Kidney Medicine Original Research

Health-Related Quality of Life in Focal Segmental Glomerular Sclerosis and Minimal Change Disease: A Qualitative Study of Children and Adults to Inform Patient-Reported Outcomes

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Rationale & Objective: Assessment of how patients feel and function is needed for clinical care and research for focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD). The objective of this study was to develop a patient-reported outcome assessment appropriate for use in children and adults with FSGS and MCD.

Study Design: Qualitative study using semi-structured interviews.

Setting & Participants: 48 semi-structured interviews with children aged 8 to 17 years (n = 11) and adults (n = 10) with FSGS and children aged 8 to 17 (n = 11) and adults (n = 16) with MCD recruited from 3 academic medical centers.

Analytical Approach: Latent content analysis.

Results: FSGS and MCD have a pervasive and comparable impact on physical, social, and mental health-related quality of life regardless of age or diagnosis. Physical symptoms of swelling, fatigue, and pain were articulated by most participants. Disease management was also a frequent topic of discussion; participants described their experiences with medication and associated side effects, as well as lifestyle changes made to manage their disease (ie, dietary changes and frequent medical appointments). These discussions often identified a profound impact on physical abilities and life participation. In many instances, participants described the negative impact these symptoms had on their mood and sense of self, with most participants reporting feelings of anxiety.

Limitations: Participants were primarily non-Hispanic White and English speaking, which may limit generalizability.

Conclusions: Our results suggest that there are commonalities to the FSGS-MCD patient experience of health-related quality of life that will enable the generation of a disease-specific FSGS-MCD patient-reported outcomes instrument for use in children and adults. The development of this tool is intended to facilitate better care and support clinical research for these individuals.

Visual Abstract included

Complete author and article information provided before references.

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Assessment of how patients feel and function is needed for clinical care and clinical trials for patients with focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD). Prior work by the project team and others have resulted in FSGS-specific patient-reported outcome (PRO) assessment tools, including the FSGS Symptom Diary and the FSGS Impact Questionnaire for adults.[1] These FSGS tools capture adult patient-defined domains of disease impact such as fatigue, pain, and edema. No disease-specific PROs have been generated for children with FSGS or for MCD. Therefore, the purpose of this study was to develop a conceptual framework to provide the basis for a comprehensive PRO instrument that evaluates health-related quality of life (HRQoL) that is appropriate for use in children (aged 8-17 years) and adults in the FSGS-MCD disease spectrum (FSGS/MCD).

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FSGS/MCD adversely affects both day-to-day and long-term health. These diseases may lead to a multitude of symptoms, resulting in reduced work and school participation, inability to complete activities of daily living, and excess health care use.[2-4] In the long term, uncontrolled FSGS/MCD may lead to progressive chronic kidney disease and is a leading cause of kidney failure in adults and children.[4] This can cause often unrecognized anxiety and in turn interfere with overall well-being. In current clinical research and care, urinary and serum biomarkers are used to monitor FSGS/MCD status and progression. These measures provide important information about disease activity but do not fully capture the FSGS/MCD patient experience.[5] In particular, these measures do not reflect the broader impact of FSGS/MCD on patients' HRQoL or the effect that a disease has on general physical, mental, and social health.[6,7] HRQoL is most feasibly assessed through PRO measures.

The importance of PROs have recently been recognized by the US Food and Drug Administration (FDA) as relevant and meaningful end points for clinical trials.[8] Specifically, drug efficacy is based in part on evidence that supports dosing selection, safety, tolerability, and the ability of the

PLAIN-LANGUAGE SUMMARY

This study was designed to provide the groundwork for the development of a new self-report measure for use with children and adults with focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD). Semi-structured interviews indicated that FSGS and MCD have a pervasive and comparable impact on physical, social, and mental health-related quality of life regardless of age or diagnosis. Physical symptoms (eg, swelling, fatigue, and pain), disease management (eg, experiences with medication and associated side effects and lifestyle changes), and the impact that these challenges have on physical abilities, social participation, and mood were frequent topics of discussion. Overall, these findings will be used to support the development of a self-report measure that is intended to facilitate better care for these individuals.

new drug to improve some specific facet(s) of the disease in question, including the patients' self-reported HRQoL. The FDA has published guidance for the qualification of PRO instruments for use in clinical trials to support medical labeling.[9] To gain approval as a qualified PRO, detail is needed highlighting measurement development (according to rigorous standards) and a number of distinct measurement properties must be met, including demonstration of content validity, reliability, construct validity, and the ability of the instrument to detect meaningful change.[10-14]

Generic PRO measures (PROMIS [Patient-Reported Outcomes Measurement Information System], 36-Item Short Form Health Survey, and Pediatric Quality of Life Inventory) have been used in nephrotic syndrome to describe a patient's HRQoL.[15,16] Although these generic measures allow for comparisons between nephrotic syndrome and other disease populations,[15-17] they do not have sufficient specificity to fully describe kidney disease–related patient experiences in a detailed, nuanced, and patient-centered manner. In this context, generic measures do not capture a number of key FSGS/MCD disease characteristics, including specific symptoms (eg, edema), the overall burden of symptoms, and the uncertainty caused by the disease's potential to relapse, remit, or progress. The goal of measuring and fully incorporating the FSGS/MCD patient experience into clinical decision making, therapy development initiatives, and clinical research served as motivation for this project to extend the existing FSGS PRO measure to children and adults with FSGS and MCD.

Therefore, the purpose of the current study was to identify and characterize salient domains of HRQoL that are important to children and adults with FSGS and MCD in accordance with established FDA standards.[14,18] This work will help identify and prioritize the most appropriate treatment targets for improving HRQoL in these individuals. Furthermore, this analysis will serve as the foundation for the development of a new disease-specific measure designed to capture the most relevant aspects of HRQoL for children and adults with FSGS and MCD. Our ultimate goal is to develop a validated PRO measure that can be used as a clinical tool, an outcome in observational research, and an end point for interventional trials targeted at improving the lives of these individuals.

