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Cognitive Function in Children with Lupus Nephritis: A Cross-Sectional Comparison with Children with Other Glomerular Chronic Kidney Diseases

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Abstract

Objective—To identify factors contributing to cognitive impairment in children with lupus nephritis.

Study design—A cross-sectional analysis of a large multicenter national cohort of children with chronic kidney disease (CKD) using standardized measures to determine baseline neuropsychiatric function and health-related quality of life (HRQoL) in children with lupus nephritis ($n = 34$), and to compare baseline function with that in children with other forms of glomerular CKD (gCKD; $n = 171$). We used inverse probability weighting via a logistic model for propensity score analysis to achieve balance between children with lupus nephritis and those with other glomerular causes of CKD, adjusting for known confounders. We used linear regression models to compare neurocognitive outcomes between exposure groups, adjusting for current prednisone use and testing for an interaction between current prednisone use and lupus nephritis, and to test for an association between cognitive function and HRQoL.

Results—Current prednisone use was independently associated with worse attention ($P < .01$) and better adaptive skills ($P = .04$), and there was a significant interaction between current prednisone use and lupus nephritis for internalizing problems, with worse parent-reported internalizing problems in children with lupus nephritis on prednisone ($P = .047$). Better parent-

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Data in this manuscript were collected by the Chronic Kidney Disease in children prospective cohort study (CKiD) with clinical coordinating centers (Principal Investigators) at Children's Mercy Hospital and the University of Missouri - Kansas City (Bradley Warady, MD) and Children's Hospital of Philadelphia (Susan Furth, MD, PhD), Central Biochemistry Laboratory (George Schwartz, MD) at the University of Rochester Medical Center, and data coordinating center (Alvaro Muñoz, PhD) at the Johns Hopkins Bloomberg School of Public Health

reported HRQoL was associated with better visual memory ($P = .01$), and better child-reported HRQoL was associated with better attention ($P < .01$) and inhibitory control ($P < .01$). Both parent and child HRQoL were associated with better measures of executive function ($P = .02$ and $< .001$, respectively).

Conclusion—Children with lupus nephritis have comparable or better cognitive function than their peers with other gCKDs, which is reassuring given the multiorgan and lifelong complications associated with lupus.

Children with chronic kidney disease (CKD) are at risk for poor clinical and psychosocial outcomes because of kidney dysfunction, living with childhood chronic illness, and effects of treatments. Cognitive impairment in children with CKD is a known comorbidity, and studies indicate impaired function across several neurocognitive domains, including IQ, memory, and executive function.¹⁻³ Psychosocial functioning also may be adversely impacted in children with CKD, who suffer from higher rates of depressive and anxiety symptoms⁴⁻⁸ and exhibit poorer health-related quality of life (HRQoL) compared with healthy peers.⁹ Cognitive and behavioral dysfunction may adversely impact HRQoL, but little is known about this potential impact in children with CKD. Glomerular CKD (gCKD) may arise from several etiologies that may differentially impact cognitive and psychosocial functioning. Understanding these differences may yield insight into the pathophysiological mechanisms of cognitive and psychosocial dysfunction, as well as inform interventions to improve overall functioning and HRQoL in these children.

Fifty-five percent of children with systemic lupus erythematosus have gCKD,¹⁰ and >20% exhibit moderate renal impairment by 10 years after diagnosis.¹¹ Children with lupus nephritis also may have central nervous system (CNS) involvement, including neurocognitive impairment in up to 50%.¹²⁻¹⁴ Inflammation of both the kidney and brain in children with lupus nephritis may exert concurrent adverse effects on cognitive and psychosocial function, and higher disease activity is associated with depression, anxiety, and poor HRQoL in these patients.^{15,16} In addition, management of lupus nephritis carries a high burden of immunosuppressive medication use¹⁷ and of psychosocial stress due to uncertainty resulting from the episodic nature of lupus and the potential for stigmatizing skin lesions.¹⁸⁻²¹ Thus, children with lupus nephritis may have worse cognitive and psychosocial impairment than children with other forms of gCKD, but this has not been examined.

