickly**."*

When patients were questioned whether they noticed reductions in the symptoms of their disease or other health benefits after reaching remission, they uniformly noted positive effects of remission.

> ***"Some of the remissions were spontaneous and some were induced by treatments that I had received. During remission my symptoms would go away and my life was pretty normal with no symptoms … I would think for a brief moment, I'd beaten the disease, but MN would creep back in."***

> *"The obvious physical side effects like **edema and foamy urine, things like that, they're just not around anymore** **[during remission]** … **I feel better mentally** … There's a good chance that it* [MN] *could come back one day. **It just feels good for right now to be in remission** and not having to take those medications that I've had to take forever. Just enjoying it right now."*

During the audience discussion, patients were asked whether partial remission would be a goal for them. They responded affirmatively.

> *"Yes, it* [partial remission] *would* [be a goal]*. **Without a doubt**, because … I believe that **that would lead to an improved quality of life** … in a partial remission, your symptoms are lessened, which leads to an improved quality of life. Ultimately prolonging life."*

> *"**For me … it's mostly about quality of life**. I was miserable for … two and a half years, and … I think **even partial remission is absolutely worth it** – just because you go through so much for so long. **You feel like you can't do it anymore and even just the littlest bit of relief is beneficial**."*

> *"**Absolutely**. Because … even **in partial remission, you'll still feel much better than if you're in a full-blown episode**."*

Perspectives on an Ideal Treatment for Membranous Nephropathy

Patients emphasized the need for a treatment option specifically for MN. They expressed the frustration of needing to piece together a therapeutic strategy from drugs designed to treat other diseases that happened to also control some of their symptoms. Often these drugs exacerbated other symptoms or created new ones that required additional treatment, complicating the therapy.

When asked to describe their ideal treatment for MN, participants emphasized the need to reduce symptoms and side effects and to make treatments more accessible.

> *"I just wish there was **a treatment that would put those of us with MN in long-term remission quickly and not cause other diseases or serious side effects**."*
>
> *"Any future treatment ideally would be **oral medication instead of an infusion**."*
>
> *"I'd like to **avoid life-changing side effects** like incontinence, impotence, et cetera."*
>
> *"**I would be most concerned of** [sic] **side effects that cause lasting damage**: cancer, other disease, etc."*
>
> *"**The toxicity of the medications is something that weighs heavily on my mind and heart** in deciding if I will even choose treatment. The **side effects can take me from a functioning individual to a non-functioning individual**."*
>
> *"… the mental health effects of my MN are the single most important aspect of my disease experience … **I really wish the patient's mental health played a larger role in treatment because it's just as important as treating the physical symptoms of membranous nephropathy [MN]**."*
>
> *"If they can target something to **address the filtration and the resulting proteinuria** …"*

In polling questions, over three quarters (78%) of respondents felt that, regardless of side effects, reversing or halting the decline in kidney function was the most important factor for them in a future treatment. Nearly a quarter (22%) of patients reported that improving their quality of life, preventing additional reduction in quality of life, reducing symptoms, or preventing progression of symptoms were most important to them in a new treatment. None of the respondents cited prolongation of life as an important factor in a new therapy (Appendix 5.2; Topic 2; Question 5; Appendix 6; Figure 16)

> *"I think **I would rather preserve/increase kidney function and delay the need for dialysis**. **Enjoying life is much more important to me than suffering through it**."*
>
> *"[An* ideal] ***treatment program*** [includes] ***quality of life***, *because **the current treatments for MN take away that quality of life**, even though they're treating the kidney, they're taking away the quality of that life."*
>
> *"**I wouldn't want to prolong the life if the life that I have here is full of trash** … **Let's improve the day-to-day**. Let's get up and still go to work; let's be able to hang out and have fun with our friends and family and enjoy the days that we are here. **And if we can do that pain-free, that'd be awesome**."*

As noted above, a majority (78%) of patients reported (Appendix 6; Figure 16) that, without regard to side effects, their preference was for an agent that halts or reverses the decline in kidney function.

> *"*[A treatment that could] ***reverse or halt the progression of the disease****, because that is the gold ring out there."*

As described above, patients agreed that a drug that achieved even a partial remission would be favorable, since the effects of the disease itself are so debilitating.

> *"****A partial remission is a win****, because at the end of the day, some or many of these* [cases] *may be even genetic, where the genes are always going to be that way. So,* ***what are we going to do to remediate what's going on****?"*
>
> *"****Getting that partial remission to me would be most helpful,*** *because it's addressing the eGFR, it's addressing the kidney decline ..."*

Female participants also expressed a need for treatment options that are compatible with pregnancy, and that a treatment option is needed that is indicated during pregnancy and family planning.

> *"My nephrologist has* ***recommended Cytoxan®*** *as the next best treatment option, but among the side effects of this drug is early menopause,* ***which would make it impossible for me to have children****. I have declined this line of treatment twice, so he told me that,* ***with my condition, I could have a risky pregnancy*** *if don't get my disease under control.* ***So, where do I go from here****?"*

CONCLUSIONS

This virtual Externally Led Patient-focused Drug Development Meeting held by the National Kidney Foundation and NephCure® provided the FDA, product developers, clinicians, and academic researchers an opportunity to hear in-depth patient views on the challenges of living with MN, the impact on patients' daily lives, their experiences with, and views on, clinical trials, and their experiences with currently available treatment options.

Major themes that emerged from patient discussions in the meeting were:

- The fatigue associated with MN and some treatments significantly affect patients' daily lives and their ability to participate in work, school, and social activities.
- The unpredictability of the disease and the risk for recurrence and treatment failure contribute to depression and anxiety in patients with MN. Additionally, this uncertainty can make planning for the future difficult, contributing to a sense of hopelessness and further affecting day-to-day life. Patients expressed the importance of treating and supporting mental health, in concert with treating the disease.
- The invisible nature of MN causes social isolation and a disconnect between patients and their friends, family, coworkers, and peers.
- Currently available treatment strategies are based on a trial-and-error approach to therapy and are often associated with a host of negative side effects that may be worse than the disease itself. These side effects, particularly for steroid-based treatments, contribute to a lower quality of life, anxiety and depression, weight gain, and self-esteem issues. Additionally, long-term side effects may occur. Patients stressed the need for safe, effective, and affordable MN-specific treatments.
- Patients expressed concerns about their ability to bear children with the disease, including worries about being able to parent and keep up with young children, whether patients would pass on the disease to their offspring, and frustration about having limited treatment choices regarding fertility.
- Patients often expressed a fear of progression to ESKD and voiced concerns about needing to rely on a machine for survival and the associated poor quality of life, as well as how they and their families would deal with the realities and complications of needing a transplant.
- Many patients were willing to participate in clinical trials if it meant aiding in the development of new therapies specific to their disease. The most commonly voiced concerns surrounding clinical trials were potential side effects, possibility of receiving placebo, requirement to stop current therapy, access to evidence for efficacy, and making logistics surrounding the study less burdensome. Many patients indicated they felt multiple biopsies were an acceptable cost for treatment development and symptom reduction.

The FDA expressed sincere thanks and admiration for the patients' courage and willingness to share their experiences and insights at the EL-PFDD Meeting.

INCORPORATING PATIENT INPUT INTO A BENEFIT-RISK ASSESSMENT FRAMEWORK FOR MEMBRANOUS NEPHROPATHY

In recent years, the FDA has adopted an enhanced approach to benefit-risk assessment in regulatory decision-making for human drugs and biologics toward improving clarity, transparency, and consistency of the assessment.[12] The Benefit-Risk Assessment Framework involves assessing four key benefit-risk dimensions: *Analysis of Condition*, *Current Treatment Options*, *Benefit*, and *Risk and Risk Management*. When completed for a particular product, the Framework provides a succinct summary of each decision factor and explains the FDA's rationale for its regulatory decision.

In the following Framework table, the *Analysis of Condition* and *Current Treatment Options* rows summarize both the severity of the condition as well as the nature and impact of the therapies currently available to treat the condition. The assessment provides an important context for drug regulatory decision-making, providing information that may help inform the weighing of specific benefits and risks of a particular medical product under review.

The input provided by patients and care partners through the Voice of the Patient Report on MN may inform the FDA's understanding of the *Analysis of Condition* and *Current Treatment Options* for this disease.

The information for *Analysis of Condition* and *Current Treatment Options* in the following sample Framework table for MN draws from patient contributions at the EL-PFDD Meeting on MN held on August 27, 2021. This sample Framework table contains the kind of information that may be included in a Framework completed for a drug treatment for MN under FDA review.

Analysis of Condition, Current Treatment Options, Benefit, and Risk and Risk Management

Dimension Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition	• MN affects children and adults. • The symptoms that most negatively affect daily life of MN patients include: - Fatigue, exhaustion - Edema - Anxiety/depression - Brain fog - High blood pressure - Muscle, joint pain • Emotional and social consequences are common and contribute to uncertainties and fears regarding: - Unpredictability of the disease - Prognosis - Future need for dialysis, transplant, recurrence in transplanted kidney - Lack of effective treatments - Long-term efficacy of treatments - Pregnancy - Limited daily function and ability to participate in life • Social isolation due to poor knowledge of MN by others has an important impact on patients. • Disease symptoms prevent patients with MN from engaging in activities: - Physical symptoms, anxiety/depression, and social isolation from MN can inhibit patients' ability to fully participate in work, school, physical activities, and social activities.	• Until the cause(s) of MN is (are) clarified, a cure for MN will remain elusive. • Currently available treatments for MN manage the symptoms and do not address the etiology of MN: - Off-target effects of many treatments cause additional problems for patients, requiring further treatment. - Prednisone-induced effects cause patients to resist or refuse further regimens with the drug. - Many patients are wary of long-term treatment with calcineurin inhibitors and alkylating agents due to the toxicities associated with these agents. • Patients expressed willingness to participate in clinical trials for MN if: - The treatment drug is safe. - The logistics surrounding the trial are not burdensome. - The treatment drug is effective. - The number of biopsies is not excessive. - The trial is recommended by their nephrologist. • Patients expressed concern about participating in clinical trials for MN if: - They would need to halt their current treatment. - They have the potential to receive a placebo. - The treatment delivery has side effects and/or is time-consuming. - The trial center is far from their place of residence. • Patients are hoping for the development of safe, specific treatments for MN, and for options that improve and/or preserve existing kidney function that slow or reverse the progression of disease.
Current Treatment Options	• Curative treatment options for MN do not exist. • Treatment is nonspecific and aimed at controlling proteinuria, nephrotic syndrome, edema, hypertension, and hyperlipidemia: - Patients often receive (off-label) corticosteroids (e.g., prednisone), immunosuppressants, ACE inhibitors, ARBs, diuretics, and statins. - The efficacy of these treatments is generally unsatisfactory. • Patients reported that their anxiety, depression, and pain are often unaddressed and medical management of these issues is often insufficient. • Prednisone is often associated with severe side effects: behavior changes, weight gain, metabolic changes, bone problems, and potential long-term harm to patients: - Patients often report prednisone-induced side effects are more debilitating than MN symptoms. • Dialysis and kidney transplant are options for patients in kidney failure, but recurrence of MN in the transplant is not unusual. • Treatments that are safe for fertility and for pregnancy are needed. • Non-pharmacological treatments include: - Low sodium and other diets - Exercise/physical activity	

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APPENDIX 2: RESOURCE MATERIALS

MEETING AGENDA

Agenda

SLIDE PRESENTATIONS

Dr. Ashley Jefferson

Dr. Laurence Beck

MEETING RECORDING

The meeting recording can be viewed on the websites below:

National Kidney Foundation https://*kidney.org*

NephCure *https://nephcure.org/*

APPENDIX 3: DISCUSSION QUESTIONS

Topic 1: Living With Membranous Nephropathy: Disease Symptoms and Daily Impacts

1. Out of everything that you have experienced because of your condition, what aspects of living with MN have had the most impact?
    a. In terms of symptoms, which have the biggest impact in your daily life?
2. What patient experiences that have been reported today have resonated the most with your own personal experience living with MN?
3. Are you able to predict when you've going to have a good day versus a bad day?
4. What are your worries and fears for the future, both for your symptoms and about your kidney disease overall?

Topic 2: Current Challenges to Treating MN

1. Of all of the treatments that you have tried or are currently employing – both pharmacological and holistic – have seemed to have the most success in relieving your symptoms?
2. What types of treatments have not worked and/or what are some of the treatments that have worked but their associated side effects were so intolerable that you had to discontinue the treatment?
3. When you have taken other medications to help alleviate side effects, have you noticed improvements in your quality of life?
4. What are some of the side effects that have had the greatest impact on your quality of life?
5. Which factors would be the most important when considering whether to enroll in a clinical trial and which would be a "deal breaker"?
6. In the absence of a cure, what would represent an ideal or meaningful future treatment for you?
7. Would partial remission be an acceptable end goal for a new treatment?