METHODS

Forty-eight children and adults with FSGS and MCD were enrolled in this study at the University of Michigan, New York University-Langone Health, and Levine Children's Hospital/Atrium Health to identify the most important and relevant HRQoL domains for these individuals. Diagnosis was confirmed as either FSGS or MCD by kidney biopsy or empirically assigned as MCD in childhood-onset steroid-sensitive nephrotic syndrome. Patients 8 years and older were eligible if they had an estimated glomerular filtration rate > 30 mL/min/1.73 m^2; proteinuria (urinary protein-creatinine ratio > 1 g/g urine protein/urine creatinine, 24-hour protein excretion > 1 g adjusted for body surface area or urinary dipstick protein > 2+ accompanied by edema) within the past 12 months; ability to provide informed consent and assent as appropriate; and were conversant in English. Patients with end-stage kidney disease (supported by dialysis or transplantation), a coexisting chronic or severe acute health condition, or who were unable/unwilling to complete study visits/assessments were excluded.

Recruitment included hospital, provider, and community-based recruitment efforts, as well as existing studies/registries including the Kidney Research Network and University of Michigan Nephrotic Syndrome Registry. Community-based recruitment included website posting at UMHealthResearch.org, as well as postings on advocacy group websites and through advocacy-based email solicitations including the Nephrotic Syndrome Foundation and NephCure Kidney International. Providers at participating institutions were also invited to refer their patients to the study. Potential participants were approached by a study team member at in-person visits and by telephone, email, or postal mail.

All participating sites acquired institutional review board (IRB) approval before initiation of local study conduct. All participants provided assent and/or consent before participation in this study (parental consent and child assent for ages 8-17 years and consent for adults ≥18 years). Data collection was done in accordance with an IRB-approved protocol (University of Michigan Medical School IRB HUM00124929, HUM00146689, and HUM00168763; Levine Children's Hospital Atrium Health IRB File #02-19-26E; and New York University School of Medicine IRB Study #18-01462).

Table 1. Sample Descriptive Data

Variable	FSGS (n = 21)	MCD (n = 27)	Combined Sample (N = 48)
Age			
8-13 y	5 (23.8%)	6 (22.2%)	11 (22.9%)
14-17 y	6 (28.6%)	5 (18.5%)	11 (20.8%)
>18 y	10 (47.6%)	16 (59.3%)	26 (56.3%)
Female sex	11 (52.4%)	14 (51.9%)	25 (52.1%)
Race			
White	18 (85.7%)	19 (70.4%)	37 (77.1%)
African American	2 (9.5%)	6 (22.2%)	8 (16.7%)
American Indian	0 (0%)	1 (3.7%)	1 (2.1%)
Asian	1 (4.8%)	1 (3.7%)	2 (4.2%)
Hispanic or Latino ethnicity	4 (19.0%)	2 (7.4%)	6 (12.5%)
Edema status[a]	2 (9.5%)	7 (25.9%)	9 (18.8%)
Present	7 (33.3%)	11 (40.7%)	18 (37.5%)
Past	9 (42.8%)	16 (59.3%)	25 (52.1%)
Never	5 (23.8%)	0 (0.0%)	5 (10.4%)
Estimated GFR, mL/min/1.73 m^2,[b]	69 (59.2, 91.3)	101.5 (75.8, 125.7)	89.6 (60, 109.5)
Urinary protein-creatinine ratio, g/g[c]	3.3 (1.6, 7.4)	4.6 (1.0, 7.3)	3.7 (1.0, 7.3)
Serum albumin, g/dL[b]	3.4 (2.1, 3.7)	3.5 (3.0, 4.3)	3.4 (2.6, 4.1)
Disease duration, y	6.8 (3.4, 12.0)	6.5 (1.5, 12.6)	7.3 (2.7, 12.4)

Note. Clinical laboratories were collected from the most recent assessment before study enrollment. Proportions are presented as number (percent), and continuous variables, as median (25th, 75th percentiles).
Abbreviations: FSGS, focal segmental glomerulosclerosis; GFR, glomerular filtration rate; MCD, minimal change disease.
[a]Missing for n = 21: n = 11 FSGS and n = 10 MCD.
[b]Missing for n = 1 with FSGS.
[c]Missing for n = 3: n = 2 MCD and n = 1 FSGS.

Semi-structured interviews began with broad open-ended questions, which allowed participants to express what the term "health-related quality of life" meant to them and discuss what they perceived to be the most important aspects of their HRQoL. Detailed prompts were provided across multiple domains of HRQoL (see Item S1 for a detailed interview guide). All interviews were approximately 30 minutes in duration. Interviews were recorded, transcribed verbatim, and deidentified.

Interview transcriptions were analyzed using QSR International's NVivo 11 using thematic content analysis.[19-23] This qualitative analysis approach identified concepts using a grounded theory approach.[24-26] Initially, each transcript was reviewed by at least 2 different individuals (N.E.C., or J.A.M.) who independently identified concepts; at least 1 of the raters remained blinded to disease diagnosis. After each transcript was coded, coders then met to discuss themes and reconcile discrepancies between themes and observations. When agreement was achieved, supporting quotes from each transcript were selected to demonstrate each theme.

Next, a matrix analysis[23,27] was conducted to facilitate the examination of each participant type. This included an examination of how each group: (1) children with FSGS, adults with FSGS, children with MCD, and adults with MCD; (2) children versus adults; and (3) FSGS versus MCD intersected with each code. Dyads of coders examined the matrix analysis for each theme, with the following goals: (1) explore higher-order metathemes that describe how codes relate to each other, (2) synthesize the overarching concept for each code, (3) describe commonalities and differences between each group's experiences, and (4) identify exemplary quotes to illustrate the conclusions of the matrix analysis.

Prior research has indicated that saturation (point at which no new information is learned) typically occurs after 20 to 30 interviews.[28-31] Given this, our sampling plan considered saturation by age and diagnosis, as well as an intersection between these 2 (children with FSGS, adults with FSGS, children with MCD, and adults with MCD).

RESULTS

Descriptive data for the sample are provided in Table 1. The overall percentage of coding agreement between the 2 raters was excellent; the percentage of agreement across the 48 transcripts was 98.46% (range, 97.25%-99.62%). Contemporaneous analysis indicated that saturation by diagnosis was achieved after 34 interviews. Interviews were continued through 48 to ensure saturation across age groups.