The Chronic Kidney Disease in Children (CKiD) prospective cohort study is a multicenter longitudinal investigation of children with mild-to-moderate CKD.²² A primary goal of the CKiD study is to determine how a decline in kidney function affects neurocognitive function and behavior. As such, participants entered in CKiD undergo a battery of neurocognitive and behavioral tests, as well as repeated HRQoL assessments. Given the myriad of neuropsychiatric comorbidities associated with both CKD and lupus nephritis, we aimed to (1) determine whether children in the CKiD study with CKD secondary to lupus nephritis exhibit worse neurocognitive and psychosocial functioning and HRQoL compared with children with other forms of gCKD, and (2) examine the association of HRQoL with neurocognitive and behavioral functioning in children with lupus nephritis and other causes of gCKD.

Methods

The CKiD study's design and objectives have been described previously.²² Inclusion criteria include age 1-16 years and an estimated glomerular filtration rate (eGFR) between 30 and 90 mL/min/1.73 m². Exclusion criteria include renal or other solid organ, bone marrow, or stem cell transplantation, dialysis treatment within the past 3 months, HIV or cancer diagnosis or treatment within the past 12 months, structural heart disease, pregnancy within the past 12 months, genetic syndromes involving the CNS, and history of severe to profound intellectual disability. CKiD participants undergo standardized neurocognitive testing and assessment of psychosocial function at 6 months following study entry and then every 2 years after study entry. HRQoL is assessed at 6 months and at each annual visit thereafter. We used the baseline data (first visit with a measurement available) from these measures to determine the outcomes for this analysis. The CKiD study protocol was approved by the Institutional Review Boards at all participating sites, and informed consent and assent was obtained from all participants.

Neurocognitive and Psychosocial Outcomes

The neurocognitive outcomes of interest included intelligence, measured by the Wechsler Abbreviated Scales of Intelligence (WASI)²³; academic achievement, measured by the Wechsler Individual Achievement Test, Second Edition, Abbreviated (WIAT-II-A)²⁴; memory, measured by the Digit Span Forward (verbal), Digit Span Reverse (verbal working), Spatial Span Forward (visual), and Spatial Span Reverse (visual working) portions of the Wechsler Intelligence Scale for Children, Fourth Edition, Integrated (WISC-IV-I)²⁴; attention and inhibitory control, measured by the Detectability, Response Time Variability, and Errors of Commission subscores from the Conners' Continuous Performance Test, 2nd edition (CPT-II)²⁵; and executive function, measured by the Global Executive Composite score from the Behavior Rating Inventory of Executive Function (BRIEF)²⁶ and the Achievement and Accuracy Ratio scores from Delis-Kaplan Executive Function System (D-KEFS) Tower Test.²⁷

The WASI is a standardized measure of intelligence, and the WIAT-II-A is a standardized measure of academic achievement. Both tests are used for children aged 6 years and are reported as standardized scores with a mean of 100 and SD of 15; higher scores indicate better performance. The WISC-IV-I is a measure of intelligence that also measures discrete cognitive domains for children aged 6-16 years, with a mean of 10 and SD of 3; higher scores indicate better performance. The CPT-II measures attention, and the BRIEF is a parent-completed inventory that measures executive function. They are both validated for children aged 6 years and have a mean score of 50 and SD of 10; lower scores indicate better performance. The D-KEFS is for children aged 8 years and also measures executive function, with a mean score of 10 and SD of 3; higher scores indicate better performance.

Psychosocial outcomes of interest were assessed with the Behavior Assessment of Childhood Disorders, Second Edition (BASC-2), both parent- and self-reports,²⁸ and the PedsQL 4.0 HRQoL survey.²⁹ Both versions of the BASC-2 yield a total Behavioral Symptom Index Score and scores for the Externalizing Problems, Internalizing Problems, and Adaptive Skills indices. In addition, the child report yields the School Problems score.

All scores on the BASC-2 have a mean of 50 and SD of 10. A higher score indicates better adaptive skills, and a lower score indicates worse behavioral symptoms, externalizing problems, internalizing problems, and school problems. HRQoL was assessed by the parent and self-report of the PedsQL 4.0. Domains of physical, emotional, social, school, and overall were measured. HRQoL scores range from 0 to 100, with higher scores indicating better HRQoL.