APPENDIX 4: PATIENT PARTICIPANTS AND TESTIMONIES

APPENDIX 4.1: PATIENT PARTICIPANTS

Topic 1. Living With Membranous Nephropathy: Disease Symptoms and Daily Impacts

Testimony Panelists

- Marge — *Adult patient*
- Taylor — *Adult patient*
- Alma — *Parent of child patient*
- Dean — *Adult patient*
- Safa — *Teen patient*

Discussion Panelists

- Alma — *Parent of child patient*
- Eric — *Adult patient*
- Seferiana — *Adult patient*
- Daniel — *Adult patient*
- Kim — *Adult patient*

Topic 2. Current Challenges to Treating Membranous Nephropathy

Testimony Panelists

- Mark — *Adult patient*
- Eric — *Adult patient*
- Seferiana — *Parent of child patient*
- Nina — *Adult patient*
- Eric — *Adult patient*

Discussion Panelists

- Katrina — *Adult patient*
- Taylor — *Adult patient*
- Eileen — *Adult patient*
- Daniel — *Adult patient*

APPENDIX 4.2: PATIENT TESTIMONIES

Topic 1: Living With Membranous Nephropathy: Disease Symptoms and Daily Impacts

Marge (*adult patient*)

Hi, my name is Marge. My membranous nephropathy story begins in Little Rock, Arkansas, three years ago. I was preparing for the annual Arkansas Women Can Run 5K race and I was eager to start training, as I was gaining weight like crazy, and my feet and knees were so swollen, I could hardly walk. I thought it was because I had been sick with the flu the past six months and had not been exercising. The first

training session, I knew that something was extremely wrong. While walking a short distance, I became exhausted and was gasping for breath. I saw a PCP [primary care physician] and then a nephrologist who ordered a kidney biopsy. The diagnosis was MN with a GFR of 21, stage four CKD. I was in shock. I left her office very unsure of my future and very scared. I was prescribed three rituximab infusions. After two infusions, I was a little better but was no longer able to function as a program manager for five surgeons and had to retire from my job and move to Houston to be near my son and daughter-in-law. It wasn't that I needed their help, as much as I felt my life was slipping away and I wanted to have family close by in case of emergency or to help me with day-to-day chores, such as grocery shopping, vacuuming, doctor appointments, and even preparing meals. My lack of concentration continued, along with severe fatigue and dizziness. Once, after walking the dog, I laid down on a neighbor's lawn. I was so dizzy and exhausted [that] I couldn't make it home. It was not only a matter of resting or catching my breath until I felt better—I *had* to lay down. Driving my car would require a pullover and a nap.

The heat in Houston affected me greatly. If I became overheated, I would pass out wherever I was, followed by throwing up and defecating. This happened numerous times when I was walking, grocery shopping, or riding my bike. An ambulance was called for me twice in Kroger's grocery because I fainted and fell to the floor. Those were certainly the most embarrassing times of my life.

I was disappointed that I was no longer able to walk or hike, but the biggest disappointment in having MN was having to give up my passion for pet therapy work with children in Arkansas Children's Hospital. There's nothing that compares to watching a young cancer patient smile with joy when the dog enters a room for long cuddles and silly tricks that make the child and the family laugh during dire circumstances. I was now wearing a mask long before COVID and I was immunocompromised. I could no longer work with kids or with developing other pet partner teams or testing new teams for licensing.

The third rituximab infusion was scheduled for January of 2019. The ritux was working, although slowly. I was feeling stronger. I wasn't as dizzy. I learned to recognize when I was about to pass out so I could go grocery shopping now, using the store's motorized handicap cart. I was hopeful that my third infusion would help me get back to being me, but I was unable to get the third ritux infusion. I was now retired and on Medicare, and Medicare would not cover ritux [rituximab] because it's off label for MN.

I have a medical scooter so I can walk my dog on the days when I'm not feeling well. I'm still plagued by spasms and muscle cramps when I'm dehydrated. I'm now able to recognize when I need to sit down. On my best days, I have more energy, I can dance, chase the grands [grandchildren], and swim. But I

have to crash and sleep the day after. I'm now walking the dog a half mile twice a day. I live in a senior community now and I'm enjoying the socialization with my new neighbors.

My worst days, I sleep all day and have no energy or stamina. My time with family is limited to just a few hours at a time. The grands know when grammy must lie down; they see it on my face and bring me ice water and sit beside me and read and tell me stories until I recover. My meals are pre-packaged and microwaveable to preserve my energy, as I can't stand long enough to cook or clean up afterwards.

My biggest fear in life is that the MN will come back and destroy the rest of my kidney function.

How will I treat it if rituximab is not an option? Will I need dialysis? Will I need a kidney transplant? Why be a burden instead of a helper to my family? I saw my new nephrologist this morning and the lab work was well below my expectations. I'm now waiting for that dreaded message from my nephrologist that I have been so fearful might be coming: telling me my kidney function has declined and that the MN is returning. I am terrified.

Taylor (*adult patient*)

Hello. My name is Taylor. I'm a 23-year-old registered nurse from Parkersburg, West Virginia. I live with my husband and one-year-old Labradoodle. In September of 2017, I had just started nursing school. I was more than exhausted. For the first few weeks of the semester, I had pretty much doubled my school workload and was also working a part-time job. So, I thought nothing of my newly onset fatigue. On my first day of clinicals, I noticed swelling in my lower extremities. I took a photo and sent it to my mom who is also a registered nurse and we both chalked the swelling up to having been on my feet for 12 hours on concrete flooring and not being used to that. I ordered some compression socks and went about my normal life. Over the next several days, I noticed swelling in my feet when I did almost anything other than lie on the couch or in my bed.

I made an appointment with my primary care doctor who ran some labs and referred me to a local nephrologist who then ordered a kidney biopsy and confirmed my diagnosis of membranous nephropathy. I was 19 years old and scared about how this disease was going to affect me. I had just started a rigorous nursing program that required my full dedication and attention.

My doctors were hopeful that, since I was young, my disease would be easier to control. They were wrong. We started treatment. I went through every treatment for the disease, none of which worked. Finally, we resorted to cyclophosphamide and other medications, such as diuretics and blood pressure

medication to manage my symptoms. My symptoms through nursing school were severe. I felt worthless. I was constantly exhausted, having difficulty concentrating and the swelling was so severe my skin was cracking and seeping fluid.

My face would swell, and I worried if my patients would question my ability to care for them. I was - it was obvious that I was sick myself. How could I possibly care for someone else? These symptoms made my daily life next to impossible. And every morning I looked forward to going to bed, even though I would wake up in wet sheets due to the weeping of my skin. I was in a tremendous amount of pain daily, mostly from feeling like my skin was going to burst open from swelling and the pressure that the swelling was putting on my joints. I was so fatigued and not getting good sleep due to my inability to feel comfortable. I had difficulty sitting still for long periods of time and concentrating, which was necessary since I was in college and sitting for two to three-hour lectures. The majority of the time, I felt like I was in a fog and was going about my daily routine only because I had no other choice. At one point, I was taking up to 20 different medications per day. I felt tied down to my medication regiment.

As an average college student, my life was severely affected by this disease. I was too exhausted to go out with friends in the evenings, too swollen to fit into any of my clothes and felt it was impossible to eat out while also trying to stick to my low-sodium diet.

There were many activities I could not do that I used to enjoy. I had previously taken these things for granted. I enjoyed walking in the fall when it wasn't too hot, but with membranous [nephropathy], I cannot walk more than a few blocks without feeling completely wiped out or I can’t walk at all because I was too swollen that day and it hurts so badly to take a step.

One of my favorite places on earth is Disney World. In July of 2018, my family and I took a trip to Disney World. By the end of the trip, I was miserable. Between the 16-hour drive, the Florida heat mid-July, and my disease, I couldn't walk. By the third day, I was being pushed around the parks in a wheelchair. Many people were confused when they saw me in a wheelchair, because those who had not seen me prior to the onset of my disease would often think I looked normal.

Prior to my diagnosis, I had easily put on 30 pounds of weight. I thought this was the freshman 15 as many called it, only much more severe. I even had people reaching out to me about weight loss plans and fitness classes when they noticed my weight gain, which was also very humiliating.

Currently my disease is in remission. I have been free of symptoms since October of 2019, but just because I remain in remission does not mean I can live my life as anyone without the disease. I still take medications, weigh myself daily, and have periods of exhaustion. I think about how the disease has affected me and how it will affect me in the future. I live fearful about if or when my disease will relapse. I worry about my ability to have children in the future and if my children will have the disease, too.

I think about my loved ones who will have to care for me if I need dialysis or a transplant if I progress to the end stages of my disease and the financial burden that it could cause. Since this disease has no treatment or cure, these are the things I think about daily. Thank you for letting me share my story and for listening.

Alma (care partner; parent of child patient, Lauren*)*

Hi, my name is Alma Sandoval, and I am the mother of four children. My oldest daughter, Lauren was diagnosed with membranous nephropathy in August of 2018. Lauren was 12 years old at the time. She was a healthy thriving child who only suffered from seasonal allergies and ear infections. Lauren went to sleepover camp in June of 2018, and during her fourth week at camp, the camp nurse called asking for permission to take her to urgent care. She mentioned that Lauren's eyes were swollen shut when she woke up that morning and mentioned how in the previous week, Lauren had begun to swell. Lauren was hospitalized and her dad and I were in shock. We spent four days at the St. Louis Children's Hospital getting her stabilized so she could return home to Texas. There were still so many unknowns, and the possibility of a kidney biopsy was mentioned.

My head was spinning. Looking back, I believe Lauren's symptoms started about seven or eight months prior to her hospitalization. I had noticed that she was gaining weight and her legs were getting larger. It was very gradual but still noticeable. At times you could see deep clothing marks her legs. I also noticed that she was tired more often, but I thought it was the weight gain. I also remember she had mild swelling around her eyes, but we attributed that to her allergies. When we left the hospital, Lauren was placed on a strict liquid intake and dietary restrictions. She would cry some days, saying that she was thirsty but had already had her limit of liquid for the day. We also had to do a daily log of her urine protein. She would get irritated when I reminded her about checking her morning urine. She had to learn to take pills, something she had never done before.

She had frequent urine and blood tests. And on multiple occasions, she would cry from the pain and frustration of being poked multiple times to get blood from her swollen arms. Lauren complained about

having to book doctor appointments during school because she didn't want the attention or people asking her where she was going. After Lauren's kidney biopsy, she could not do physical education class for three weeks. She was frustrated because her friends and classmates asked her why she was not participating. Lauren did not want her friends to know anything about her diagnosis. Lauren is a very friendly and social person, but her medical condition was not something she wanted to share, because she didn't want to be treated differently. Lauren also resisted scheduling 24-hour urine tests because they were awkward and disruptive to her schedule. When she had strict dietary restrictions and was invited to a friend's house for pizza and movie night, it made her feel uncomfortable that she couldn't eat.

As a parent, the diagnosis brought on feelings of guilt. What did I miss? What could I have done differently? I immediately began searching online for information and support, feeling helpless with absolutely no knowledge of this disease was frightening. Finally, NephCure connected me with parents whose kids had membranous nephropathy. Having the support and a chance to ask questions from parents who had experience with MN was informative and encouraging.

Currently Lauren's condition is stable. While on her medication, her urine protein and kidney functions have been normal. We have discussed with her nephrologist about stopping the medication and we're working through that process to see if she can come off the medication with no significant impact to her kidney function.

Every day I wake up hoping today won't be the day that Lauren's condition takes a turn for the worse. I constantly look at her eyes and touch her legs and wrists for signs of swelling. I look for clothing marks that may mean she has swelling. I asked her to check her urine for foamy pee. She told me this morning, “Mom, my urine was foamy.” I secretly started to freak out but told her, “We need to check your protein in the morning.” Mornings like this make my mind start to wonder, how much damage is this disease causing her kidneys? What are some of the long-term side effects of this medication and how will a change in her condition impact her future? As my sweet daughter will say, “Mom, we have to focus on today and hope everything will be okay.” Thank you for listening.

Dean (*adult patient*)

Hello, my name is Dean and I live in Boiling Springs, South Carolina with my wife and children. I was diagnosed with membranous nephropathy at the Naval Hospital in San Diego California when I was sixteen years old. I most likely exhibited symptoms of MN as early as fourteen years of age but didn’t

realize it. Some of those early symptoms were extreme pain in my back around my kidneys. This caused me to miss school many times; other early symptoms were moderate swelling that extended from my lower calves to my ankles, and a urinary tract infection that required testing at a hospital. I also experienced times where I was bed ridden due to back pain, I could not participate in physical sports and miss[ed] time with family and friends.

Eventually I was admitted to the hospital due to extreme swelling in my face and pitting in my legs. In a span of twenty-four hours, I had gained 24 pounds in water weight, was put on a low sodium diet and spent a week in the hospital for further testing, including a kidney biopsy that diagnosed my MN. Looking back at my medical charts recently I was shocked as to how sick I actually was during those early years. My symptoms were consistent with my disease and included swelling, migraines, and periods of back pain. After high school graduation I was in a period of denial as far as my condition goes and neglected care for a few years.

At age nineteen my blood pressure got out of control and the swelling in my legs returned. I would get flushed and my pulse was very fast. My protein spillage was very high, and I gained weight. While all these symptoms were not as severe as when I was first diagnosed, I began to see a nephrologist again because I was concerned about my kidneys and how that would impact my overall health. I had recently attempted to enlist in the U.S. Army and even though I had a letter from my nephrologists endorsing the enlistment, the U.S. Army turned me down, due to my kidney disease and high protein in my urine.

In my twenties and thirties, I had hypertension related migraine headaches. At times the headaches would be so severe that they made it impossible to work or spend time with my family. One of those times was me and my wife's wedding practice; I had to leave early due to a migraine headache, but I showed up for the wedding and that is what is important. The only relief I could find was a dark, quiet room and plenty of Tylenol®. My doctor prescribed a new blood pressure medication and it worked; I have only one to two migraines a year now.

Since my first diagnosis until 2019 I have gone into remission several times and my doctor has attributed that to my strict adherence to his protocol recommendations. Some of the remissions were spontaneous and some were induced due to treatments I received. During remission my symptoms would go away, and my life was pretty normal with no symptoms of MN. I would think for a brief moment I had beaten the disease, but MN would creep back in. In my thirties, a new symptom started: I developed gout in my big toe and my left knee. The pain felt like needles poking into my joints. I will say the gout is the most debilitating component of MN for me as it prohibits me from walking; even making it impossible to wear shoes or sleep at night due to the pain.

I had discussed dialysis and a kidney transplant with my doctor over the years, but they always seemed so far away. I tried not to dwell on what the future would hold and took it one day at a time. In February 2020 right before the pandemic started, my doctor said the scarring caused by the disease had damaged my kidneys to the point that I needed dialysis. I started peritoneal dialysis at home and I am still using the therapy today. I still have symptoms of MN that will never go away - the swelling still persists today in my lower legs. Dialysis is a burden and it does not fully replace the function of your kidneys. I have to take phosphorus blocking medicine and have monthly lab work to monitor my progress and more frequent doctor visits. A better alternative would be effective treatment of the disease and medicines that help symptoms and lead to a cure.

