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A Longitudinal Examination of Parent-Reported Emotional-Behavioral Functioning of Children with Mild to Moderate Chronic Kidney Disease

Rebecca J. Johnson, PhD[1], **Arlene C. Gerson, PhD**[2], **Lyndsay A. Harshman, MD**[3], **Matthew B. Matheson**[4], **Shlomo Shinnar, MD, PhD**[5], **Marc B. Lande, MD, MPH**[6], **Amy Kogon, MD, MPH**[7], **Debbie S. Gipson, MD**[8], **Bradley A. Warady, MD**[1], **Susan L. Furth, MD, PhD**[7], **Stephen R. Hooper, PhD**[9]

[1]Children's Mercy Kansas City, University of Missouri – Kansas City School of Medicine, Kansas City, MO

[2]Johns Hopkins Medical Institute, Baltimore, MD

[3]University of Iowa Stead Family Children's Hospital, Iowa City, IA

[4]Johns Hopkins School of Public Health, Baltimore, MD

[5]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY

[6]University of Rochester Medical Center, Rochester, NY

[7]Children's Hospital of Philadelphia, Philadelphia, PA

[8]University of Michigan School of Medicine, Ann Arbor, MI

[9]School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

Abstract

Background: Children with mild to moderate chronic kidney disease (CKD) are at increased risk for deficits in neurocognition. Less is known about how CKD affects emotional-behavioral functioning in this population.

Methods: Parent ratings of emotional-behavioral functioning at baseline and over time were examined for 845 children with mild to moderate CKD using the Behavior Assessment System for Children, Second Edition Parent Rating Scales (BASC-2 PRS). Associations with demographic and disease-related predictors were also examined.

Results: Children with mild to moderate CKD had parent-reported emotional-behavioral functioning largely within normal limits, at baseline and over time. The proportion with T-scores at least 1 SD above the mean was 24% for Internalizing Problems and 28% for Attention Problems. A greater proportion of participants scored lower than expected (worse) on scales measuring adaptive skills (25%). Persistent hypertension predicted attention problems (β = 1.59,

Corresponding Author: Rebecca J. Johnson, Division of Developmental and Behavioral Health, Children's Mercy Kansas City 2401 Gillham Road, Kansas City, MO 64113, rejohnson@cmh.edu.

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95% CI = 0.24 to 2.94, $p<.02$) and suggested worse behavioral symptoms (β = 1.36, 95% CI = −0.01 to 2.73, $p = .05$). Participants with proteinuria at baseline, but not at follow-up, had fewer attention problems than participants whose proteinuria had not resolved (β = −3.48, CI = −6.79 to −0.17, $p<.04$). Glomerular diagnosis was related to fewer (β = −2.68, 95% CI = −4.93 to −0.42, $p<.02$) internalizing problems.

Conclusions: Although children with CKD generally have average emotional-behavioral parent ratings, a notable percentage of the population may be at risk for problems with attention and adaptive behavior. Providers working with this population should facilitate psychosocial referrals when indicated.

Keywords

pediatric chronic kidney disease; CKD; CKiD; emotional-behavioral; adaptive behavior; BASC-2

Chronic kidney disease (CKD) is a progressive disease that can have a significant impact on children's health and well-being. CKD, particularly in its more advanced stages, has been shown to negatively impact physical functioning, neurocognitive development and performance, and emotional and behavioral health [1–3]. Children with CKD also report poorer quality of life [2], problems with academic achievement [4–8], and poorer vocational outcomes [9–10].

The Chronic Kidney Disease in Children (CKiD) prospective cohort study is the largest study of pediatric CKD to date. Findings from the CKiD study indicate that children with even mild to moderate CKD are at increased risk of neurocognitive dysfunction, particularly in the domain of attention regulation [7,11]. Children with advanced CKD also have higher rates of emotional-behavioral symptoms and psychopathology compared to healthy controls [12–14]. Moreira et al. [3] compared children with pre-dialysis CKD to healthy, matched controls. Children with CKD were more likely to report symptoms of anxiety and depression, which in turn were negatively associated with quality of life. Kogon et al. [15] found a rate of clinically significant depressive symptoms in 30% of their sample of children with CKD stages III-V.