A summary table of the overall frequency denoting the number of patients who articulated each theme is provided in Table 2. Physical, social, and mental health symptoms were common. Physical symptoms such as swelling, problems with sleep or fatigue, and pain were endorsed by most participants. Most participants also described

Table 2. Summary of Concept Elicitation From Children and Adults With FSGS and MCD

HRQoL Domain and Subdomains	Example Quotation	FSGS		MCD		Combined Sample (N = 48)	Overlap With Version 1 Content
		Children (n = 11)	Adults (n = 10)	Children (n = 11)	Adults (n = 16)		
Physical health							
Medication impact (including side effects)	"When I'm high on prednisone and it affects me, it makes me a little depressed, a little on edge, headaches, out of it."	100	100	81.8	100	95.8	No
Medical appointments	"Going to the doctor became like really normal."	90.9	100	90.9	93.8	93.8	No
Swelling	"Ever since I was diagnosed, I've always had a swollen stomach."	90.9	70	100	100	91.7	Yes
Pain	"Doing a task was very, very difficult because my muscles and my bones hurt so much."	81.8	60	100	100	87.5	Yes
Problems with sleep	"I am up probably 6, 7 times during the night."	90.9	50	100	100	87.5	Yes
Fatigue	"I never feel like I'm really refreshed. I mainly always just feel tired."	72.7	70	81.8	100	83.3	Yes
Changes in appetite	"There's days when I don't have an appetite at all."	72.7	100	81.8	75	81.3	Yes
Problems with mobility	"You can't move as fast as you would if you were back to normal. But you just have to move slower."	63.6	40	81.8	100	75	Yes
Changes in appearance (due to swelling)	"When I look at pictures of myself, it's like, look at my face. It's just round and red and my cheeks are like burning, you know?"	54.5	40	81.8	100	72.9	Yes
Problems with ADLs or IADLs	"Getting dressed, there has been times where I can't even put my socks on."	45.5	40	72.7	93.8	66.7	Yes
Relapses	"I would say like 3 years ago I had swelling every time I relapsed, which was very often."	27.3	50	45.5	81.3	54.2	No
Nausea	"There are at least 2 days a week to where I can be in bed all day. Just from nauseousness…"	27.3	0	36.4	31.3	25	No
Dizziness or shortness of breath	"Just a simple walk through the house, I would have to stop and rest to catch my breath."	45.5	10	9.1	31.3	25	Yes
Temperature fluctuations	"Sometimes I am hot, very hot. I feel like I am a pressure cooker."	27.3	0	9.1	6.3	10.4	No
Foamy urine	"A good day, I feel normal but still have foamy urine."	0	0	0	25	8.3	Yes
Mental health							
Concerns with future	"I'm worried that I might have it for my whole life."	90.9	100	72.7	100	91.7	Yes
Feelings of positive well-being	"It showed me to be my own advocate and advocate for others. And it's also shown me that I'm stronger than I thought I was."	81.8	90	81.8	87.5	85.4	No
Feeling sad or depressed	"You know, it's just it's kind of sad. I feel like I've lost a few things because of it."	54.5	60	81.8	81.3	70.8	Yes
Feelings of anger/ frustration	"Where did it come from and why did it choose to bother me?"	63.6	50	63.6	87.5	68.8	Yes
Feelings of general anxiety	"I kind of do get a little anxious sometimes. And that typically is around my doctor appointments and around changing of medications."	45.5	60	72.7	87.5	68.8	Yes

(Continued)

Table 2 (Cont'd). Summary of Concept Elicitation From Children and Adults With FSGS and MCD

HRQoL Domain and Subdomains	Example Quotation	FSGS		MCD		Combined Sample (N = 48)	Overlap With Version 1 Content
		Children (n = 11)	Adults (n = 10)	Children (n = 11)	Adults (n = 16)		
Cognitive concerns/ mentally tired	"There'll be things that I don't remember at all […] Or I'll be trying to focus on something, and I can't remember. I don't know, it's just like, it's hard to explain. It's just kind of like a brain fog."	60	63.6	54.5	68.8	62.5	No
Negative impact on self-esteem	"It definitely makes me feel insecure. Because I feel like everybody is staring at me if I go into a public place."	36.4	60	54.5	75	58.3	Yes
Perceptions stigma	"Well, with the edema a lot of times [people] would stare."	36.4	40	45.5	75	52.1	No
Feeling stressed or overwhelmed	"You know everybody's kind of got their breaking point."	9.1	10	0	50	20.8	No
Mood swings	"Almost on a daily basis, I could go from super-angry to tears of joy in the matter of 20 minutes."	9.1	10	18.2	25	16.7	No
Social health							
Missing out on recreational activities	"I had to quit sports because I didn't… Like when I was swollen it was hard to work out and stuff…[I used to play] volleyball and basketball."	100	100	100	100	100	Yes
Impact on work or school life	"This up and down and up and down is more than I want to cope with on top of my current job."	100	100	100	100	100	Yes
Family impact	"On Halloween, I can't walk my daughter around trick-or-treating."	72.7	80	100	93.8	87.5	No
Impact on friendships or other relationships	"You hear about your buddies going out and they're going snowmobiling and stuff, and that's what you used to love to do."	90.9	40	90.9	100	83.3	No
Financial impact	"I even had to make severe changes in my life…it's really affected my finances."	0	20	9.1	43.8	20.8	No
Religion or spirituality	"My religious relationship is a lot better and stronger and deeper."	0	0	0	18.8	6.3	No
Loss of independence	"I became dependent on family members…even things that I wanted to do, I wasn't able to."	0	0	0	6.3	2.1	No

Note. Data are presented as percentage of patients endorsing theme. Percentages of number of participants reporting the specific domain/total within-column participant sample.
Abbreviations: ADLs, activities of daily living; FSGS, focal segmental glomerulosclerosis; HRQoL, health-related quality of life; IADLs, instrumental activities of daily living; MCD, minimal change disease.

problems with mobility and activities of daily living, as well as physical changes in appearance caused by swelling. In addition, participants commonly described their experiences with medication and associated side effects. Participants also described lifestyle changes made to manage disease (ie, diet and medical visits). Participants universally described problems with work or school as a result of symptoms; this included absences related to active disease or regular medical appointments, and for children, the impact that multiple absences had on the ability to keep up with the current curriculum.