Safa (young adult patient)

Hi, my name is Safa. I'm 18 and I live in California with my parents and four siblings. I graduated high school this summer and I'm starting community college in the fall. I was diagnosed with nephrotic syndrome in February of sixth grade, then membranous nephropathy around May. At first, we didn't know something was wrong. I'd been noticing for a couple of weeks that my legs were hurting, but it didn't seem concerning. Growing up, I always had growth pains and that's what we shrugged this off as. This went on for weeks until my dad noticed that my nose looked extra big. When he saw that my legs were also swollen, I went in to see my doctor. My pediatrician referred me to a nephrologist. It took over a month to be seen. That month felt extremely long. We were beyond stressed with my parents continuously researching nephrotic syndrome. Between the referral and starting treatment, I noticed more things that were different - that the edema caused my face and ankles to become puffy too.

The first couple of years with MN, I wasn't myself. My dad says I was the loudest, most outspoken and happy kid in the family. But after my diagnosis, I withdrew from everyone. I became depressed, spending most of my time alone or crying and being comforted by my dad at least once a week. Because of the depression, I wasn't able to get out of bed and missed school. I would sit with my dad as he just hugged me, because nothing else made me feel better. I didn't know what was going to happen, how long I'd have MN or what it would mean in the future. I was just so scared of having to live with MN for the rest of my life. On most of the days that I did go to school, I didn't participate in PE [physical education class] because the edema in my legs and pain in my ankles made it too difficult.

[While] my close friends knew about my diagnosis and, while they were supportive, others would make hurtful comments implying I was lying about my pain to get out of class. Because of my pain, my family had to cut down on our outings. We couldn't go out on hikes, visit downtown San Francisco, or tour

lighthouses. Whenever I felt down, I wrote letters. Sitting in our home office, I filled pages with my fears, explaining why I felt the way I did. I wrote about how I was scared my kidneys would fail, that I would never be myself again, and that I would always be sad and angry. I would leave the letters for my dad to read so he could begin to understand what I was going through. I needed someone to understand because all these fears were eating away at me. I was angry at everyone for saying I'd get better because there just wasn't any guarantee. I even began seeing a therapist to talk about my fears and the negative ways MN was affecting my life. Even years later, every time I felt depressed, I would pull out those letters and reread them. But a couple years ago, I destroyed every single one because they brought back such bad memories. Taking me back to a time in my life when I felt hopeless and alone.

Because of MN, I couldn't do things I found joy in. Before my diagnosis, I always slept over at my cousin's house. We'd stay up all night watching *Lord of the Rings* and eating Doritos®, then make pancakes for everyone in the morning. After my diagnosis, these sleepovers became scarce because, as an 11-year-old, I wasn't able to dip my urine alone, my parents didn't trust me to take my meds on time, and I'd eat too much sodium - easily triple my allowed amount. And so, I was usually always home where my parents could keep an eye on me. This chipped at the close relationship I had with my cousin, and we began to grow apart.

My diagnosis impacted my entire family. Everyone kept an eye on the sodium entering our house and the food I ate. We stopped dining out because we couldn't calculate the sodium in dishes. I couldn't even eat store-bought naans, since each had nearly 500 milligrams of sodium. My mom had to make everything she cooked from scratch, including naans, ketchup, and yogurt. At the mall one day, there was a seasoned fries stall, meaning they'd be delicious, but full of sodium. My family bought tubs, but I wasn't allowed to taste even one and felt angry at being left out. This consciousness of sodium is so instilled in us that even now when grabbing anything, even though my protein levels are much lower and I no longer need to watch my sodium, the first thing we do is check the sodium.

One of the biggest changes from MN relates to Ramadan. Since [I was] seven years old, I've looked forward to fasting each year. I was devastated when I was told it was out of the question with all my meds. Now that I can fast, I worry about my labs and if my meds will need to be increased after. MN doesn't just dictate whether or not I can fast - it robs me of the joy of Ramadan. Even if I can fast, I can't pray Taraweeh at night because I can't stand on my feet for long. For an entire month, I feel separated from my family because instead of focusing on what Ramadan symbolizes, I'm preoccupied with concerns. Today, I have the same fears as six years ago: I’m scared of being on meds forever, of never

being in full remission, and that my kidneys will fail to the point of needing dialysis. Every so often these thoughts plague my mind, and I am fearful of what my life could become.

Topic 2: Current Challenges to Treating MN

Mark (*adult patient*)

Hello, my name is Mark Parisi. I'm 63 years old. I live in Newburyport, Massachusetts with my wife, Laura, and we are both retirees. We're physically fit and socially active. I was diagnosed with MN at age 43. I was experiencing fatigue, swelling in my ankles, blurred vision, and muscle spasms for many months. A kidney biopsy confirmed that I had irreversible damage to my kidneys and had advanced MN. I realized how serious my diagnosis was when my doctor suggested that I attend a pre-dialysis class at a local clinic the following week.

My MN treatment started immediately. I was instructed to stop the use of over-the-counter anti-inflammatories such as Advil, Aleve, and Motrin, as they could cause further damage to my kidneys. Blood pressure and cholesterol medications were prescribed to help control the progression of the disease. My nephrologist explained there were no drugs developed specifically for MN and that my treatment would consist of trying off-label drugs developed for other diseases, such as cancers and organ transplant rejection. He said if one does not work, you typically move to the next. He confirmed that MN studies have shown that these off-label drugs can help control the disease but not cure it.

I felt confused and stressed, especially when I tried to explain my extremely limited choices to friends and family. For the next 12 years, I was prescribed and endured the existing standard of treatment for my MN. The treatments were prescribed for an eight to twelve-month period with blood work monitored every other week. I remember being overwhelmed with fear and anxiety after researching each drug and their side effect profile. We started with Cytoxan, then tacrolimus, and then cyclosporine. These were supplemented with prednisone and an antibiotic that would help my depleted immune system fight seasonal infections.

During the twelve years of treatments, I suffered debilitating side effects, such as severe headache, nausea, vomiting, extreme high blood pressure, muscle cramps, joint pain, episodes of painful gout, and excessive weight gain. My overall mental and physical health had deteriorated to a point where my life had been so negatively affected that I could not travel, socialize with friends, or collaborate in person with work colleagues for fear of being exposed to common illnesses.

In 2013, my local nephrologist referred me to a Boston hospital for an MN consult. I was sent to a renal dietician for the first time since my MN diagnosis and another nephrologist from Boston who enrolled me in his MN research study in which patients were being treated with four rituximab infusions. The study also included the development of a diagnostic test to detect [anti-]PLA2R [antibody] levels in patient blood samples that provide a direct correlation to the overall level of disease activity in an MN patient. In coordination with my scheduled rituximab treatments, I incorporated the lifestyle changes that the renal dietician recommended. I controlled my overall protein intake to 70 grams per day, controlled my salt and sugar intake, cut down the consumption of dairy products, controlled portion sizes, minimized the use of alcohol, eliminated soft drinks and fruit juices, and increased my hydration level with water. Some substitutions included regular (dairy) milk to coconut or almond milk, white bread to whole wheat bread, white pasta to wheat pasta, regular salt products to low salt products, and low fiber to high fiber products.

After four to six months of these dietary changes, my energy levels increased. I lost weight. The swelling in my ankles disappeared, and my muscle and joint pain subsided. The rituximab infusions were easy to schedule and were accessed through my local hospital. I had minimal side effects from the rituximab. There were temporary fatigue and minor headaches that subsided two to three days after the infusions. Three months after my first series of rituximab infusion, my [anti-]PLA2R [antibody], urine protein, and creatinine and were down significantly. At six months, my lab tests were close to the normal range. At twelve months, my lab results stabilized and my PLA2R was undetectable. After enduring 13 years of treatment using the existing standard of care for MN, my MN was officially declared in remission after only 12 months of the rituximab infusions.

In 2018, after five years in remission, my lab test in PLA2R started to increase. After monitoring them for an additional three months, it was confirmed that my MN was re-emerging. It was recommended that I have a maintenance infusion of rituximab, two infusions for the study to help control my relapse. Then, after three to four months of completing the prescribed maintenance infusions, my lab test results improved, and my PLA2R test was in the undetectable range again. I'm happy to confirm that today, my MN is still in remission. I am hopeful that my experience will help industry leaders recognize the overwhelming need and opportunity for the development of new drug therapies for the increasing population of MN patients.

Eric H. (*adult patient*)

Hello. My name is Eric. I'm a 52-year-old attorney, songwriter, husband, and father living in Central New Jersey. In the spring of 2019, I noticed with my annual physical that my cholesterol had shot up. My internist put me on a statin, which I did not consider it to be a big deal. I figured that this was a changing metabolism with middle age. Several months later, I was constantly bragging to my wife about how my new workout regimen was building up bulk in my calves, which were previously scrawny. I went for repeat blood [and urine] work to see if the statin was working, and I found that it was working but that I had alarmingly low protein levels in my blood and alarmingly high protein levels in my urine. A couple of blood tests later and a biopsy confirmed that I had membranous nephropathy.

I started taking a diuretic to deal with the swelling. That was not much of a big deal. I just had to get up a couple of times a night to go to the bathroom, had to cut down on coffee. As for the disease itself, I started the conventional approach of taking high amounts of high blood pressure medication and a blood thinner. I noticed that the combination or maybe just the high blood pressure medication made me dizzy. As a performer, musically, I would normally stand up, and I'd found that after a couple of songs, I would need to have a seat because I would get very lightheaded. My harmonica playing, which I used to incorporate into live performance, was no longer possible, which actually is a good thing because I'm an atrocious harmonica player, but the conventional approach wasn't working, and my numbers were getting worse.

So, a few months after we commenced the conventional approach, my nephrologist recommended Rituxan, otherwise known as rituximab. It's not approved for the treatment of MN. It is approved for several types of cancer and rheumatoid arthritis. For this reason, my doctor and I had to fight mightily with my insurance company to get approval for it. A lot of calls and letters and delays of my initial infusion ensued as a result of that. I finally got my first infusion on March 13th, 2020, a date that a lot of us remember because it was the first day of the great COVID shutdown across most of our nation. Second infusion was six weeks later.

Unfortunately, the blood levels after those two infusions suggested that it might not be the drug for me. My 24-hour urine output went from eight grams to five grams, which is an improvement, but five grams is still unacceptably high, so we were a little worried we might have to go in a different direction. But, a few months later, I had my third and fourth infusions. A few months after that, I'm happy to say that it brought my levels down to the point where I am now considered to be fully in remission.

I continue to maintain by taking 40 milligrams daily of candesartan high blood pressure medication. I do my best to minimize sodium in my diet, staying away from cheeses and cured meats. My MN-related symptoms have pretty much been held at bay. I have occasional lightheadedness from the blood pressure meds and decreased endurance when I'm speaking for prolonged periods of time. This is a byproduct of lower blood pressure and what is perhaps a good sign for my kidneys but a blow to my ego. My calves are now back to their pre-MN level of scrawniness.

In terms of future treatment, I have a demanding job. I have two hormonal teenagers at home. I generally do not have a lot of time to worry about what's going to happen if I relapse. If and when I do relapse, I would like to know that Rituxan is still a viable option, a safe option, and an effective option. I read up on the Ponticelli method, which, before Rituxan, was the gold standard, consisting of prednisone and cyclophosphamide for six months. I know that that carries some attendant risks that are not there with Rituxan.

I've read about other modes of treatment. The common reality appears to be a lack of robust longitudinal data to support both efficacy and safety, which certainly I would like to see. Any future treatment ideally would be oral medication instead of an infusion. I'd like to avoid life-changing changing side effects like incontinence, impotence, et cetera. I really appreciate this opportunity to speak to you and to help my fellow MN patients and the medical community addressing this disease. Thank you very much.

Seferiana (*adult patient*)

My name is Seferiana. I'm 35 years old and live in Seattle, Washington. I own and run a political consulting firm where my work is dynamic and fast-paced. I was diagnosed with membranous nephropathy in February 2016 at the age of 30. I remember waking up one morning to swelling in my ankles that I had never experienced before. This heaviness subsided throughout that first day only to return after a long day's work. I began a pattern of sleeping off this mystery swelling until it stopped going away on its own.

I soon saw my doctor, and she ran a gamut of tests due to the high level of protein I was losing in my urine. She ordered a kidney biopsy, and I was diagnosed with primary membranous nephropathy and stage one chronic kidney disease. I was spilling 13 grams of protein in 24 hours. My treatment started right away with furosemide to ease the water retention, lisinopril, and prednisone. Soon after beginning lisinopril, I came down with a persistent cough and face swelling that sent me to the emergency room.

My doctor immediately ordered me off the lisinopril and switched me to the losartan. On the prescribed 75 milligrams per day, I experienced tingling in my arms and hands, so my dose was limited to 50 milligrams.

The prednisone caused me to be hungry all the time and never full. I was moody at work, and my colleagues noticed that I was always on edge. At the time, I worked for the city council, and I found myself impatient and short with constituents calling in for help. Within six months of my diagnosis, I gained 30 pounds. I carried weight all over my body and I didn't know if the weight was caused by water retention from the disease or the prednisone treatment.

In the fall of 2016, I began cyclosporine, which caused a severe reaction of face swelling, wheezing, and fever. I went to the emergency room because the swelling in my face came on so suddenly. My doctor considered this a reaction to the dose of cyclosporine. My doses were lowered, and the acute side effects subsided. The cyclosporine diminished my immune system, and I was sick multiple times over the course of treatment. I caught every cold and bug that went around.

This medication also caused my skin to bruise at the slightest contact. While on cyclosporine, I had a test for the PLA2R antibody, which came back positive. After seeing no real improvement from cyclosporine in my protein loss, my nephrologist ordered off-label rituximab treatments. I began one gram of four infusions over the course of one month, each lasting about four or five hours. The infusions left me physically exhausted, and I would have to take a full day off work to accommodate the treatments.

The treatment itself is physically uncomfortable and anxiety producing, having an IV inserted each time and not knowing if my body would have an allergic reaction. Once, I made the mistake of looking at the infusion site and promptly fainted. Three months after the rituximab treatment, my [anti-]PLA2R antibody level came down, and my swelling went down significantly. Even though the treatment reduced many of the visible signs of my disease, I still have symptoms that were not reduced by treatment. My proteinuria is still high, and a recent kidney biopsy showed permanent scarring and a slight presence of the [anti-]PLA2R antibody in the kidney.