We hypothesized that a greater proportion of children than expected would place in the at risk range for emotional-behavioral symptoms. We also hypothesized that renal function (estimated glomerular filtration rate [eGFR]) would be significantly associated with parent-report of emotional-behavioral functioning (internalizing symptoms, externalizing symptoms, and adaptive functioning), with parent-reported symptoms negatively correlated with eGFR. We also hypothesized that CKD progression would be associated with increased parent report of emotional-behavioral symptoms for their children.

With regard to specific comorbidities of CKD, and consistent with available literature [16–17], we hypothesized that hypertension would be associated with increased parent-reported attention problems as measured by the Attention Problems subscale. In addition, very little is known about the natural progression of emotional functioning as children progress to ESRD. Earlier work by CKiD investigators indicates that only about 5% of children with mild to moderate CKD self-report elevated depressive symptoms [18], but we know that by the time

children reach end stage renal disease, a much higher proportion report depressive symptoms [13, 19–21]. Thus, we hypothesized that depressive symptoms would be associated with declining renal function in longitudinal analyses.

The aims of the current study were: 1) to describe parent-reported emotional-behavioral functioning of children with CKD at baseline, including the percent "at risk" for deficits in emotional-behavioral functioning compared to normative data; and 2) to examine emotional-behavioral functioning longitudinally as CKD progresses and determine which, if any, disease-related variables are associated with changes in emotional-behavioral functioning. This is the largest study to date to examine emotional-behavioral functioning of children with mild to moderate CKD, and the first to do so longitudinally.

Method

Participants

Participants were 845 children, 2–18 years of age at baseline, enrolled in the CKiD prospective, observational cohort study [22], which recruits from approximately 50 sites across North America. The CKiD study is funded by the National Institutes of Health to study mild to moderate CKD (estimated glomerular filtration rate [eGFR] of 30–90 ml/min/1.73m^2 at time of study enrollment). Exclusion criteria included a history of solid organ, bone marrow, or stem cell transplant; cancer/leukemia; and HIV. Children with central nervous system dysfunction related to genetic syndromes and those with intellectual disabilities were also excluded. CKiD participants have detailed assessment of renal function [23] in addition to assessment of complications of CKD progression, including, but not limited to: anemia, proteinuria, and hypertension.

Measures

As part of the CKiD study, parents were asked to complete the Behavior Assessment System for Children, Second Edition, Parent Report Scale (BASC-2 PRS) every two years, over a span of up to 10 years. The BASC-2 PRS is a norm-referenced, psychometrically sound, comprehensive assessment of behavior and emotions in children [24]. Parents are asked to rate the frequency with which a child has experienced a symptom or behavior in the previous month using a four-point Likert scale (never, sometimes, often, almost always). These ratings result in standardized age-based T-scores for nine clinical scales, five scales of adaptive behavior (e.g., social skills, communication skills), and four composite scales. Composite scores include Internalizing Problems (calculated from Anxiety, Depression, and Somatization scales), Externalizing Problems (calculated from Hyperactivity, Aggression, and Conduct Problems scales), and Adaptive Skills (calculated from Adaptability, Social Skills, Leadership, Functional Communication, and Activities of Daily Living). A Behavioral Symptoms Index (BSI) T-score is also calculated and serves as a measure of overall behavioral and emotional problem severity.

Procedure

The BASC-2 PRS is administered as part of CKiD at study entry and every 2 years thereafter (i.e., years 3, 5, 7, 9, 11 of the study), the same time points at which the neurocognitive

battery is administered. BASC-2 results were available for a total of 845 participants. For 148 participants, we had BASC-2 PRS data from a single time point; for 280 from two time points; the remaining 417 participants had between three and six time points. Twenty-nine participants had follow-up covering a period of ten years.

The CKiD protocol received approval by the Institutional Review Board at each center. Parents or legal guardians provided informed consent for children's participation. Assent from child participants was obtained.