Social health concerns suggested that FSGS/MCD has a profound impact on both relationships and recreational activities. In particular, participants universally discussed "missing out" on social events (eg, being able to spend time with their friends and family due to their disease). Most participants described the diverse ways that having FSGS/MCD affected their interpersonal relationships, especially their relationships with family and friends.

In addition, participants reported how certain leisure activities, especially those that involve physical exertion, were limited. For children, this included being unable to participate in school sports in times of active disease or an inability to consistently commit to regular practice/games. Adults focused primarily on having to modify or limit regular exercise during periods of active disease or simply not having the same stamina as before disease. Regarding mental health, most individuals highlighted concerns

Table 3. Relative Importance of Each Topic That Was Discussed

	Overall Thematic Breakdown			
	FSGS		MCD	
HRQoL Domain and Subdomains	Children (n = 11)	Adults (n = 10)	Children (n = 11)	Adults (n = 16)
Physical health	(55.7%)	(61.8%)	(56.4%)	(55.7%)
Medication impact (including side effects)	12.8%	22.4%	12.0%	17.7%
Swelling	16.0%	10.2%	12.2%	9.3%
Medical appointments	8.8%	9.9%	8.8%	9.0%
Fatigue	6.1%	5.6%	3.4%	6.1%
Problems with sleep	7.2%	3.3%	7.4%	4.0%
Changes in appearance (due to swelling)	3.4%	2.6%	4.8%	6.3%
Pain	14.2%	10.5%	14.5%	6.5%
Problems with mobility	5.6%	2.6%	6.9%	5.3%
Problems with ADLS or IADLS	3.6%	4.3%	3.8%	3.6%
Changes in appetite	5.0%	8.9%	5.9%	4.8%
Relapses	2.9%	2.8%	6.5%	6.4%
Nausea	1.1%	0%	2.9%	1.1%
Dizziness or shortness of breath	2.0%	0.3%	0.2%	0.6%
Temperature fluctuations	0.9%	0%	0.2%	0.2%
Foamy urine	0%	0%	0%	0.5%
Mental health	(18.6%)	(19.2%)	(17.1%)	(22.8%)
Concerns with future	19.6%	23.0%	16.0%	12.14%
Feelings of positive well-being	16.2%	23.8%	16.7%	18.1%
Feelings of general anxiety	12.8%	13.1%	12.5%	11.5%
Feelings of anger/frustration	14.9%	5.7%	9.0%	12.4%
Feeling sad or depressed	8.8%	9.8%	14.6%	11.0%
Cognitive concerns/mentally tired	10.1%	5.7%	5.6%	6.4%
Negative impact on self-esteem	4.7%	6.6%	12.5%	8.2%
Perceptions of stigma	5.4%	6.6%	7.6%	7.1%
Feeling stressed or overwhelmed	4.1%	1.6%	0%	3.3%
Mood swings	1.4%	0.8%	1.4%	1.5%
Social health	(25.7%)	(18.9%)	(26.5%)	(21.5%)
Missing out on recreational activities	29.8%	33.3%	30.0%	29.3%
Impact on work or school life	30.2%	30%	27.4%	21.6%
Family impact	13.2%	12.5%	16.1%	17.1%
Impact on friendships or other relationships	15.6%	13.3%	14.3%	13.8%
Financial impact	0%	2.5%	0.4%	5.4%
Religion or spirituality	0%	0%	0%	1.2%
Loss of independence	0%	0%	0%	0.5%

Note. The percentage reports the proportion of time the overall interview discussion that was spent on a given topic. Percentages for domains reflect the total percentage of comments related to this specific domain (domain percentages should sum to 100 with rounding); percentages within each subdomain reflect the percentage of comments within each domain (should sum to ~100).
Abbreviations: ADLs, activities of daily living; FSGS, focal segmental glomerulosclerosis; HRQoL, health-related quality of life; IADLs, instrumental activities of daily living; MCD, minimal change disease.

about their future, as well as general anxiety, feelings of sadness or depression, and anger/frustration. However, most participants also discussed the positive impact from a supportive medical and patient community, as well as being more appreciative of positive life experiences and times of good health.

Although a number of these themes were represented in version 1.0 of the FSGS PRO,[1] there are several others that were not well represented. Notable areas that are not represented in version 1.0 include the impact that the disease has on social relationships (including family, friends, and other relationships), the substantial side effects that are encountered for commonly prescribed medications (the most common symptoms were side effects related to steroids, such as increased appetite, weight gain, difficulty sleeping, and moodiness), the large number of doctor appointments needed for disease management, the unpredictable nature of relapses, and any positive impact that is related to having FSGS/MCD.

Table 3 provides a summary of the relative importance of each theme determined by the percentage of time during the overall interview that was spent on a given topic. Participants spent 55% of the interview time discussing physical symptoms and 20% focused on mental health, regardless of age and diagnostic group. Children and adults, regardless of diagnostic group, spent ~25%

Table 4. Matrix Analysis Summary for Physical Health: Comparison Across Ages and Diagnosis Groups