For the last two years, my treatment has consisted of 50 milligrams of losartan per day, Lipitor to lower my heightened cholesterol brought on by my MN, daily aspirin to lower the possibility of blood clots, calcium supplements, and 10,000 IUs of vitamin D. I haven't seen drastic improvements with this treatment, but I'm no longer spilling upwards of 10 [grams] of protein as I was a couple years ago.

My nephrologist has called mine a tricky case, and at times, I felt like I'm in a dead end with no viable treatment or remission in sight. It is frustrating to feel like I've plateaued, and the lack of a viable [treatment] option has made it impossible to plan for my life. My nephrologist has recommended Cytoxan® as the next best treatment option, but among the side effects of this drug is early menopause, which would make it impossible for me to have children. I have declined this line of treatment twice, so he told me that with my condition, I could have a risky pregnancy if I don't get my disease under control. So, where do I go from here?

After consulting my case with fellow nephrologists, my doctor has proposed another round of rituximab, which would prolong getting pregnant by a year from the end of treatment. I will be 37 then. At this very moment, I'm weighing my options. I could do nothing, wait and see if my proteinuria continues to lower on losartan, or move forward and prolong starting a family. As a 35-year-old woman, I feel like there's no viable treatment for me that does not risk my fertility. I hope that a treatment can be found that centers on women's health, that acknowledges this disease can impact anyone at any age, and that this disease deserves a cure.

Nina (*adult patient*)

Howdy. My name is Nina, and I live in Richmond, Texas, close to Houston with my husband of 31 years. I have two grown boys who live close to us. I have resigned from my dream job a few years ago as a preschool teacher because of my MN and the immunosuppressive drugs that I was on. I didn't want to leave, but I had no energy to be the motor skills teacher every day. The principal thought it wouldn't be fair to the children if I had to keep taking time off. She made a very strong suggestion that I stay at home and take care of myself. I never did return.

Since 2017, I take cyclosporine and prednisone and supplements twice a day. The nephrologist adjusts the dosages based on lab results and how I am feeling. Usually, within a year, this can occur four to six times, which includes increasing or decreasing the cyclosporine based on the cyclosporine levels in my blood and the protein spilling in my urine. Valsartan has to be adjusted at least twice a year because my blood vessels will burst in my eyes if my blood pressure gets too high. This feels like someone took a knife and stabbed me in the eyeball. Not very pretty for people to look at.

My body is so tense and nervous the week before labs. Will the doctor have to increase the dosages and will my body respond with worsening side effects? Will I have muscle spasms where the feeling of two hands inside my legs twisting in opposite directions will have me limping around the house in pain? Will

I have increased night sweats where I wake up literally drenched from head to toe - my pajamas and sheets soaked as well? Will the nerves in my fingers again be sensitive to hot water in the shower where I have to take a cold shower because my fingers tingle so much and I can't hold onto a bar of soap or wash my own hair? Or if the doctor decreases my meds, will the disease rev up again?

Never a day goes by that MN is not on my mind. I have to give myself a shot of Repatha in the leg every other week for high cholesterol caused by either MN or possibly the cyclosporine. The Alexa chiming to remind me to take the shot makes me nervous, and I get mad that because of MN, I have to do this. This shot is painful. It feels like a wasp sting. As I push the button to administer the drug into my leg, it brings tears to my eyes every time.

I also have to take Prolia® shots every six months in my stomach because of the osteoporosis caused by the long-term use of prednisone. All the weightlifting I do has not helped prevent bone loss, and that frustrates me tremendously. Prednisone also causes easy bruising, cuts, bleeding, scarring and contributes to the lengthy healing time of those cuts and bruises. I work very hard to keep my body in shape, and I'm proud of my legs, but because of the prednisone, if I bump up against something or seriously cut myself, the scarring is so bad and embarrassing. It makes me sad when I look at the scars, and I remember that this is my reality.

After four years of taking prednisone and cyclosporine every day, my numbers for my protein:creatinine ratio are in remission levels. My nephrologist wants me to stay on this protocol for another nine months, but I brought it to his attention that, yes, this combo has helped my MN, but it's causing permanent damage to my bones. I am nervous because I tried getting off prednisone and cyclosporine in 2019 after two years of being on them, but that only lasted five months until I noticed I was very tired with edema in my legs - Silly Putty, I call it - trembling and of course, bubbles in my urine.

When we ran the blood work, of course, my protein:creatinine ratio had gone up significantly, and I had a relapse. So, back on both drugs immediately. I can remember the feeling of victory weaning off these drugs in 2019, and I could remember the defeat I felt to jump right back into the protocol.

Why can't this disease just stay away? I don't want to be this disease. I've never taken this disease lying down. I've tried the paleo and Plant Paradox Diets, no alcohol, and no protein, and none of these have seemed to help me. Working out helps keep me sane. I have been taking CBD oil, which has helped decrease the muscle cramps, tingly fingers, and night sweats from happening three to four times a week to maybe one or two times a month. Very thankful for that.

I just wish there was a treatment that would put those of us with MN in long-term remission quickly and not cause other diseases or serious side effects. Also, it's very important to have a treatment that has been tested specifically for MN patients and was successful in its treatment, affordable, and can be done at home. To be able to get out of bed, have energy, and be present in life is not something now that I take for granted. And yes, this combo of drugs has helped me to do this, but at a big price. Thank you.

Eric R. (*adult patient*)

Hi, my name is Eric. I live in Jasper, Alabama, with my wife and four cats. I'm a data scientist working with healthcare claims data. I was diagnosed with membranous nephropathy when I was around 16 years old and I'm about to be 35. So, I'm approaching my 20th anniversary. When I first began treatment, I started with 250 milligrams of cyclosporine every 12 hours along with warfarin, a blood thinner, atenolol, and at least one other blood pressure medication to bring it under control. The first month was terrible starting these medications. I had bouts of stomach pain and nausea very frequently that I never had before. I remember driving to school one morning and having to pull over because I felt like I was going to throw up or pass out. It was very scary. I also lost a lot of weight the first month because of the nausea. The blood pressure medications also cause numerous side effects. I passed out in Walmart one day and had to be taken to the ER. My nephrologist attributed it to a blood pressure drop. And even today I still become lightheaded from the blood pressure medicine if I happen to bend over and stand up too quickly.

All of the issues I mentioned previously were worth it though, as within a year or so, my disease was under control, but not quite what we would call remission. Perhaps interestingly, my first few nephrologists never attempted prednisone with cyclosporine, which is a commonly used treatment protocol for MN. The rationale was that due to being overweight, the prednisone could cause further weight gain. When I was around 20 years old, we tried rituximab for about a week or two. I did not have many side effects that I could point to from this medication other than to say I was given high doses of Benadryl to try to ward off any allergic reaction. The Benadryl made me very tired and, unfortunately, we didn't achieve our mission, but we were able to reduce my cyclosporine from 250 milligrams every 12 hours to over 150.

I began a serious diet around 2011 and lost nearly a hundred pounds over a year or two by eating lots of vegetables and calorie counting. After losing about 60 pounds, my labs showed signs of remission. I didn't have insurance at the time so we couldn't consider doing a biopsy. My nephrologist speculated that there was a small chance that my MN could have gone away and that the proteinuria might have

been weight related. I was weaned off cyclosporine but, unfortunately, I relapsed about two months later. I had control of my blood pressure, but my lowered weight and increased vegetable intake caused my potassium to spike. As a result, I had to follow a low-potassium diet, which was extremely difficult to follow because most of the foods I ate to help with weight loss were high in potassium.

I eventually began gaining weight once I started substituting more unhealthy foods. Between 2017 and 2019, my treatment remained the same (besides the short remission), though with low levels of proteinuria and blood creatinine levels that fluctuated from normal to high. I was on losartan plus two or so additional blood pressure medications that were prescribed when my blood pressure fluctuated too much. At it's worse - the blood pressure reached 150 over 90 in the office and was lower at home. I have edema, which is typically in my legs, and never fully goes away. The cyclosporine also typically causes nausea within an hour of taking the dose, even when I take it with food.

Gout has been a recurring issue for me throughout my disease. When I received my undergraduate degree, I walked across the stage on crutches because of the gout flare. In 2019 because of the recurring gout, I was prescribed a daily dose of 10 milligrams of prednisone and 100 milligrams of allopurinol. Prednisone caused some sleep issues, so I started taking it early in the morning, which helped. I also noticed I was more hungry than normal.

Soon after starting prednisone, I began moving toward remission. The PLA2R tests and related labs were within normal limits, so I was first weaned off the prednisone and then the cyclosporine. That was almost a year ago and this is the longest I've ever been in remission. Besides allopurinol, I currently take losartan, chlorthalidone and diltiazem to control my blood pressure, which has been in a good range for a while.

Finally, the mental health effects of my MN are the single most important aspect of my disease experience, especially when I was young, but they were never treated. Being diagnosed with such a serious and rare illness at a young age forced me to confront my mortality before my brain was ready. My mental health suffered enormously. I was 15. And when my friends were worried about what they were getting for Christmas, I was trying to figure out how we can afford medications or whether or not I was on my way to kidney failure and ultimately death. The disease definitely put a dark cloud over my teenage years and beyond. I take Lexapro now to help manage my anxiety and it changed my life. I really wish that a patient's mental health played a larger role in treatment, because it's just as important as treating the physical symptoms of membranous nephropathy. Thank you.

APPENDIX 5: MEETING POLLING QUESTIONS

APPENDIX 5.1: DEMOGRAPHICS OF PARTICIPANTS

1. I am:
    a. An individual living with MN
    b. A care partner of someone with MN

2. Where do you or your loved one live?
    a. U.S. East Coast (Eastern time zone)
    b. U.S. Midwest (Central time zone)
    c. U.S. West (Mountain time zone)
    d. U.S. West Coast (Pacific time zone)
    e. Canada
    f. Mexico, Caribbean Islands
    g. Outside of North America (Europe, South America, etc.)

3. What is your or your loved one('s) age?
    a. Younger than 18
    b. 18-29
    c. 30-39
    d. 40-49
    e. 50-59
    f. 60-69
    g. 70 or older

4. Do you or your loved one identify as:
    a. Male
    b. Female
    c. Non-binary or non-gender-confirming
    d. Prefer not to say.

5. Is your or your loved one's ethnicity/race:
    a. Caucasian
    b. African American
    c. Native American
    d. Latinx
    e. Asian American
    f. Other

6. What is the length of time since your diagnosis of MN?
    a. Less than 1 year ago
    b. 1 to 2 years ago
    c. 2 to 5 years ago
    d. 5 to 10 years ago
    e. More than 10 years ago
    f. I'm not sure.

7. You or your loved one are:
    a. Not currently on dialysis and have never received a kidney transplant.
    b. Currently on dialysis and have never received a kidney transplant.
    c. A kidney transplant recipient in remission.
    d. A kidney transplant recipient with recurrent MN.
    e. A kidney transplant recipient and currently on dialysis (e.g., failed transplant).

APPENDIX 5.2: TOPIC POLLING QUESTIONS

Topic 1. Living with Membranous Nephropathy: Disease Symptoms and Daily Impacts

1. Have you experienced any of the following difficulties? (Select all that apply.)
    a. Muscle and joint aches and pains, including gout
    b. Bones/teeth problems
    c. Issues with eyes
    d. High blood pressure
    e. High blood sugar/diabetes
    f. Anxiety and/or depression
    g. "Brain fog" (forgetfulness, poor concentration, lose track of time)
    h. Being tired or exhausted
    i. Gastrointestinal problems
    j. Recurrent infections
    k. Swelling (ankles, face, etc.)
    l. Other
    m. I do not have symptoms.

2. Which THREE of the following symptoms or conditions most negatively impact your daily life? (Select top three.)
    a. Muscle and joint aches and pains, including gout
    b. Bones/teeth problems
    c. Issues with eyes
    d. High blood pressure
    e. High blood sugar/diabetes
    f. Anxiety and/or depression
    g. "Brain fog" (forgetfulness, poor concentration, losing track of time)
    h. Being tired or exhausted
    i. Gastrointestinal problems
    j. Recurrent infections
    k. Skin problems
    l. Swelling (ankles, face, etc.)
    m. Other
    n. I do not have symptoms

3. How much does your MN impact your daily life in general?
    a. Not at all
    b. Minimally
    c. Moderately
    d. Significant amount

4. Which of the following statements is true for you as related to living with MN? (Select all that apply.)
    a. My general daily function is limited by MN.
    b. I miss work or school more than I am comfortable with.
    c. Family stress is common in my life.
    d. Others don't know what it's like to live with MN.
    e. I cannot participate in sports or other physical activities I enjoy.
    f. I cannot participate in other hobbies I enjoy.
    g. None of the above.