Statistical analyses

Descriptive statistics at baseline (defined for this analysis as the first visit with BASC-2 results available) were calculated to describe BASC-2 data and demographic information for children whose parents completed the BASC-2. To address the primary research questions, linear mixed models were utilized to estimate participant scores on the Behavioral Symptoms Index (BSI), and for Internalizing Problems, Externalizing Problems, and Adaptive Skills, as well as two key clinical scales (Depression and Attention Problems) longitudinally. All BASC-2 PRS data was included (i.e., between one and six records per subject); models included random intercept and slope at the subject level, with unstructured covariance. Models were adjusted for demographic and medical covariates including baseline age, time on study, sex, race (African-American or non-African-American); ethnicity (Hispanic or non-Hispanic); maternal education (high school or less, some college, college or more); household income (above or below $36,000 per year); baseline full scale intelligence quotient (FSIQ); history of low birth weight or designation as small for gestational age (LBW/SGA); history of seizures; years since onset of CKD; glomerular vs. non-glomerular diagnosis; baseline renal function (eGFR estimated using the 2012 CKiD equation [23]; ; change in renal function (current minus baseline); nephrotic range proteinuria (urine protein/creatinine>2); anemia (hemoglobin < 5^{th} percentile or current use of erythropoiesis-stimulating agent); and hypertension (systolic blood pressure or diastolic blood pressure ≥ 90^{th} percentile OR self-reported hypertension plus current anti-hypertension medication use).

Proteinuria, anemia, and hypertension were each included as three different variables, calculated using each participant's first available and most recent time points: persistent (present at both baseline and follow-up, relative to absent at baseline and follow-up); acquired (absent at baseline, present at follow-up, relative to absent at baseline and follow-up); and resolved (present at baseline, absent at follow-up, relative to present at baseline and follow-up). As this was the first longitudinal examination of BASC-2 data in this cohort, the models should be considered exploratory, with all covariates being understood as potential predictors of behavioral functioning.

Results

Sample Characteristics

Table 1 presents descriptive statistics for participant demographic characteristics and disease-related variables from the first study visit at which BASC-2 data were available for

each participant (n = 845). The median baseline age was 11.8 years (interquartile range [IQR] 8.2, 15.2). Sixty-one percent were male, 22% were African-American, and 14% reported Hispanic ethnicity. The median Full Scale IQ (FSIQ) score of the sample at baseline was 97 (IQR 85, 107), which is in the average range of functioning. With regard to maternal education, 28% of mothers reported attending some college and 33% of mothers reported having at least a college degree. Household income was greater than $36,000/year for 60% of families.

The median eGFR of the sample was 52 ml/min/1.73m^2 (IQR 39, 66) and the median time since diagnosis was 8.6 years (IQR 4.1, 12.7). Thirty percent of the sample had glomerular disease. Nephrotic range proteinuria was present for 13% of the sample. Anemia and hypertension were present in 33% and 55%, respectively. More than one-fourth had a history of low birth weight or small for gestational age status (27%), and 12% reported a history of seizures.

Baseline Assessment (Aim 1)

Composite scores.—For BASC-2 clinical composite scores, T-scores below 60 are considered average; T-scores 60–69 are in the at-risk range; and those 70 and higher are considered clinically significant. At baseline, the median BASC-2 composite scores placed in the average range (Externalizing Problems 49 [IQR 43, 56]; Internalizing Problems 51 [IQR 45, 59]; Behavioral Symptoms Index (BSI) 50 [IQR 44, 57]). For the Adaptive Skills composite, scores above 40 are considered average, scores 31–40 are considered at-risk, and scores 30 and below are considered clinically significant. At study entry, the median score on the Adaptive Skills composite placed in the average range (47 [IQR 40, 54]; see Table 2).

The proportion of participants with BASC-2 composite scores 1 SD or more above the mean (i.e., more dysfunction) was 24% for Internalizing Problems, 15% for Externalizing Problems, and 19% for the BSI. For Adaptive Skills, 25% scored greater than 1 SD below the mean (indicating poorer adaptive skills). We would expect approximately 16% to score 1 SD or more above or below the mean in a normal distribution.