Statistical Analyses

The primary outcomes of interest were the neurocognitive measures and BASC-2 and HRQoL scores. Descriptive statistics for the demographic, neurocognitive, BASC-2, and HRQoL variables were generated to characterize the study sample. For examination of differences in neurocognitive and psychosocial outcomes by disease group, the categorical exposure was lupus nephritis vs other gCKDs. To balance covariates between groups, we derived propensity scores from a logistic regression model containing the following variables: age, sex, height Z-score, race, ethnicity, maternal education, eGFR,³⁰ urine protein/creatinine ratio, systolic blood pressure Z-score, and anemia status. These variables were selected a priori to be likely risk factors and confounders for the outcomes. Three participants with unknown ethnicity were imputed as non-Hispanic based on the demographics of the sample. Inverse probability weighting based on the propensity score was used to adjust for exposure group differences within regression models. Weights were winsorized at the 1st and 99th percentiles for stability. Linear regression analyses were used to determine the differences in neurocognitive and psychosocial outcomes between the children with lupus nephritis and those with other gCKDs. Median regression was used to determine differences in HRQoL outcomes. Current prednisone use (yes/no) was included as a covariate and potential effect modifier.

To examine the relationship of HRQoL to the neurocognitive and psychosocial outcomes, we used a nonweighted linear regression model to assess the effect of a 10-point increase in HRQoL on the outcomes. Covariates included maternal education, eGFR, urine protein/creatinine ratio, and systolic blood pressure Z-score. Lupus nephritis status was included as a covariate and potential effect modifier. Inverse probability weights were not used for this analysis, because the primary interest was in the effect of HRQoL, which was assumed to be equal in the children with lupus nephritis and those with other gCKDs unless the interaction indicated otherwise.

We performed a sensitivity analysis comparing the lupus nephritis group with a subgroup of participants with other gCKDs that excluded those with the following systemic vascular glomerular diseases: chronic glomerulonephritis (n = 16), Henoch–Schönlein nephritis (n = 9), and idiopathic crescentic glomerulonephritis (n = 7). This was done to determine whether our findings may be related to overall systemic inflammation as opposed to specific effects of lupus nephritis.

All *P* values were 2-sided, at a significance level of .05. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina). No adjustment was made for multiple comparisons.

Results

We identified 34 participants with lupus nephritis and 171 participants with other gCKDs with baseline data for the inverse probability-weighted analysis. The specific diagnoses included in the other gCKD group are listed in Table I (available at www.jpeds.com). Compared with participants with other gCKDs, those with lupus nephritis had a shorter median duration of CKD (1.6 vs 4.0 years) and a higher rate of prednisone use (59% vs 23%). Additional demographic and disease characteristics are presented in Table II.

Neurocognitive Outcomes

In adjusted analyses, compared with the other gCKD group, the lupus nephritis group had better performance for attention on the CPT-II Detectability test ($\beta = -7.41$; $P < .01$) and better executive function on the D-KEFS Achievement test ($\beta = 1.66$; $P = .03$) (Table III). There were no differences for the other cognitive measures, and no significant interactions between current prednisone use and lupus nephritis. Current prednisone use was independently associated with worse attention on the CPT-II Detectability test ($\beta = 4.48$; $P = .01$) and showed a significant association with better achievement on the WIAT-II-A ($\beta = 8.62$; $P = .05$).

Psychosocial Outcomes

In adjusted analyses, there were no statistically significant differences between the lupus nephritis and other gCKD groups in overall behavioral symptoms, externalizing problems, internalizing problems, adaptive skills, or school problems on the parent-reported BASC-2 (Table IV). Current prednisone use was independently associated with better adaptive skills ($\beta = 3.43$; $P = .04$). There was a statistically significant interaction indicating worse parent-reported internalizing problems in the children with lupus nephritis receiving prednisone ($\beta = 10.18$; $P = .047$). There were no significant differences between the lupus nephritis and other gCKD groups in parent- or child-reported HRQoL measures.

Association of Neurocognitive Outcomes with HRQoL

The Figure displays the effects of HRQoL on neurocognitive and behavioral outcomes. To simplify the presentation, effects have been scaled to SD units for each instrument and oriented so that higher scores consistently indicate better performance. Better parent-reported overall HRQoL was associated with better executive function on the D-KEFS Achievement test ($\beta = 0.33$; $P = .03$) and better visual memory on the WISC-IV Spatial Span Forward test ($\beta = 0.56$; $P = .01$) (Figure). Better child-reported overall HRQoL was associated with better executive function on the BRIEF ($\beta = -2.23$; $P < .001$), better inhibitory control on the CPT-II Errors of Commission test ($\beta = -1.89$; $P < .01$), and better attention regulation on the CPT-II Detectability test ($\beta = -1.61$; $P < .01$). Compared with the other gCKD group, in the lupus nephritis group there was a statistically significant interaction indicating better executive function on the BRIEF with an equivalent parent-reported HRQoL score ($\beta = -2.47$; $P = .03$). There were no statistically significant interactions between child-reported HRQoL and lupus nephritis for the neurocognitive outcomes.