HRQoL Subdomains for Physical Health	Overall Thematic Breakdown Example Quotation FSGS	MCD
Swelling		
Children	"Swelling in my stomach. It's, like, probably the most uncomfortable place to have swelling."	"Sometimes when I'm swollen, my stomach will hurt. Or my feet will hurt. Or when I wear jeans, at school, they sometimes… It gets really tight."
Adults	"The swelling can actually get painful when it gets to be quite a bit […] I'll have my shoes tied and they'll feel very constricting on my feet and things like that. Same for my belts, when I have abdominal swelling…I think the pain is primarily related to the tightness."	"There's a component of it that's painful because I get so much… I would get so much swelling, it would start to compress on my organs. Like just the little amount of water I'd be carrying."
Medication impact (including side effects)		
Children	"I mean, I don't like the side-effects of prednisone. Every time like I dread it. And then it's like, because the rounder face and all that kind of stuff."	"Eating, whenever I'm on prednisone, I eat a lot. So, I start to gain a lot of weight."
Adults	"[The steroids caused] A whole lot of weight gain and sweating really bad. It was difficult to do anything because every bone and muscle in my body hurt. I couldn't even vacuum or carry groceries. I gained a whole lot of weight, which was sad.	"From steroids, I know a lot of people have different kinds of responses to them. For me, I developed a stomach irritation, which led to a feeling of being bloated."
Medical appointments		
Children	"Since I had to get biopsies, my last biopsy was pretty painful. And whenever I'm in the hospital and I have to get an IV or I have to get medical procedures done, it's not the most pleasant experience."	"For my legs, sometimes – the last 2 times I've been admitted, it's taken a week each time for my legs to get better. It takes a while for the swelling to go down."
Adults	"I passed out at work from low sodium level, and ended up in the hospital for 4 days."	"A month and a half I was in and out of hospitals and they couldn't figure it out."
Fatigue		
Children	"I wouldn't just have the energy to do anything…I always feel tired."	"I really don't have a lot of energy to do the things with… Like I would just have enough energy to go up and down the stairs."
Adults	"I don't have the physical energy to do anything. You know? I'm afraid to start projects because I know I can't finish them. You know? I just physically don't have the energy to do it."	"My body felt tired. It wasn't I was sleepy. It was more my body. Because when my body's carrying all this extra weight, it feels like someone's breaking down my body, basically."
Problems with sleep		
Children	"I wake up tired. Then after that, I just go to sleep and wake up again, I feel like way more tired. I always wake up tired."	"I used to wake up at 8, and now I wake up at like 12. Yeah, [I sleep] a lot longer."
Adults	"I sleep a lot now. You know? I think I sleep too much. And you know, I just don't have a regular sleep pattern anymore."	"I sleep a lot. I personally require 8 hours of sleep a night or else I am just exhausted. Now, I do tend to be more tired. I definitely, at 9 o'clock, I'm ready for bed."
Changes in appearance (due to swelling)		
Children	"Getting dressed, it can be a struggle because I have… a lot of my outfits, they look pretty, but I can't normally wear them because they're smaller."	"Sometimes when I have swelling, some of my clothes don't fit me, so I have to wear something different. I'd wear a different shirt or different pants that are like a different size."

(Continued)

Table 4 (Cont'd). Matrix Analysis Summary for Physical Health: Comparison Across Ages and Diagnosis Groups

HRQoL Subdomains for Physical Health	Overall Thematic Breakdown Example Quotation FSGS	MCD
Adults	"I had to buy all new clothes, shoes, everything. And I figured I'd lose my weight, you know? So… I just recently got rid of a lot of my old clothes; I can't fit in them anymore."	"When you're symptomatic and you're swollen, you're not able to really fit your normal size. I would have to wear, probably, some jogging pants… …to be loose, to be able to move around, to be able to do everyday activities without me feeling like I'm being squashed to death."
Pain		
Children	"I have pain in my back. And then, wherever I have the swelling. So, sometimes my stomach or my legs. Or sometimes my eyes, when they're swollen, hurt."	"I used to get sharp pains in the back area because when I'm swollen, you can just feel the fluid."
Adults	"It was difficult to do anything because every bone and muscle in my body hurt."	"Yes, in my lower back. Like right where my kidneys are. I always know something is wrong when my back gets real sensitive in those areas, like right where your kidneys are. You can feel it in your lower back."
Problems with mobility		
Children	"It hurts a lot when I go down or up [the stairs], so someone used [or "needs"] to carry me down or up."	"It makes it hard to do like a lot, a lot of physical activity at once…I can't run very far…it makes my legs hurt a lot."
Adults	"[Exercise is] Very minimal. I have a hard time going up and down a flight of stairs."	"[I feel tired from] Walking short distances, doing stairs, things that you would normally take for granted…doing stairs would put me out of breath."
Problems with ADLS or IADLS		
Children	"Bathing, sort of, because heat can make your headaches worse. So, bathing can be a…can hurt really, really bad."	"When I'm in a relapse, all the water weight, it's harder to move and get around to the bathroom and stuff like that."
Adults	"I had to be a little bit more careful in the shower. I don't know that my balance was off as much as just moving, walking sometimes…"	"When I take a shower, I don't have enough energy to stand in there and blow-dry my hair. So, I'll lie in the bed and blow-dry my hair."
Changes in appetite		
Children	"When I'm really swollen in my stomach, the pressure on my stomach just makes me feel like I don't want to eat."	"I get really hungry with all the prednisone but I can't eat anything...because I'm swollen up."
Adults	"If I'm really inflamed, my appetite will go down, and I will not want to eat."	"It reduced my stomach capacity, so I could not eat very much, and then absorption in my body was reduced, so whatever I ate would linger for very long."
Relapses		
Children	"If I'm in relapse, then I just am more annoyed."	"Right before relapse, if I have – right before relapse, I'm usually super-grumpy and in a really bad mood."
Adults	"So, if I'm really swollen and having a flare up, then when I'm walking or if I'm standing or doing anything like that, I am aware that I am swelling."	"I get very kind of like moody, and confused would probably be a symptom. Like almost like PMS. Like I feel real irritable when I'm starting to relapse. And then, that too, I feel kind of like just off."