Topic 2: Clinical Trials in Membranous Nephropathy

1. Of the following factors related to a test drug in a clinical trial, select UP TO THREE that you rank as most important to your decision about participating in a clinical trial: (Select top 3.)
    a. Whether I might get placebo ("sugar pill")
    b. Whether I need to stop my current treatment
    c. Potential side effects from a new drug
    d. How the drug is taken (by mouth, IV, injection in muscle)
    e. In earlier trials, whether drug effective for specific benefits most meaningful to me
    f. Knowing if I can make the commitment to participate in a clinical trial
    g. Frequency of exam appointments
    h. Distance to trial site
    i. Length of trial
    j. Whether a kidney biopsy is required
    k. Negative things I have heard about clinical trials
    l. Whether my nephrologist recommends enrolling in the trial
    m. Other

2. Would you enroll in a clinical trial if it required? (Select greatest number of biopsies you would accept.)
    a. No kidney biopsy
    b. 1 kidney biopsy within 1 year
    c. 2 kidney biopsies within 1 year
    d. 3 kidney biopsies within 1 year

Topic 3: Current Challenges to Treating Membranous Nephropathy

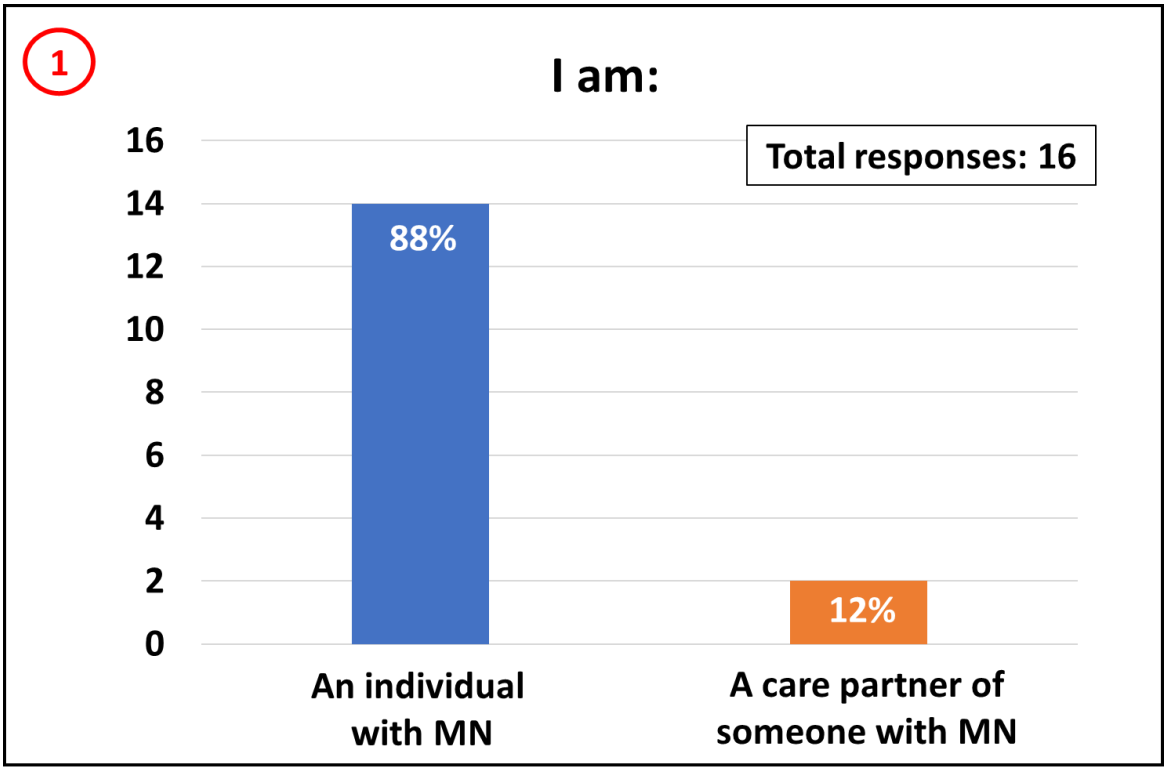
1. Select the medications you use for MN: (Select all that apply.)
    a. ACE inhibitors, ARB, beta-blocker, diuretic = "water pill" (or other drug for blood pressure)
    b. Allopurinol (for gout or high uric acid)
    c. Statin (or other drug for cholesterol)
    d. Veltassa® (or other drug for high potassium)
    e. Sevelamer® (or other drug for high phosphate)
    f. Antidepressant or antianxiety drug
    g. Drugs affecting immune system (anti-inflammatories, immunosuppressants, etc.)
    h. Other (including nonprescription remedies)
    i. I do not take medication.

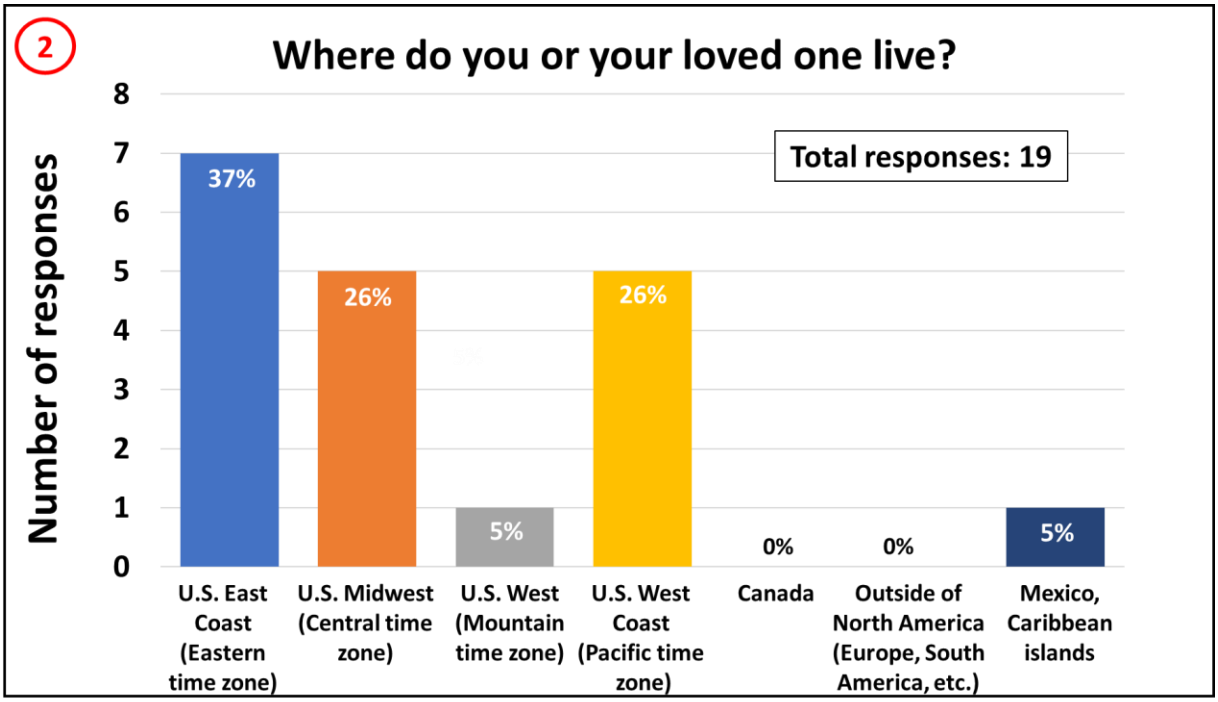
2. How well does your current treatment reduce the most significant symptoms of your disease?
    a. Very well
    b. Moderately well
    c. Somewhat
    d. Not at all
    e. I do not currently take any treatments.

3. Without considering side effects of a drug, which ONE of the following would be the most important to you in a future therapy?
    a. Reverse/halt decline in kidney function (i.e., halt progression of MN, delay need for dialysis)
    b. Improve your quality of life/symptoms or prevent future reduction in quality of life/symptom progression
    c. Prolong your life

APPENDIX 6: RESULTS FROM POLLING QUESTIONS

DEMOGRAPHIC QUESTIONS





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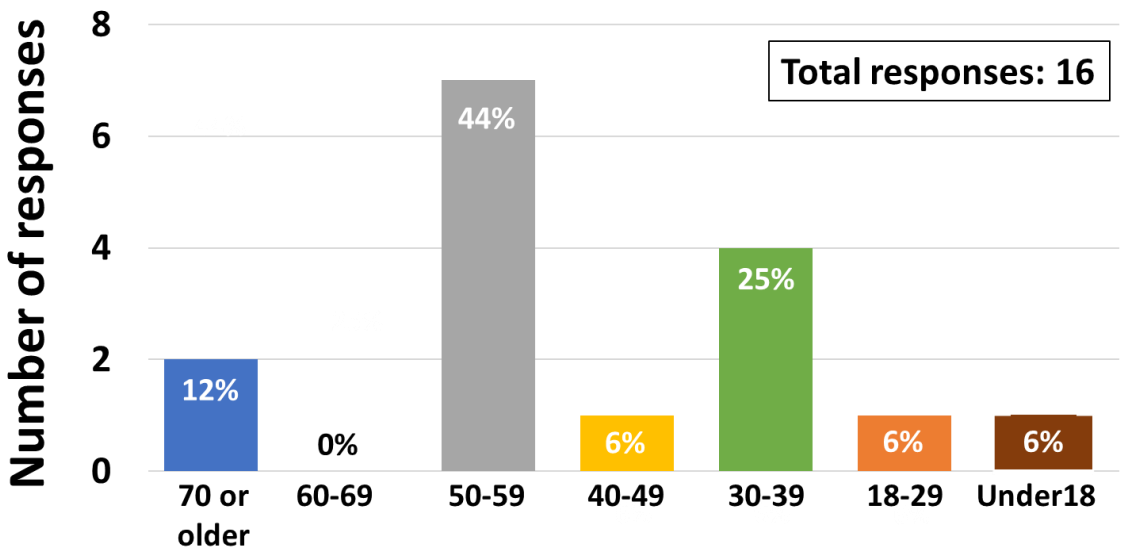
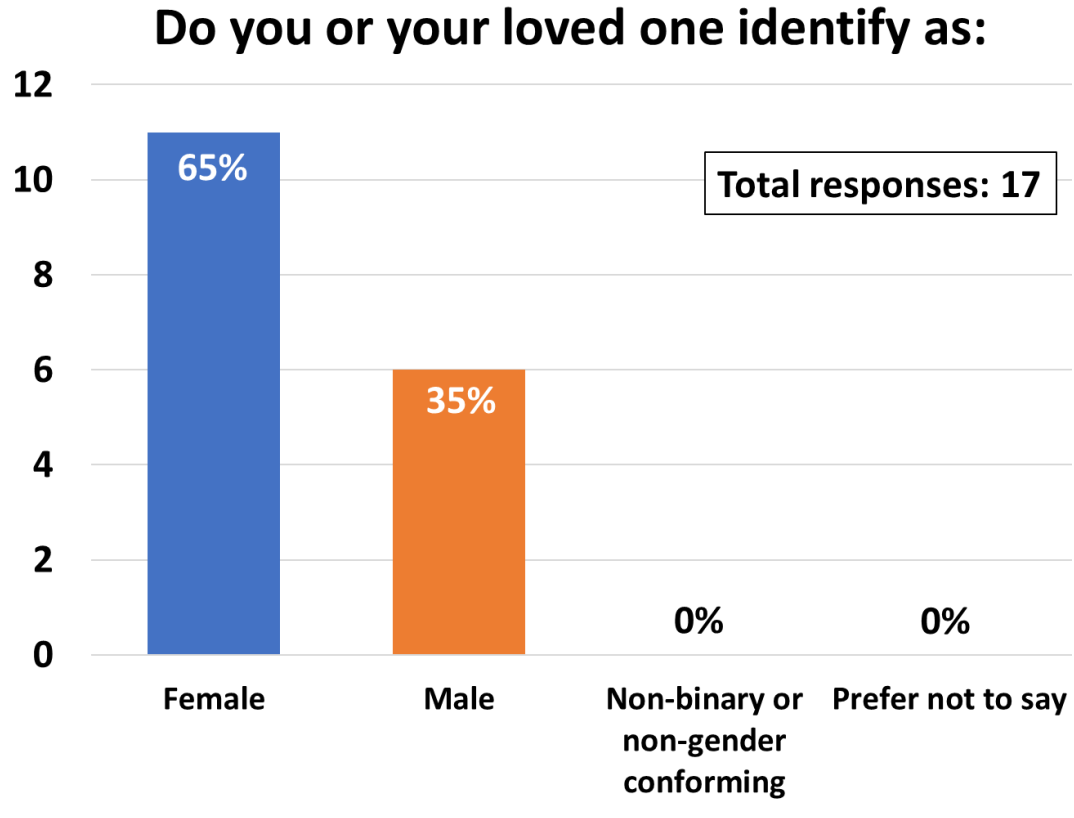
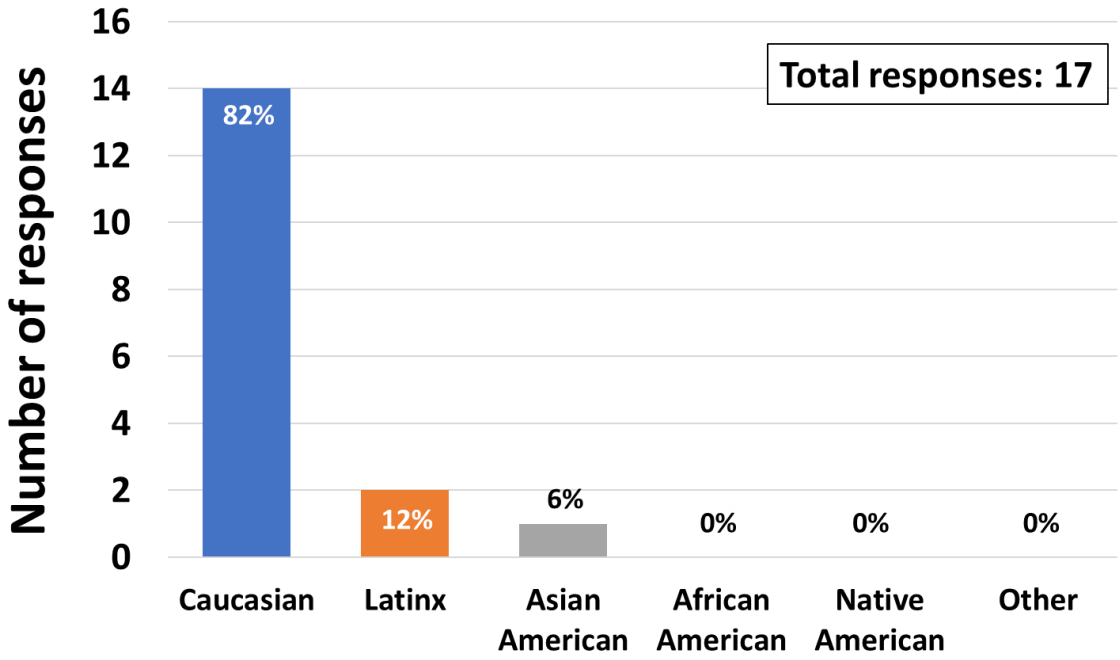