Association of Psychosocial Outcomes with HRQoL

Better parent-reported overall HRQoL was associated with less parent-reported overall behavioral symptoms ($\beta = -2.93$; $P < .001$), externalizing problems ($\beta = -1.58$; $P < .001$), and internalizing problems ($\beta = -3.44$; $P < .001$) and better adaptive skills ($\beta = 2.10$; $P < .001$). Better parent-reported HRQoL also was associated with fewer child-reported school problems ($\beta = -1.99$; $P < .01$) and internalizing problems ($\beta = -1.46$; $P < .01$) (Figure). Better child-reported overall HRQoL was associated with less parent-reported overall behavioral symptoms ($\beta = -2.14$; $P < .001$), internalizing problems ($\beta = -3.63$; $P < .001$), and adaptive skills ($\beta = 1.50$; $P < .01$) and fewer child-reported internalizing problems ($\beta = -2.36$; $P < .001$). There were no significant interactions between HRQoL and lupus nephritis for the psychosocial outcomes.

Sensitivity Analysis

In sensitivity analyses, compared with the gCKD ($n = 139$), the lupus nephritis group ($n = 34$) had higher intelligence scores on the WASI ($\beta = 9.43$; $P = .03$), higher executive function scores on the D-KEFS Achievement test ($\beta = 1.56$; $P = .03$), and better performance for attention/inhibitory control on the CPT-II Errors of Commission test ($\beta = -5.86$; $P < .001$) and Detect-ability test ($\beta = -7.97$; $P = .02$). There were no between-group differences for the other cognitive measures, and there were no significant interactions between current prednisone use and lupus nephritis. Current prednisone use was independently associated with better parent ratings of global executive function on the BRIEF ($\beta = -4.12$; $P = .05$), but worse inhibitory control and attention regulation on the CPT-II Errors of Commission test ($\beta = 4.70$; $P = .04$) and Detectability test ($\beta = 5.52$; $P = .008$).

Sensitivity analyses showed no statistically significant differences between the lupus nephritis and other gCKD groups in terms of psychosocial measures. Current prednisone use was not independently associated with the psychosocial measures; however, there was a statistically significant interaction indicating worse parent-reported internalizing problems in children with lupus nephritis on prednisone ($\beta = 13.64$; $P = .004$). There were no statistically significant differences in the HRQoL measures between the lupus nephritis and other gCKD groups. Current prednisone use was independently associated with decreased child-reported overall HRQoL ($\beta = -7.00$; $P = .04$).

Results of the sensitivity analysis did not differ for the associations of HRQoL with the neurocognitive or psychosocial outcomes, except for a statistically significant interaction indicating fewer parent-reported internalizing symptoms in the lupus nephritis group compared with the other gCKD group with an equivalent parent-reported HRQoL score ($\beta = 2.54$; $P = .02$).

Discussion

Although children with gCKD are known to be at risk for poor cognitive and psychosocial outcomes, there has been little study of potentially important differences among children with different etiologies of gCKD. This analysis provides results from a cross-sectional study of a large prospective cohort of children with CKD that showed comparable or better

cognitive and psychosocial functioning in children with lupus nephritis compared with those with other causes of gCKD. Our study also provides new insight into the relationship between HRQoL and specific domains of cognitive and psychosocial function in this population. Our findings may begin to inform differences in pathophysiology and intervention targets.