(Continued)

Table 4 (Cont'd). Matrix Analysis Summary for Physical Health: Comparison Across Ages and Diagnosis Groups

HRQoL Subdomains for Physical Health	Overall Thematic Breakdown Example Quotation FSGS	MCD
Nausea		
Children	"[My nephrotic syndrome can affect my] Eating, it just depends if I'm nauseous."	"I throw up everything I eat. Half the times, it doesn't even get to my stomach before it comes back up."
Adults		"You just feel like you have the worst hangover, blue, everything."
Dyspnea or shortness of breath		
Children	"I can't breathe well….It's like I'm breathing hard."	"[Nephrotic syndrome] affects my ability to be active [because of] shortening of breath."
Adults	"You go into work and maybe you go up a couple flights of stairs, and next thing you know is you're feeling more winded and out of breath…"	"It reduced my lung capacity, so I had shortness of breath very quickly. Even simple things like speaking tend to be worse."
Temperature fluctuations		
Children	"[I feel] Kind of like sick or like that my body is way too hot."	"Sometimes, I am hot, very hot."
Adults	NA	"My hands and feet burn all the time. And what makes that worse is like doing dishes or walking outside when it's cold without an extra pair of socks on…"
Foamy urine		
Children	NA	
Adults	NA	"A good day, I feel normal but still have foamy urine."

Abbreviations: ADLs, activities of daily living; FSGS, focal segmental glomerulosclerosis; HRQoL, health-related quality of life; IADLs, instrumental activities of daily living; IV, intravenous access; MCD, minimal change disease; NA, not applicable; PMS, premenstrual syndrome.

Table 5. Matrix Analysis Summary for Mental Health: Comparison Across Ages and Diagnosis Groups

HRQoL Subdomains for Mental Health	Overall Thematic Breakdown Example Quotation	
	FSGS	MCD
Concerns with future		
Children	"You don't know if you're going to have to get a kidney transplant, or if they're going to find a cure. A cure. Or if you have a big opportunity, but then you have to miss out of it because you have this chronic disease."	"Sometimes it makes me worry I will never [going to] grow out of it."
Adults	"I would say it's always a player in the back of your mind…That it changes somewhat and becomes not necessarily a minimal change disease, but actually changes into a real kidney issue where your kidney starts losing function instead."	"In the worst case, that the disease…if it continues progressing, can lead to kidney failure. So those are sort of things that I do… I am somewhat concerned about."
Feelings of general anxiety		
Children	"Well, my kidney disease, it makes me really nervous that it's going to be a problem for like… I always worry about if I never go into remission, I always worry about what I'll do if I never go into remission."	"I'm worried that I might have it for my whole life."
Adults	"Yeah, I mean I get anxious, I think, thinking long-term. Well, not knowing if the treatment is going to last."	"My biggest concern, for myself, would be… Well, before that there's like no concoction for me."
Feelings of anger/ frustration		
Children	"If I wake up swollen, and I had plans to do that day, and my swelling is not going down, then it makes me like mad and upset. Because I'm like, I had things to do, and plans. And this hinders that."	"[It makes me feel] upset. Because I can't be active like I was last times."
Adults	"I could get very frustrated. That this is how science is and it is unpredictable and it's trial and error."	"I guess I'm angry because, you know, everything I used to do, I can't no more. So, it does… it wears on you after a while. You know?"
Feeling sad or depressed		
Children	"Sometimes I'm a little bit sad because I don't… because I have it. And sometimes at school, I miss things that I was looking forward to because I have to go to the doctors."	"Yeah, because I can't – especially when I'm in the hospital because like then, sometimes I don't feel good and then, I can't hang out with friends and stuff."
Adults	"I don't… really know, because I pretty much shut everybody out. I don't really think about it. And I don't really see a lot of the people that I used to see anymore."	"I was always pretty social, but you don't feel like connecting, so a lot of connections drop off, and that feeds the fire. That's kind of a… that's a side effect of depression, but it's also a cause of depression."
Mood swings		
Children	"It makes me moody…probably because I don't feel really feel well."	"When I'm… Usually on prednisone, I get really sad or I'll get really moody. Because I guess that's what one of the symptoms is. It changes your mood."
Adults	"While I was on the heavy dose of steroids, that definitely affected mood swings."	"I can't really control my emotions like… almost on a daily basis, I could go from super-angry to tears of joy in the matter of 20 minutes. And it's not really anything I can control."
Negative impact on self-esteem		
Children	"I normally always have a… more of a swollen stomach. And so that can embarrass me. And swollen eyes. Like the swollen face. It… That will embarrass me."	"I definitely don't like going in public when I have a relapse, besides when I'm at the hospital. Because I just get too self-conscious. Like, I think they might think he's a fat boy or something like that."
Adults	"I was a little bit upset that I couldn't control the things; that I had gotten so big when I'm usually a very small person. Yeah. It was kind of embarrassing."	"For me, it was embarrassing because I was at my biggest I ever been at in my whole entire life. Like, I couldn't… like, sociably, I could not socialize."

(Continued)

Table 5 (Cont'd). Matrix Analysis Summary for Mental Health: Comparison Across Ages and Diagnosis Groups

HRQoL Subdomains for Mental Health	Overall Thematic Breakdown Example Quotation	
	FSGS	MCD
Perceptions of stigma		
Children	"If I go out or go to school when my eyes are really swollen, I notice like maybe…like sometimes people are looking at me like they're wondering why my eyes are swollen."	"I guess I get really discouraged in like whenever I do get self-conscious, I don't want to go to school because people make fun of you, I guess, for being swollen."
Adults	"With the edema a lot of times [people] would just stare. You know, and there was the assumption that I was just morbidly obese, and they would act like that."	"I had people ask me like hey, how come one week you were this size and then this week you're like bigger than what you usually are?"
Feelings of positive well-being		
Children	"I got to take part in a study that was in Florida. So, I got to go to Florida for a whole month and go to Disneyland and stuff during the study. So, that was one good thing that came from it."	"It doesn't necessarily stop me from doing anything, because the only time I get to do arts and crafts is basically when I'm at the hospital."
Adults	"I get to meet other people who are… I'm not going to say just like me, but people who are going through the same thing. And it's like kind of like encouraging to let them know that everything is going to be okay."	"I mean, it makes you be happy for the good days and try to be productive on those days when you can, even though there's, you know, the lack of motivation and stuff. It makes you realize that, you know, nobody's guaranteed good health."
Feeling stressed or overwhelmed		
Children	"I'm one of the people who gets more stressed out when you do miss school…I feel really overwhelmed."	NA
Adults	"Back when I was first diagnosed with it, I was having a hard time thinking clearly there, because I had to take a few tests for my job at work there and I think I ended up failing one of them at the time there."	"In terms of what I'm looking for in a job, I feel like this up and down and up and down is more than I want to cope with on top of my current job, which is pretty demanding."
Cognitive concerns/ mentally tired		
Children	"If I'm swollen, my head is always hurting, when… if my face is swollen. So, I can't concentrate on that. Or if I'm trying to take a test, I get brain fog and I can't remember, even though I did like three hours of studying two days in a row."	"School stuff […] I'm like totally out of it, so I can't even be there. My head is hurting, everything – everything is heavy, and everything is – I'm not into it. Not a clear mind."
Adults	"I know in the last couple of years, I've had some episodes of maybe a little bit worse memory or thinking clearly."	"Going back to school has been night and day. I feel like my brain just shuts down when I get too afraid. And I just can't remember things like I used to. I don't know why […] but what I do know is that I've lost memory."