Clinical scales.—For the clinical scales, higher scores indicate greater parent-reported problems or dysfunction. At baseline, median scores for all of the clinical scales placed in the average range (see Table 2). The proportion scoring greater than 1 SD above the mean was about what might be expected in a population of healthy children for the majority of clinical scales (see Table 2); however, there were higher than expected ratings on the somatization and attention problems scales (32% and 28% of the sample, respectively, scoring 1 SD or more above the mean).

Adaptive scales.—For the adaptive scales, lower scores represent poorer adaptive functioning. At baseline, all median scores for the adaptive scales were in the average range (see Table 2). For these scales, the percentage of participants with parent ratings 1 SD or more below the mean were 21% (Adaptability), 24% (Social Skills), 26% (Leadership), 31% (Activities of Daily Living), and 27% (Functional Communication).

Longitudinal Assessment (Aim 2)

Linear mixed models were used to examine emotional-behavioral functioning over time (Table 3). Outcome variables included the four BASC-2 composite scores (Internalizing Problems, Externalizing Problems, Behavioral Symptoms Index, Adaptive Skills) as well as two clinical scales (Attention Problems and Depression, seen in Table 4).

Composite scores.—All composite scores were significantly associated with time on study, such that parent ratings improved over the course of the study (see Table 3). Higher baseline FSIQ and household income greater than $36,000/year were associated with better scores on all composite variables, indicating that higher IQ and income were associated with better adaptive behavior and fewer externalizing and internalizing problems. Being male was related to higher (worse) scores on the BSI (β = 1.42, $p<0.04$) and Externalizing Problems composite (β = 2.43, $p<0.0003$); lower (worse) scores on Adaptive Skills (β = −3.27, $p<0.0001$); and lower (better) scores on the Internalizing Problems composite scale (β = −2.99, $p<0.0001$). Hispanic ethnicity was associated with lower (better) scores on the BSI (β = −1.99, $p<0.05$).

With regard to disease-related variables, glomerular diagnosis was associated with lower (better) scores on Internalizing Problems (β = −2.68, $p<0.02$); history of seizures was associated with higher (worse) scores on Internalizing Problems (β = 2.18, $p<0.03$). Persistent HTN was associated with higher (worse) scores on the BSI (β = 1.36, $p = 0.05$). Change in eGFR was not related to any of the composite scores.

Depression scale.—On the Depression scale, household income and baseline IQ were associated with depressive symptoms: both higher income (β = −2.96, CI [−4.48, −1.44] $p<0.0002$) and higher baseline IQ (β = −0.36, CI [−0.59, −0.14] $p<0.002$) predicted fewer depressive symptoms. Time on study was also associated with lower scores on the depression scale ((β = −0.41, CI [−0.64, −0.18] $p<0.0004$).

Attention problems.—In the longitudinal model, several variables were significantly associated with parent-reported attention problems. Resolution of proteinuria was negatively associated with attention problems, indicating that for participants with proteinuria at baseline that had since resolved, fewer problems associated with attention were reported compared to those whose proteinuria had not resolved (β = −3.48, CI [−6.79, −0.17] $p<0.04$). Persistent hypertension (present at baseline and follow-up) was associated with more attention problems (β = 1.59, CI [0.24, 2.94] $p<0.02$), indicating that those with persistent hypertension had more parent-reported attention problems than those who had never had HTN.

Parents reported more symptoms of inattention for boys versus girls (β = 3.81, CI [2.44, 5.17] $p<0.0001$). Hispanic ethnicity (β = −2.31, CI [−4.26, −0.36] $p<0.0001$), higher household income (β = −2.13, CI [−3.68, −0.57] $p<0.007$), and higher baseline IQ (β = −0.84, CI [−1.07, −0.61] $p<0.0001$) were all associated with fewer attention problems. Longer time on study was associated with ratings of fewer attention problems, (β = −0.37, CI [−0.67, −0.07] $p<0.02$).