Contrary to our hypothesis, we found that neurocognitive outcomes in children with lupus nephritis were the same as or better than those of their counterparts with other causes of gCKD. Although we found differences in attention/inhibitory control (CPT-II Detectability test) and executive function (D-KEFS Achievement test) between the groups, they were quite subtle, approximating 0.5 SD in standardized T-score. Nevertheless, these findings held in our sensitivity analyses, which also indicated higher scores for intelligence and CPT-II Errors of Commission in the children with lupus nephritis. One explanation for our findings may be that children with lupus nephritis have a shorter disease duration compared with children with other causes of gCKD, resulting in less cumulative CNS effects and a lower psychosocial burden due to CKD. It is possible that over time, children with lupus nephritis may experience deteriorating cognitive functioning, although the difference between groups may persist. In addition, there may be a worse developmental impact due to the presence of a neurocognitive insult at an earlier age in children with other causes of gCKD compared with children with lupus nephritis, although this hypothesis has not been demonstrated in other CKiD studies.^{1,31} A third possible explanation is that children with lupus nephritis experience less CNS effects than children with other causes of gCKD due to greater use of immunosuppression, such as prednisone and other chemotherapeutic agents. In our cohort, prednisone use was greater in the lupus nephritis group and was independently associated with better executive function in sensitivity analyses; however, this effect was not present across cognitive domains, prednisone was associated with worse attention, and we had no data on past prednisone exposure. Finally, it is possible that the pathophysiology of lupus nephritis may portend less brain inflammation, given that lupus has heterogeneous clinical manifestations and likely heterogeneous pathophysiology. Counter to this theory, a post hoc analysis revealed that a history of seizures was more common in the lupus nephritis group (21% vs 13%).

Our study did not find differences in the psychosocial functioning of children with lupus nephritis compared with children with other causes of gCKD. Behavioral and HRQoL outcomes were similar in the 2 groups, despite the multiorgan effects of systemic lupus erythematosus and the higher burden of systemic medications in the lupus nephritis group. More than 70% of the children in the lupus nephritis group were being treated with corticosteroids, compared with 30% in the other gCKD group. This suggests that the reason for the similar performance is not similar disease treatment effects, and that despite intense treatment, children with lupus nephritis are maintaining appropriate psychosocial functioning and are not experiencing detriments to their quality of life. It is also possible that because most children with lupus nephritis are seen by caregivers from at least 2 subspecialties (nephrology and rheumatology), they are better supported from both a medical and psychosocial standpoint, allowing them to maintain a high level of functioning despite the challenges of living with a complex chronic disease.

Interestingly, we found associations between HRQoL and the domains of cognitive and psychosocial functioning. For cognitive outcomes, lower parent-reported HRQoL was associated with worse visual memory, but lower child-reported HRQoL was associated with worse executive function, including attention regulation and inhibitory control. For psychosocial symptoms, unsurprisingly, worse overall symptoms were associated with worse parent- and child-reported HRQoL, but only child-reported internalizing problems and adaptive skills were associated with worse HRQoL. These results support previous findings of differences between child-reported and parent-reported HRQoL,³² showing the different information obtained from the different perspectives. Our findings also indicate that factors affecting parent-reported HRQoL may differ among different gCKD etiologies. For similar parent-reported HRQoL, parents of the lupus nephritis group reported worse executive function but fewer internalizing problems and less adaptive dysfunction compared with parents of the other gCKD group. These findings merit further study given their implications for addressing HRQoL for different forms of CKD.

Our study has several limitations. First, the small sample size reduces our ability to detect small differences between the lupus nephritis and other gCKD groups. This is of particular concern in our attempts to determine the extent to which corticosteroid treatment may be either mitigating or exacerbating the effects of disease on functioning. Second, the study's cross-sectional design precludes the generation of conclusions about causality regarding associations between HRQoL and cognitive and psychosocial functioning. Third, although we adjusted for the duration of CKD, we were unable to adjust for the duration of the disease causing CKD, which may be longer for those 1 year of diagnosis in 85% of patients.¹⁰ Fourth, there may be selection bias if the children participating in CKiD are more likely to have better cognitive and psychosocial functioning than those choosing not to participate. However, we would expect this to be a nondifferential bias affecting generalizability, but not our comparison of lupus nephritis and other gCKDs. Finally, our results are from children with a median eGFR of ~ 60 mL/min/1.73 m² and might not be generalizable to children with poorer kidney function, who may have worse cognitive and psycho-social outcomes.^{1,33} Finally, when developing weights for our propensity scores, we used all 205 subjects. Because not all subjects are included in each model, these weights might not be valid if the missingness in the outcome is not independent of covariates in the weighting model.

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Glossary

BASC-2	Behavior Assessment of Childhood Disorders, Second Edition
BRIEF	Behavior Rating Inventory of Executive Function
CKD	Chronic kidney disease
CKiD	Chronic Kidney Disease in Children
CNS	Central nervous system
CPT-II	Conners' Continuous Performance Test, 2nd Edition
D-KEFS	Delis–Kaplan Executive Function System

eGFR	Estimated glomerular filtration rate
gCKD	Glomerular chronic kidney disease
HRQoL	Health-related quality of life
WASI	Wechsler Abbreviated Scales of Intelligence
WIAT-II-A	Wechsler Individual Achievement Test, Second Edition, Abbreviated
WISC-IV I	Wechsler Intelligence Scale for Children, Fourth Edition, Integrated

Figure.