What is your loved one('s) age?
Number of responses
8
6
4
2
0
Total responses: 16
12%
0%
44%
6%
25%
6%
6%
70 or older
60-69
50-59
40-49
30-39
18-29
Under18

4


Do you or your loved one identify as:
12
10
8
6
4
2
0
Total responses: 17
65%
35%
0%
0%
Female
Male
Non-binary or non-gender conforming
Prefer not to say

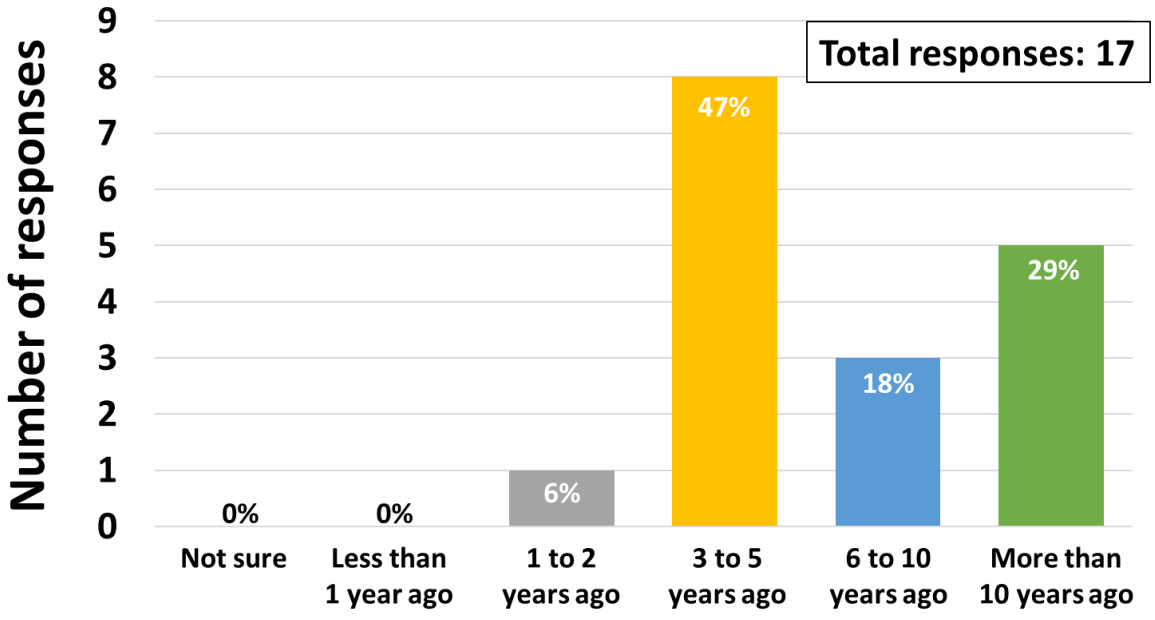
5

Is your or your loved one('s) ethnicity/race:



6

What is the length of time since your diagnosis of MN?



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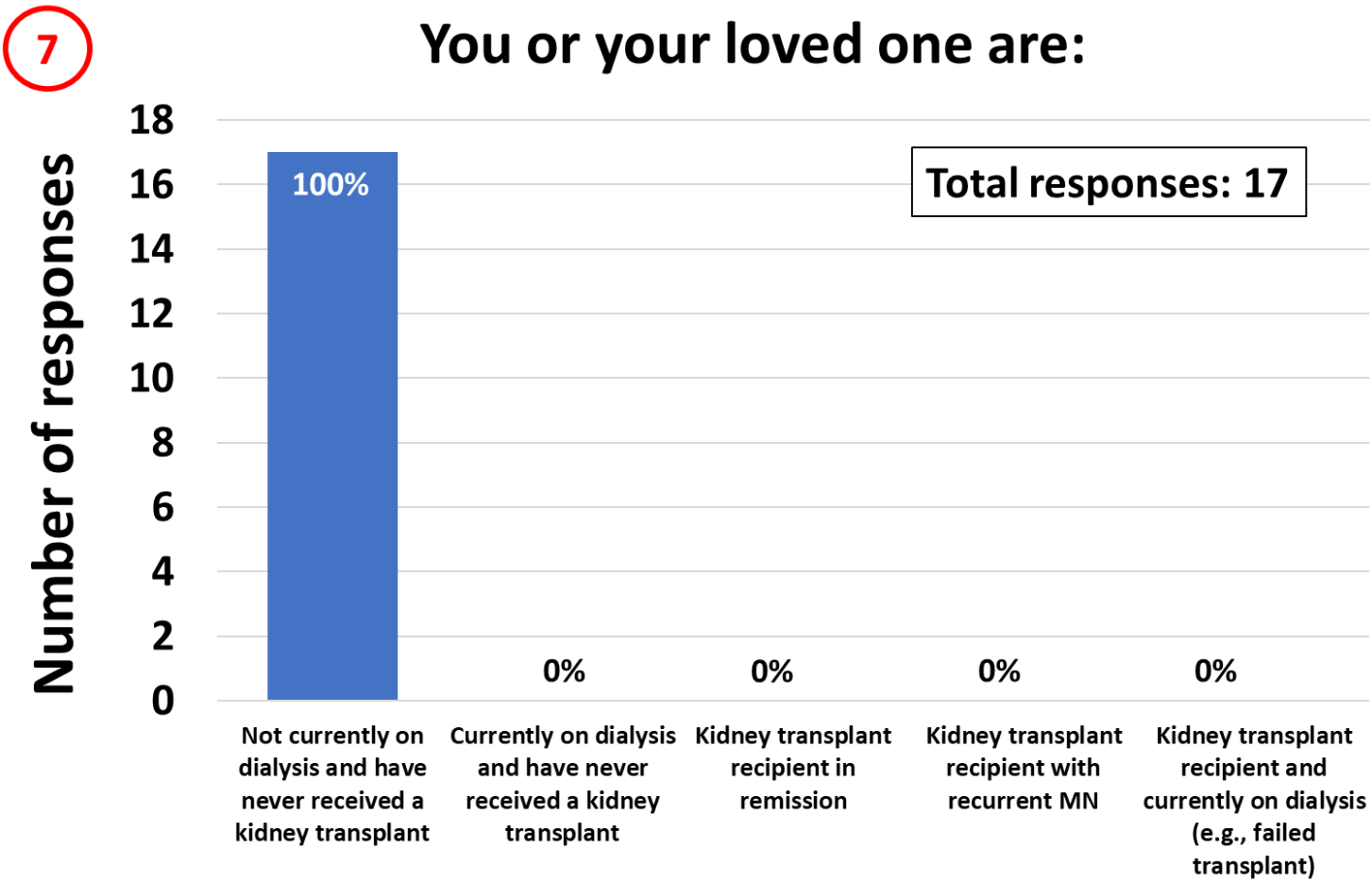
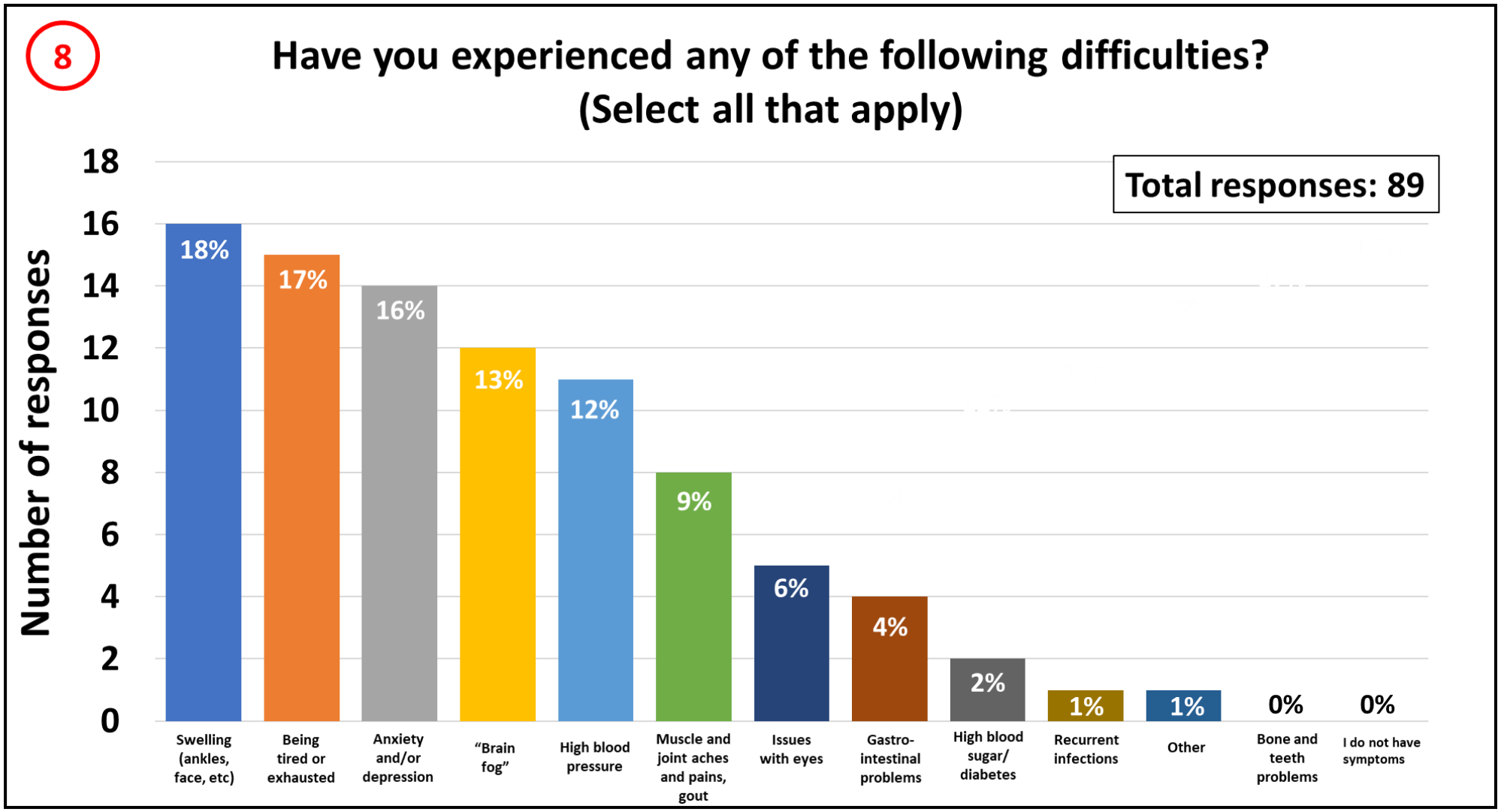
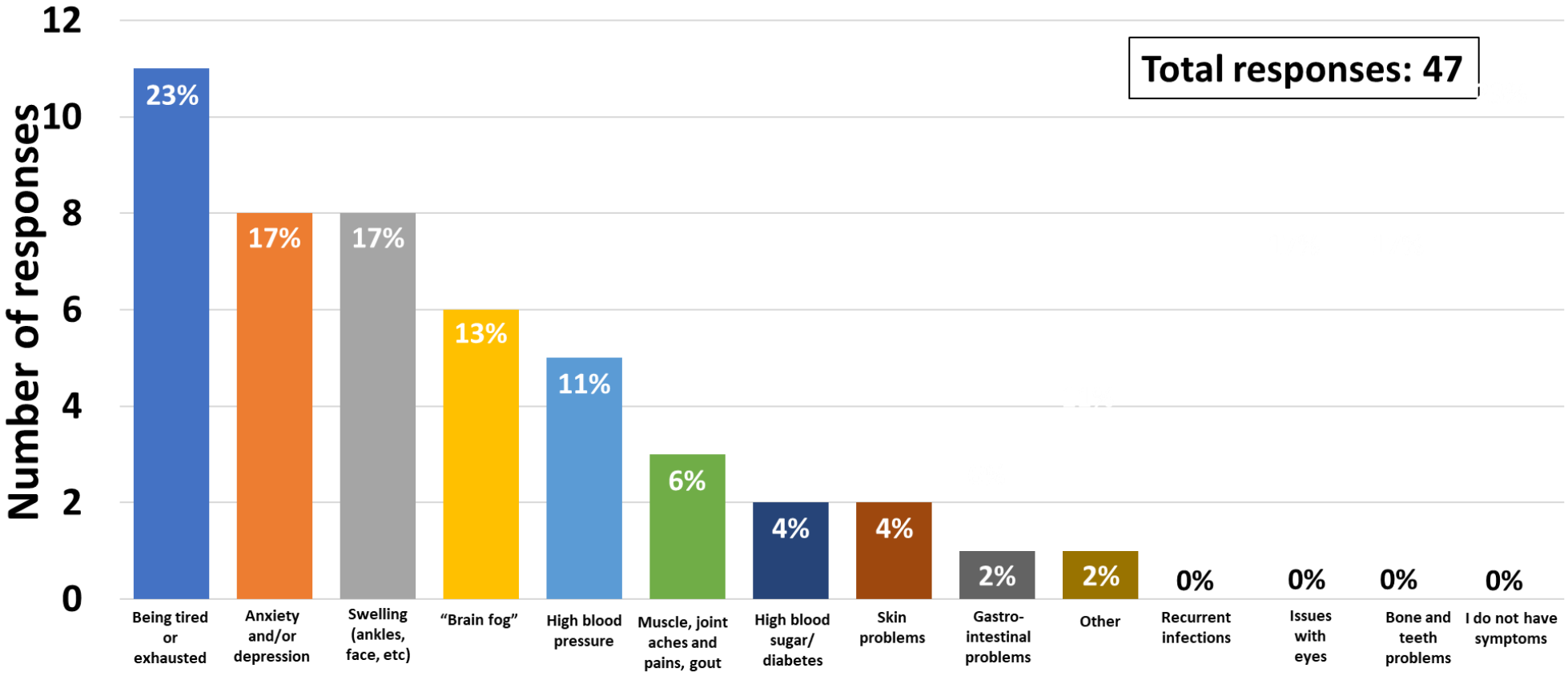