Abbreviations: FSGS, focal segmental glomerulosclerosis; HRQoL, health-related quality of life; MCD, minimal change disease; NA, not applicable.

and ~20% of the time, respectively, discussing social health. In total, the matrix analysis indicated that FSGS and MCD have a profound and comparable impact on HRQoL regardless of age or diagnosis (see Tables 4-6 for exemplar quotations).

DISCUSSION

FSGS and MCD have a profound impact on HRQoL. Thus, a quantifiable understanding of the global and specific consequences that FSGS and MCD have on how patients feel and function is paramount. We undertook this study to elicit the disease-specific concepts that represent how adults and children feel and function with FSGS or MCD in accordance with established best practices for PRO development.[14] The findings presented in this report illustrate the common impact on HRQoL themes across both FSGS and MCD in children and adults. These results will be used in future initiatives to generate a new FSGS/MCD disease-specific PRO measure.

There was notable concordance with respect to a number of generic aspects of HRQoL that are common to both persons with FSGS/MCD and individuals with other chronic conditions, including generic aspects of physical health (ie, fatigue and sleep), mental health (ie, anxiety, depression, and positive well-being), and social health (ie,

Table 6. Matrix Analysis Summary for Social Health: Comparison Across Ages And Diagnosis Groups

HRQoL Subdomains for Social Health	Overall Thematic Breakdown Example Quotation	
	FSGS	MCD
Missing out on recreational activities		
Children	"Sometimes when my brother stretches, I like to do, but sometimes I can't really do a lot of those advanced ones because… like all those advanced back ones because sometimes it hurts me."	"Whenever I run on a treadmill, I have to slow down the speed, because then I feel like I get tired easily, and I have to stop."
Adults	"When that kind of stuff [feeling off during exercise] happens, I just get a little worried. And it kind of makes me not want to do it like as much."	"The 2 times when I had progressed into nephrotic syndrome, then yes, it was keeping me from those things [outdoor activities]."
Family impact		
Children	"I would say it [FSGS] has stopped me before [from spending time with family]."	"Besides when I'm in the hospital, I don't get to see all my family. Because it's either mom and dad. Or mom. Or just dad. Or just both of them. But I don't get to see my brothers and sisters."
Adults	"I'll still be there, but I just don't be like as open to like, or engaged, if that makes sense."	"If there's an outbreak of flu or something going on, then I tend to not be involved in things that are going on because of my immune system."
Impact on friendships or other relationships		
Children	"Like if I want to hang out with my friends, but I'm swollen, or my head is hurting. Like, I can't do that, so…"	"If I'm swelling a lot in my legs, then yeah. Like I don't get to hang out with my friends that often.
Adults	"I can't really relate to active people. You know, if you go out and talk to all your friends, and they're all doing things, and doing this and doing that, and then well, what have you been doing?"	"It has stopped me. I can't stop it. I mean, on Halloween, I can't walk my daughter around trick-or-treating… There are definitely times that I have missed out because of my minimal change disease."
Impact on work or school life		
Children	"I'm missing information during school when I'm at the doctor, that I could be using for the test, to study with."	"Worried about like, I don't know, worried about my grades, too. Because I don't know. Like I, I missed the first week of the semester at school. That was a big deal."
Adults	"I'm not able to hold down a job. I can't work at all. If I ever had to go get a job where I had a timeline and I had to be there for 8 to 10 hours a day, I couldn't do it."	"I was in full-time school, and I had to do a medical withdraw."
Financial impact		
Children	NA	"[The most concerning thing to me would be] Medication, hospital visits. Because even just the nephrotic syndrome medication is a lot of it."
Adults	"I even had to make severe changes in my life…it's really affected my finances."	"Through the fifteen years, there's been times when I haven't had insurance and stuff and not able to stay on top of medical care."
Religion or spirituality		
Children	NA	NA
Adults	"My religious relationship is a lot better and stronger and deeper."	"I have a faith in God and he knows and controls tomorrow and whatever comes, he'll be there with me through it."
Loss of independence		
Children	NA	NA
Adults	NA	"I became dependent on family members. I couldn't do much myself and then even things that I wanted to do, I wasn't able to."

Abbreviations: FSGS, focal segmental glomerulosclerosis; HRQoL, health-related quality of life; MCD, minimal change disease; NA, not applicable.

social participation and social satisfaction).[32] However, there were several disease-specific aspects of HRQoL that were raised within this FSGS/MCD patient sample. These include physical symptoms, such as swelling, which affected multiple aspects of physical health, including breathing, mobility, pain, appearance, and appetite, as well as social health, including recreational activities (especially those involving mobility). Side effects from the medications used to treat FSGS/MCD were commonplace. Concerns about the unpredictability of the disease including relapse and the potential for disease progression were frequent across the different groups.

From a metatheme perspective, these findings serve to highlight and illustrate the interrelated and consequential ways in which the routine care and monitoring associated with FSGS/MCD can affect routine activities, personal interactions, and daily life. Patients described an array of challenges, including the negative impact that medications, especially steroids, have on health, mood, and appearance. They elaborated on how routine doctor visits and hospitalizations had a negative impact on social/recreational activities, as well as school and work. In addition, swelling, which was experienced at one time or another by most patients, affected diet and appetite, mobility, interpersonal interactions (including stigma and unwanted attention because of appearance), and self-esteem.