Association of HRQoL with neurocognitive and behavioral outcomes among children with gCKD. The effect of HRQoL is shown in SDs of T-scores for neurocognitive and behavioral outcomes. Linear regression models were adjusted for eGFR, urine protein/creatinine ratio, systolic blood pressure Z-score, and maternal education. An interaction between lupus nephritis and HRQoL was significant only in the model for the effect of Parent Overall HRQoL on the Global Executive Composite.

Table I
Diagnoses of children with other gCKDs (n = 171)

Diagnoses	n (%)
Focal segmental glomerulosclerosis	74 (43)
Familial nephritis (Alport)	19 (11)
IgA nephropathy (Berger)	16 (9)
Chronic glomerulonephritis	16 (9)
Membranoproliferative glomerulonephritis type I	11 (7)
Henoch–Schonlein nephritis	9 (5)
Idiopathic crescentic nephritis	7 (4)
Other	7 (4)
Membranous nephropathy	4 (3)
Congenital nephrotic syndrome	4 (3)
Membranoproliferative glomerulonephritis type II	3 (2)
Sickle cell nephropathy	1 (<1)

Table II
Subject demographic and disease characteristics

Characteristics	Lupus nephritis, unweighted (n = 34)	Lupus nephritis, weighted	Other gCKD, weighted	Other gCKD, unweighted (n = 171)
Baseline age, y, median (IQR)	15.4 (12.2-16.6)	15.8 (13.3-16.1)	14.6 (12.4-16.0)	14.4 (11.9-15.9)
Male sex, n (%)	9 (26)	13.5 (46)	92.6 (54)	102 (60)
Height Z-score, median (IQR)	-0.06 (-0.75 to 0.86)	-0.50 (-1.59 to 0.59)	-0.19 (-1.03 to 0.47)	-0.25 (-1.06 to 0.51)
African-American race, n (%)	7 (21)	9.0 (31)	54.9 (32)	59 (35)
Hispanic ethnicity, n (%)	9 (26)	3.6 (12)	29.0 (17)	27 (16)
Maternal education, n (%)				
High school or less	15 (44)	17.2 (58)	85.1 (50)	87 (51)
Some college	8 (24)	5.8 (20)	33.4 (20)	32 (19)
College or more	11 (32)	6.5 (22)	52.4 (31)	52 (30)
eGFR, mL/min/1.73 m ² , median (IQR)	60.1 (49.3-80.0)	58.5 (43.1-72.1)	60.4 (43.3-77.3)	60.4 (42.2-77.3)
Urine P/C ratio, median (IQR)	0.58 (0.15-0.96)	0.86 (0.21-1.50)	0.87 (0.28-3.17)	0.95 (0.32-3.66)
Systolic BP Z-score, median (IQR)	0.14 (-1.05 to 1.03)	0.56 (-0.36 to 1.38)	0.24 (-0.41 to 1.15)	0.44 (-0.39 to 1.23)
Anemia, n (%)	14 (41)	12.4 (42)	69.5 (41)	70 (41)
Years with CKD, median (IQR)	1.5 (0.8-2.5)	1.6 (0.8-3.0)	3.9 (1.5-8.2)	4.0 (1.4-8.2)
Prednisone use, n (%)	20 (59)	21.0 (71)	40.7 (24)	39 (23)
Nephrotic proteinuria, n (%)	3 (9)	6.7 (23)	50.1 (29)	55 (32)
C-reactive protein	0.83 (0.30-3.18)	1.20 (0.30-2.60)	0.50 (0.30-1.95)	0.50 (0.30-1.95)

BP, systolic blood pressure; P/C, protein:creatinine.

Shown are the demographic and disease variables characterizing the unweighted and inverse-probability-weighted samples of patients with lupus nephritis and other gCKDs.