You or your loved one are:
Number of responses
18
16
14
12
10
8
6
4
2
0
100%
0%
0%
0%
0%
Total responses: 17
Not currently on dialysis and have never received a kidney transplant
Currently on dialysis and have never received a kidney transplant
Kidney transplant recipient in remission
Kidney transplant recipient with recurrent MN
Kidney transplant recipient and currently on dialysis (e.g., failed transplant)

TOPIC 1. LIVING WITH MEMBRANOUS NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS



9

Which THREE of the following symptoms or conditions most negatively impact your daily life? (Select top three)



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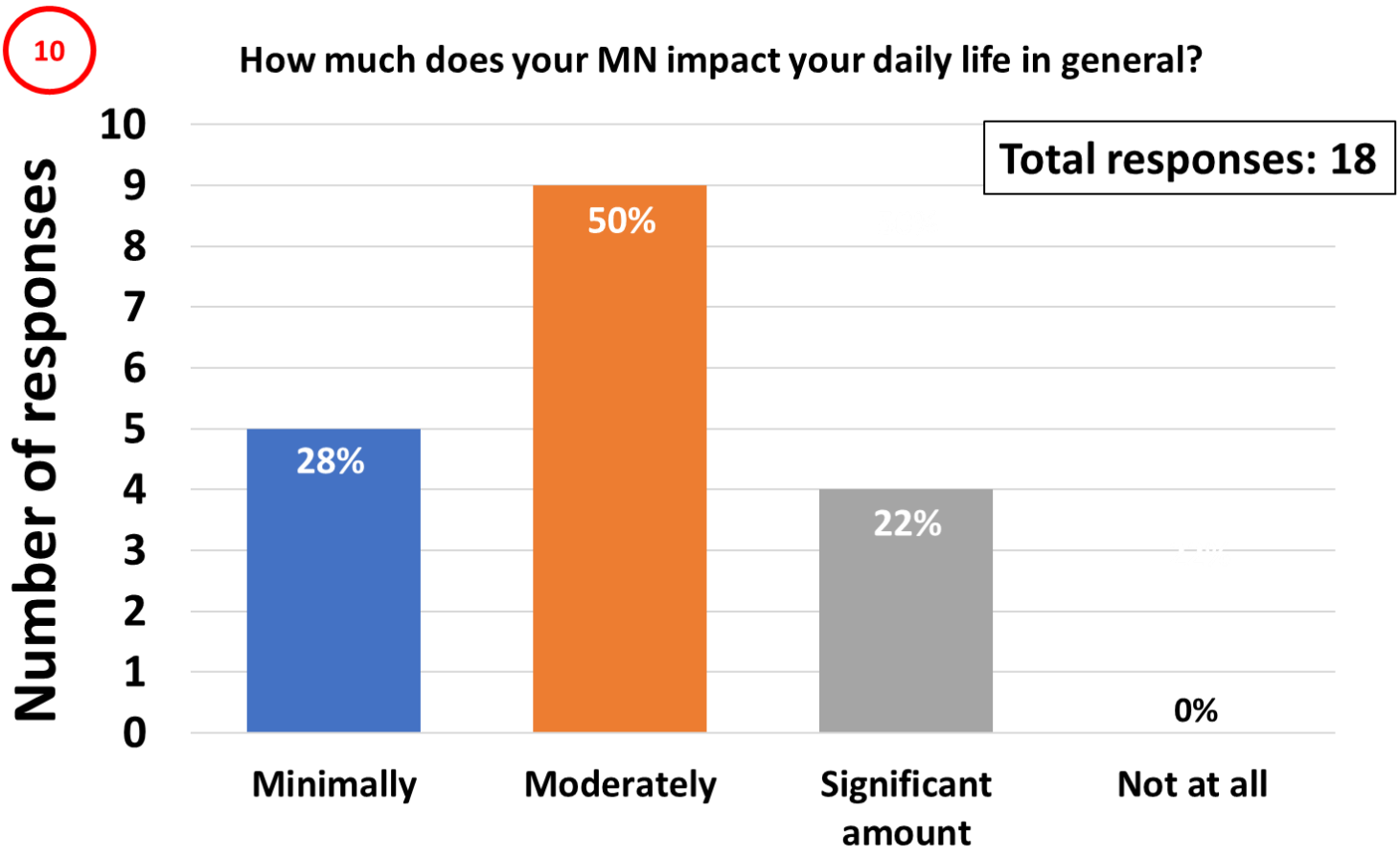
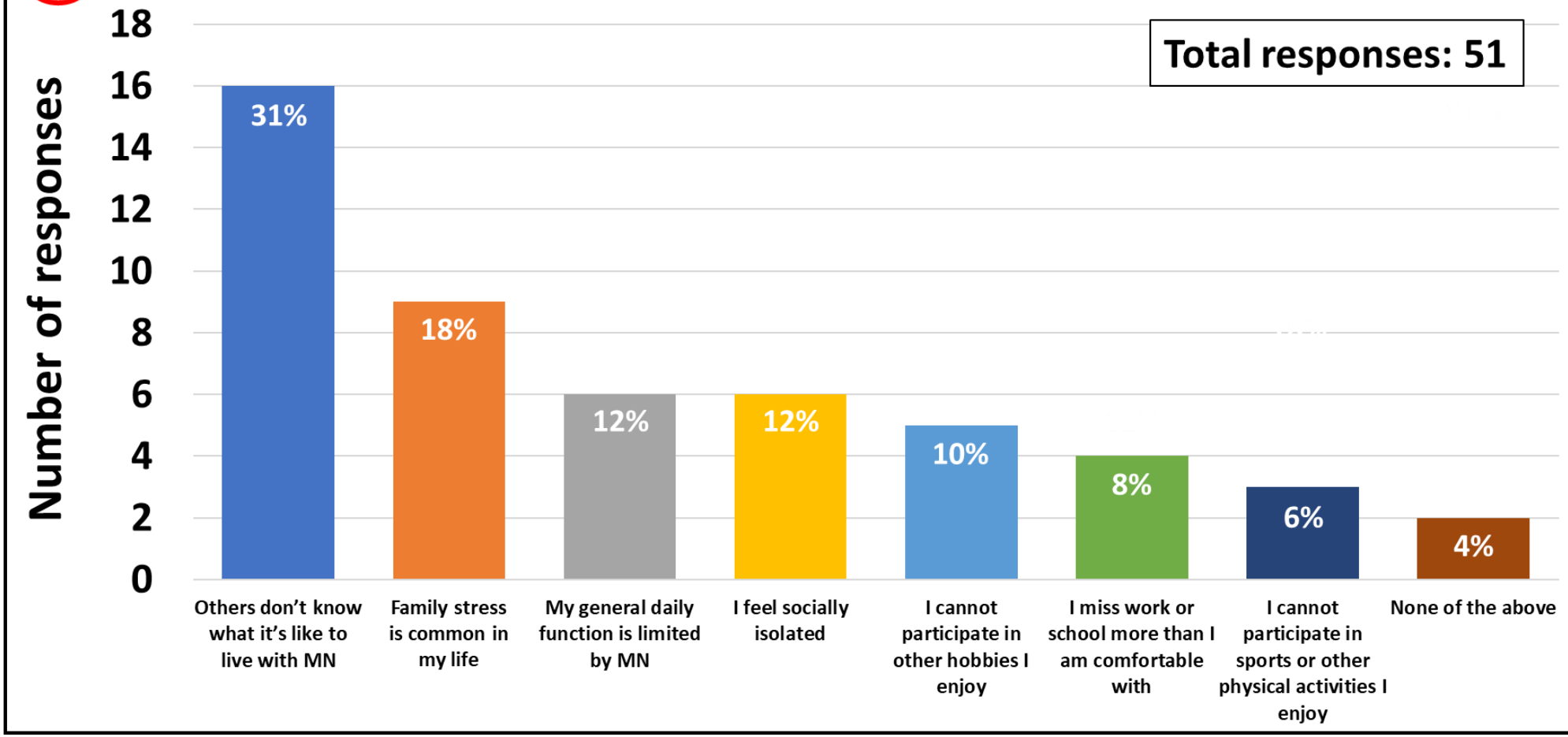

How much does your MN impact your daily life in general?
Total responses: 18
Number of responses
10
9
8
7
6
5
4
3
2
1
0
28%
50%
22%
0%
Minimally
Moderately
Significant amount
Not at all

11

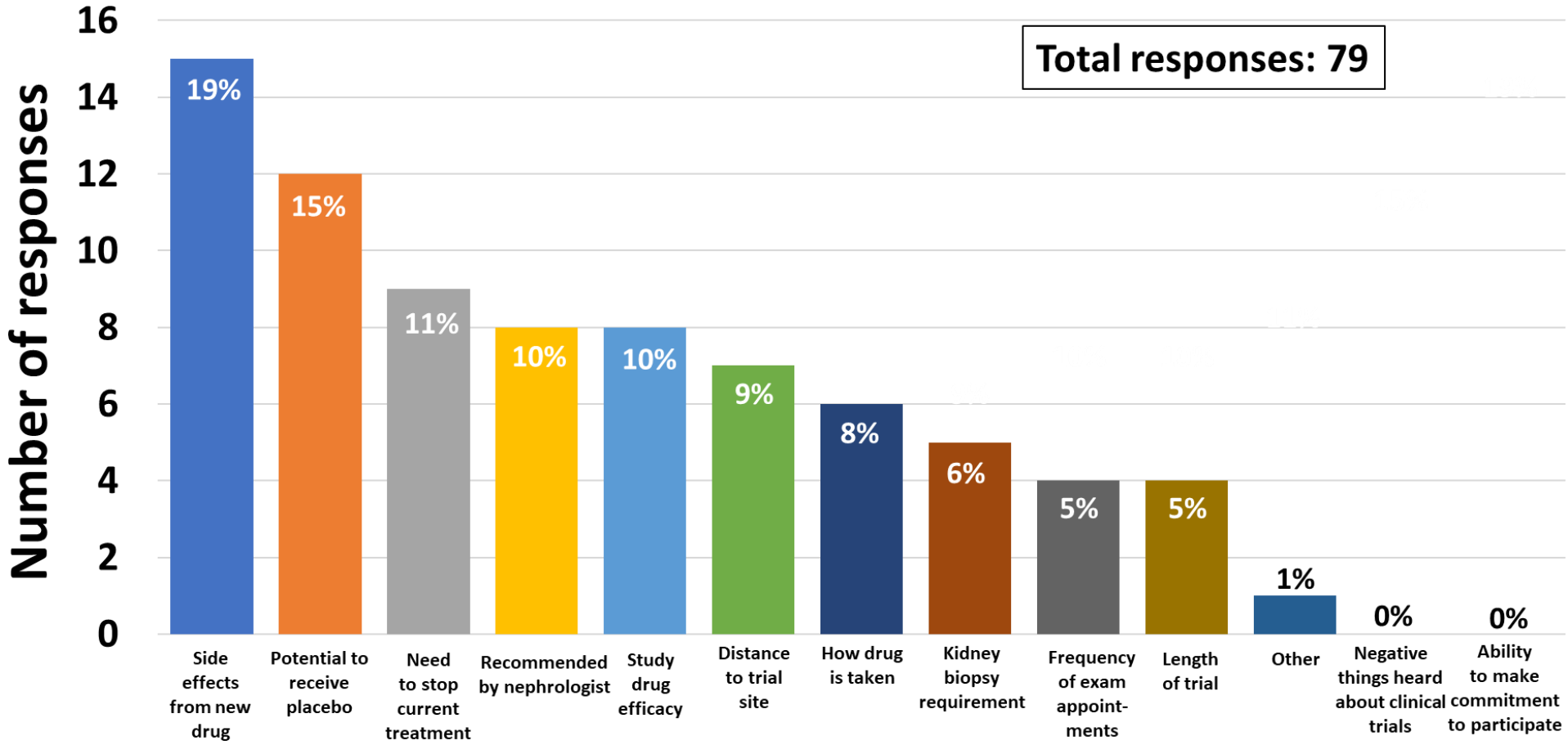
Which of the following statements is true for you as related to living with MN?