Although this study elucidates the experiences of children and adults with FSGS and MCD, it is important to acknowledge the limitations. First, although the sample is intentionally heterogeneous in terms of age and diagnosis, more research focusing on racial and ethnic minorities with FSGS/MCD is needed to ensure the generalizability of findings to these groups. The study cohort was limited to patients who were conversant in English and it will be necessary to extend the findings to patients who speak other languages. Because studies of rare diseases such as FSGS and MCD are often international, future work will need to include the global community. In addition, children too young to self-report are also affected by FSGS and MCD. Future work is needed to develop a companion Observer Reported Outcome measure to address this important gap.

In summary, the findings presented are consistent with previous research in FSGS, MCD, and nephrotic syndrome that has demonstrated that although generic HRQoL measures capture important aspects of HRQoL and that PROs can sensitively capture some outcomes in this population, the generic measures do not adequately capture the unique disease-specific aspects of FSGS/MCD.[16,33-35] These findings support our hypothesis that HRQoL measures for individuals with FSGS/MCD should incorporate both disease-specific and generic HRQoL concepts. Furthermore, the findings from this study suggest that the commonalities between HRQoL in FSGS and MCD, as well as the commonalities in HRQoL between adults and children, should allow for the development of an HRQoL PRO measure that can be used in children (aged ≥8 years) and adults, as well as in both disorders, and is appropriate for use supporting FDA-based labeling claims.[14,18] To this end, the findings from this study will be used to help develop a new measure of HRQoL enabling a more holistic assessment of patient health beyond clinical metrics for use in clinical practice, observational research, and clinical trials.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Item S1: Detailed interview guide.

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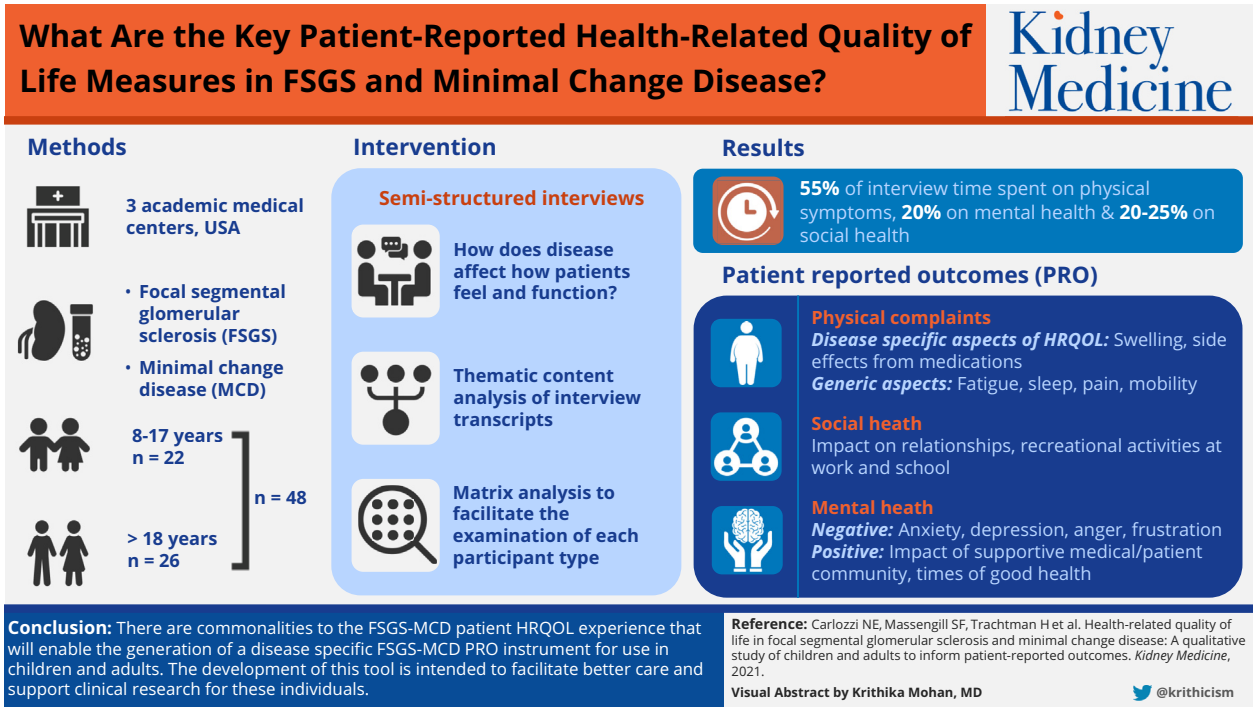
What Are the Key Patient-Reported Health-Related Quality of Life Measures in FSGS and Minimal Change Disease?
Kidney Medicine
Methods
3 academic medical centers, USA
• Focal segmental glomerular sclerosis (FSGS)
• Minimal change disease (MCD)
8-17 years n = 22
> 18 years n = 26
n = 48
Intervention
Semi-structured interviews
How does disease affect how patients feel and function?
Thematic content analysis of interview transcripts
Matrix analysis to facilitate the examination of each participant type
Results
55% of interview time spent on physical symptoms, 20% on mental health & 20-25% on social health
Patient reported outcomes (PRO)
Physical complaints
Disease specific aspects of HRQOL: Swelling, side effects from medications
Generic aspects: Fatigue, sleep, pain, mobility
Social heath
Impact on relationships, recreational activities at work and school
Mental heath
Negative: Anxiety, depression, anger, frustration
Positive: Impact of supportive medical/patient community, times of good health
Conclusion: There are commonalities to the FSGS-MCD patient HRQOL experience that will enable the generation of a disease specific FSGS-MCD PRO instrument for use in children and adults. The development of this tool is intended to facilitate better care and support clinical research for these individuals.
Reference: Carlozzi NE, Massengill SF, Trachtman H et al. Health-related quality of life in focal segmental glomerular sclerosis and minimal change disease: A qualitative study of children and adults to inform patient-reported outcomes. Kidney Medicine, 2021.
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