Table III
Neurocognitive outcomes for children with lupus nephritis vs other gCKDs

Neurocognitive outcomes	T-score, median (IQR)		Adjusted effect of lupus nephritis	
	Lupus nephritis (n = 34)	Other gCKD (n = 171)	Estimate (95% CI)	P value
Intelligence (WASI)	103 (90.5-114)	93.5 (83-104)	7.63 (−0.7 to 16.0)	.07
Academic achievement (WIAT-II-A)	100 (93-122)	89.5 (77-100)	8.29 (−3.1 to 19.6)	.15
Memory (WISC-IV)				
Digit span forward (verbal)	10 (5-11)	7 (5-10)	0.93 (−0.7 to 2.6)	.26
Digit span reverse (verbal working)	9 (8-11)	9 (7-11)	0.28 (−1.2 to 1.8)	.71
Spatial span forward (visual)	9.5 (8-11)	9 (7-11)	1.20 (−0.9 to 3.3)	.26
Spatial span reverse (visual working)	10.5 (8-12)	10 (7-12)	0.67 (−1.5 to 2.9)	.55
Attention/Inhibitory Control (CPT-II)				
Detectability	50 (42-55)	53 (45-58)	−7.41 (−11.8 to −3.0)	<.01
Response time variability	48 (41 -63)	50 (43-58)	−0.18 (−5.0 to 4.7)	.94
Errors of commission	48 (41-55)	49 (41-58)	−4.74 (−9.8 to 0.3)	.07
Executive Function				
BRIEF Global Executive Composite	46.5 (41-58)	53 (45-61)	−0.99 (−5.8 to 3.8)	.68
D-KEFS Achievement	10 (8-13)	9 (8-11)	1.66 (0.2 to 3.1)	.03
D-KEFS Accuracy Ratio	9 (8-10)	9 (7-11)	−0.52 (−2.1 to 1.0)	.50

Shown are actual standardized T-scores for the neurocognitive outcomes and estimates from the adjusted linear regression comparing children the outcomes for children with lupus nephritis to those with other gCKDs (reference group). Higher scores indicate better performance for the WASI, WIAT-II-A (mean, 100; SD, 15), WISC-IV, and D-KEFS (mean, 10; SD, 3). Lower scores indicate better performance for the CPT-II and BRIEF (mean, 50; SD, 10). Significant *P* values are in bold type.

Table IV
Psychosocial outcomes for children with lupus nephritis vs other gCKDs

Psychosocial outcomes	T-score, median (IQR)		Adjusted effect of lupus nephritis	
	Lupus nephritis (n = 34)	Other gCKD (n = 171)	Estimate (95% CI)	P value
Behavior (BASC-2)				
Overall behavioral symptoms	46.5 (42-54)	50 (44-57)	0.35 (−3.85 to 4.55)	.87
Externalizing problems	45.5 (43.5-53.5)	49 (43-55)	−1.06 (−5.11 to 3.00)	.61
Internalizing problems				
Parent-reported *	49 (44.5-60)	52 (45-59)	−4.29 (−12.11 to 3.52)	.28
Child-reported	48 (40-54)	46.5 (42-51)	0.59 (−4.69 to 5.87)	.82
School problems	46 (41-56)	47 (41-56)	5.08 (−2.68 to 12.85)	.20
Adaptive skills	50 (43.5-63)	47 (41-54)	0.44 (−3.88 to 4.77)	.84
HRQoL (PedsQL 4.0)				
Parent				
Overall	79 (67-90)	75 (60-87)	−1.00 (−13.42 to 11.42)	.87
Physical	78 (63-91)	81 (56-91)	−6.00 (−31.36 to 19.36)	.64
Emotional	80 (65-95)	80 (60-90)	0.00 (−12.14 to 12.14)	>.99
Social	90 (70-100)	80 (60-100)	10.00 (−15.56 to 35.56)	.44
School	80 (55-90)	65 (45-80)	10.00 (−11.97 to 31.97)	.37
Child				
Overall	75 (66-90)	79 (65-87)	−4.00 (−14.67 to 6.67)	.46
Physical	88 (69-94)	81 (71-94)	3.00 (−11.84 to 17.84)	.69
Emotional	75 (60-90)	80 (60-90)	5.00 (−7.29 to 17.29)	.42
Social	90 (65-100)	90 (75-100)	0.00 (−13.68 to 13.68)	>.99
School	70 (50-80)	65 (50-80)	5.00 (−8.80 to 18.80)	.48

Shown are actual standardized T-scores for the psychosocial outcomes. Linear regression models compared behavioral outcomes and median regression compared HRQoL between children with lupus nephritis and those with other gCKDs (reference group), adjusting for prednisone use.

* Significant interaction with prednisone use; interaction estimate, 10.2 (0.1-20.2); $P = .047$.