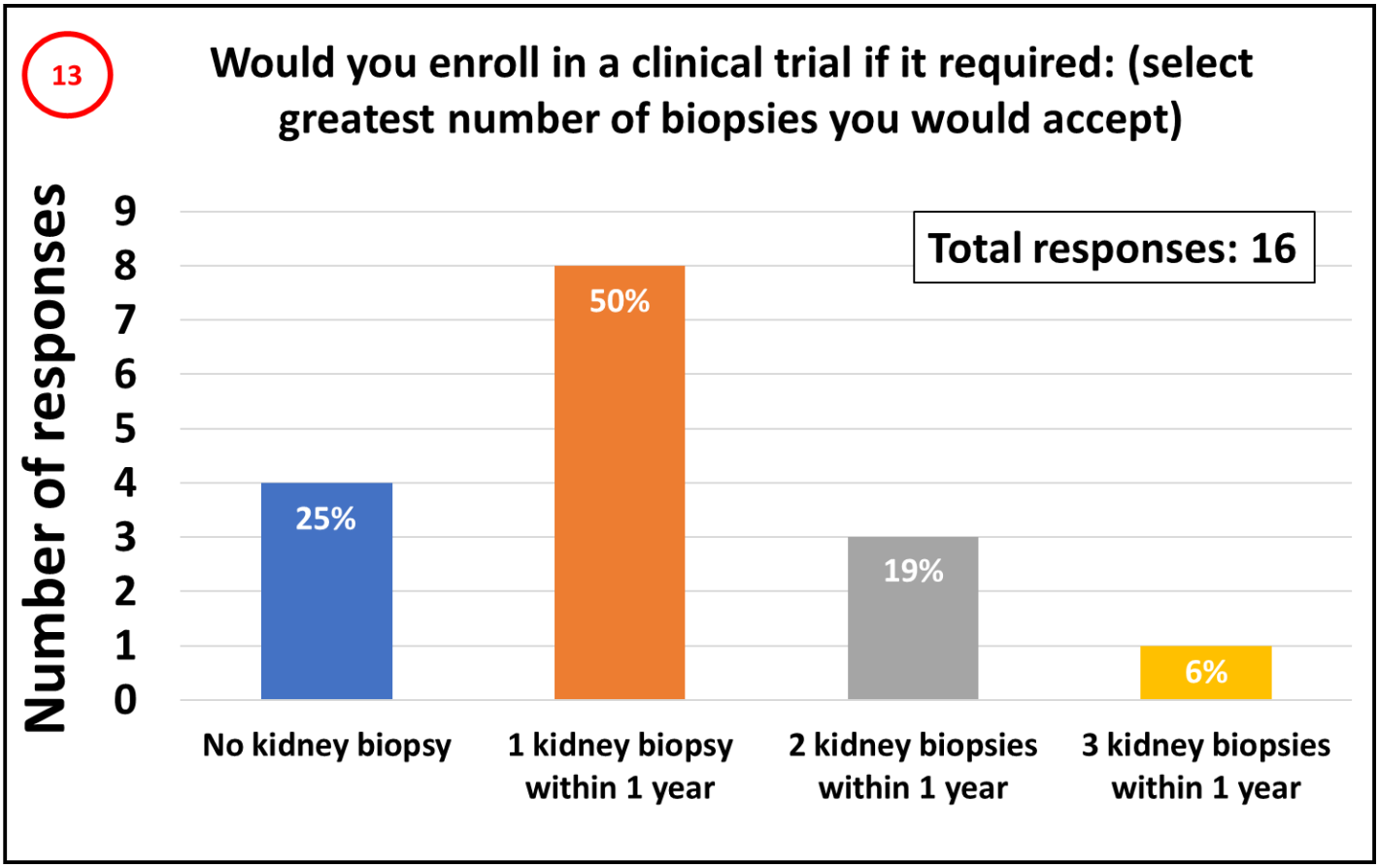
TOPIC 2. CLINICAL TRIALS IN MEMBRANOUS NEPHROPATHY

12

Of the following factors related to a test drug in a clinical trial, select UP TO THREE that are most important to your decision about participating in a clinical trial

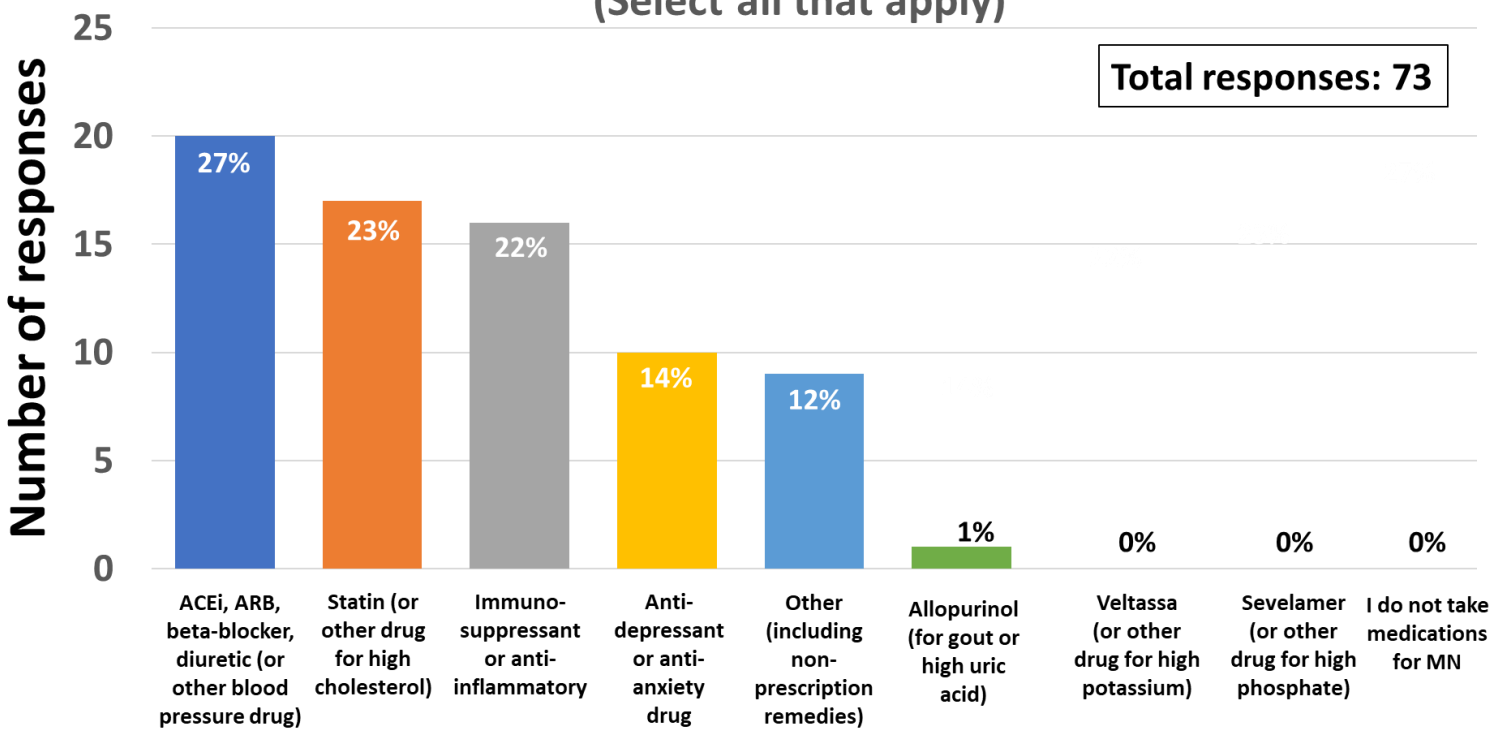


13


Would you enroll in a clinical trial if it required: (select greatest number of biopsies you would accept)
Number of responses
9
8
7
6
5
4
3
2
1
0
Total responses: 16
25%
50%
19%
6%
No kidney biopsy
1 kidney biopsy within 1 year
2 kidney biopsies within 1 year
3 kidney biopsies within 1 year

TOPIC 3: CURRENT CHALLENGES TO TREATING MEMBRANOUS NEPHROPATHY

14



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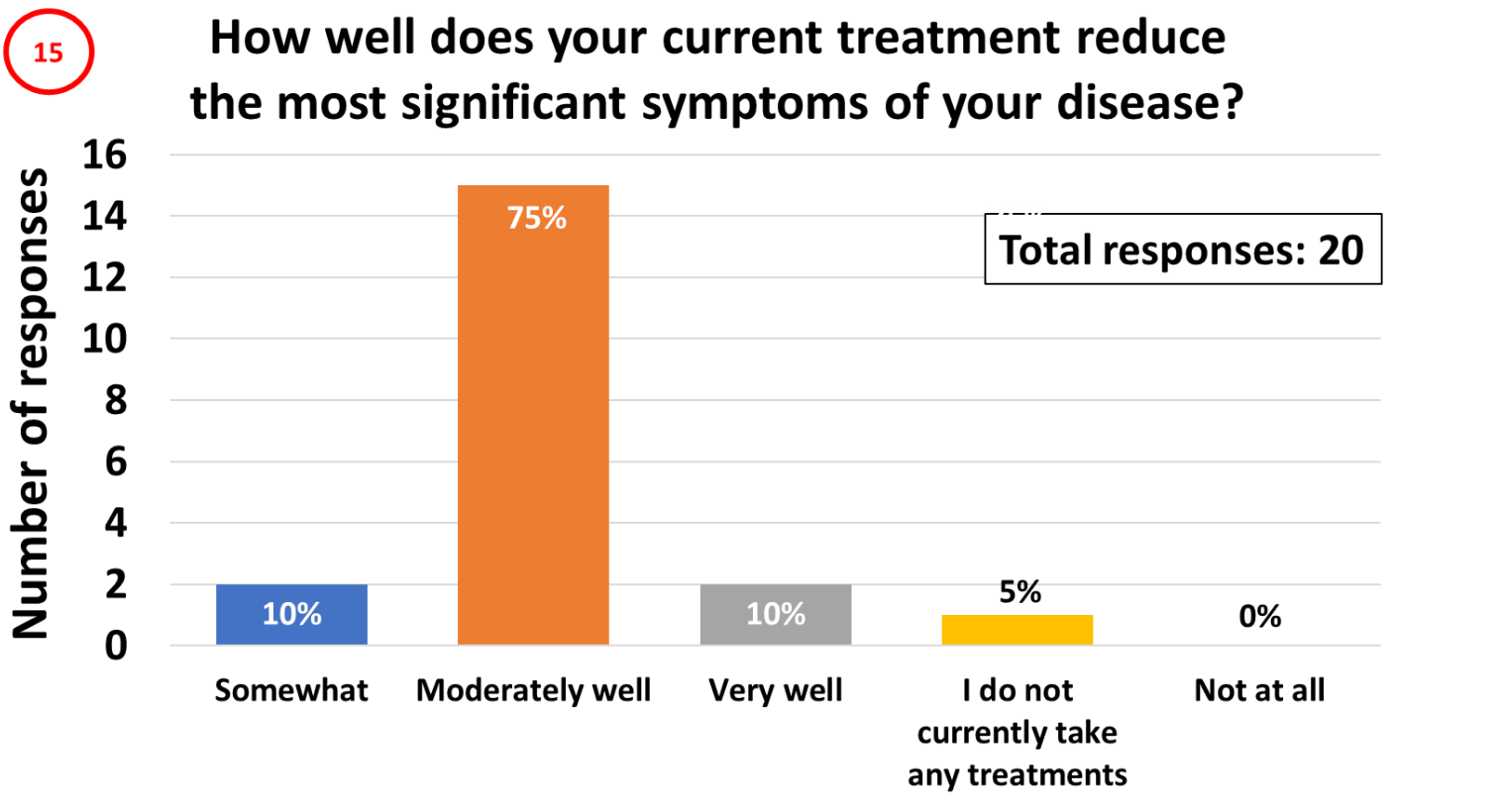
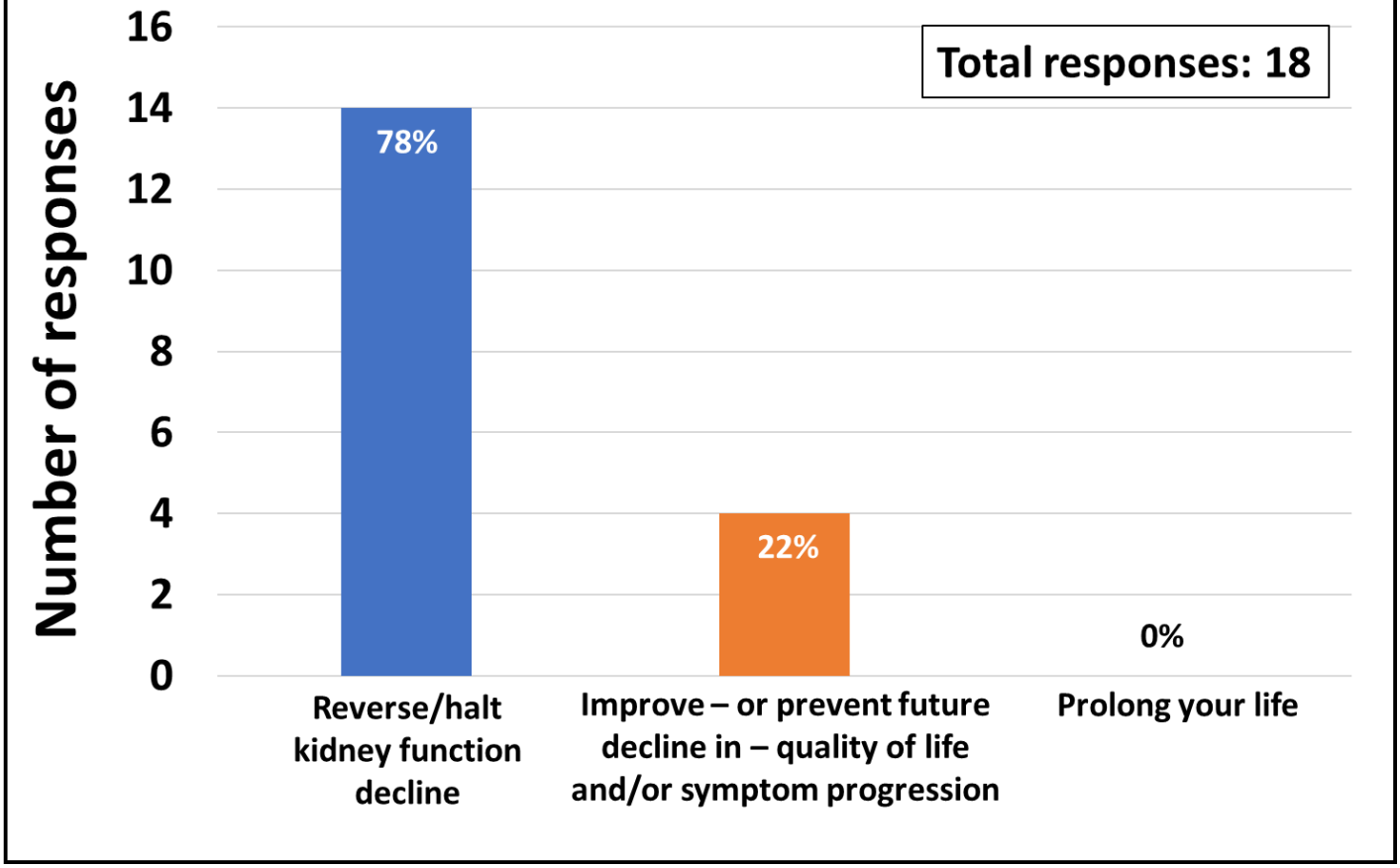


16

Without considering side effects of a drug, which ONE of the following would be the most important to you in a future therapy?



APPENDIX 7: ACKNOWLEDGEMENTS

The National Kidney Foundation and NephCure Kidney International® gratefully acknowledge the generous support of this meeting by:

- Alexion Pharmaceuticals
- BioCryst Pharmaceuticals
- ChemoCentryx
- Mallinckrodt Pharmaceuticals
- Novartis Pharmaceuticals
- ValenzaBiotech