Discussion

This study represents the largest evaluation to date of the longitudinal emotional-behavioral functioning of children with mild to moderate CKD. The results are reassuring in that, by and large, children with mild to moderate CKD have normal parent-reported emotional-behavioral functioning both at baseline and over time. Overall, parent ratings improved over the course of the study. We hypothesize this is related to a low baseline level of emotional-behavioral problems from the study outset in this population of mildly affected children. Looking at the pediatric literature more broadly, few studies have examined emotional-behavioral functioning in children with chronic health conditions longitudinally. More commonly, measures of health-related quality of life are used, including ratings of emotional functioning, and suggest that decline in emotional health may be related to gender, comorbidities, or side effects of treatment [25–26].

While the findings from our study are reassuring overall, at baseline we did uncover a higher proportion of children than expected to be more than one standard deviation above or below the mean on several of the ratings, suggesting that children with mild to moderate CKD are at greater risk than healthy children for specific emotional-behavioral problems and poorer development of adaptive skills. These findings are consistent with another study that compared children with CKD to a healthy control group using the BASC and found “at risk” rates of 12–24% for children with CKD, compared to 0–9% in the healthy group [12]. Our findings are also in line with a recent meta-analysis examining symptoms of anxiety and depression among youth with a range of life-limiting health conditions which concluded that the prevalence of anxious and depressive symptoms among children with chronic conditions is higher than the general population and warrants psychological assessment and monitoring [27].

Our findings also suggest that this population of children is at increased risk for problems with adaptive skills. At baseline, the percent at risk was greater than expected on all five adaptive scales and included nearly a third of the sample for subscales examining leadership skills, activities of daily living, and functional communication. This may reflect the impact of CKD on overall health and functioning, as these children may have less energy, miss more school, or participate in fewer extra-curricular activities; or the impact of the disease on neurocognitive skills, which may be prerequisites for or promote development of adaptive skills.

We hypothesized that disease-related variables would be associated with attention problems. For children with mild to moderate CKD, higher blood pressure and greater blood pressure variability have been associated with poorer performance on neurocognitive measures of attention [16–17, 28]. Evaluations of children with advanced CKD show similar findings, with earlier disease onset, elevated blood pressure, and more severe disease associated with more extensive neurocognitive deficits [8, 12, 29–31]. Consistent with this literature, children enrolled in the CKiD study do appear to be at increased risk for attention problems, with 28% of the sample receiving parent-rated scores on the Attention Problems scale that were 1 SD or greater above the mean at baseline. Persistent hypertension was associated with worse scores on the Attention Problems scale in longitudinal analyses. In addition to

hypertension, children with persistent proteinuria (compared to those with resolved proteinuria) had more parent-reported attention problems in the longitudinal model. These findings bolster the conclusion that comorbidities associated with CKD place children at risk for difficulty with attention regulation. Notably both hypertension and proteinuria have been associated with increased systemic inflammation, a factor potentially associated with vascular injury, suggesting one possible mechanistic link to altered cognitive function [32–33]. Long-standing proteinuria is a risk factor for progression of renal disease [34]; thus, clinicians often utilize angiotensin converting enzyme inhibitors (ACE-I) for anti-proteinuric effect. These agents are widely used in the treatment of pediatric hypertension. We considered it plausible, then, that children with proteinuria at baseline may have been prescribed ACE-inhibitors, which may have led to both improved proteinuria and blood pressure control, with a potential favorable impact of improved attention. Furthermore, centrally active ACE inhibitors may be associated with decreased cognitive decline in the elderly, suggesting a possible direct neuroprotective effect [35]. We examined our data and found 27 patients whose proteinuria resolved. Of those, 22% (n = 6) resolved after initiation of ACE-inhibitor. This finding is far from clear and deserves additional study.

In addition to the above findings, a number of other disease-related and demographic variables were related to BASC-2 scores. In longitudinal analyses, glomerular diagnosis was associated with better scores on the Internalizing Problems composite measure, possibly due to the later onset of glomerular disease and thus shorter disease course at study entry. History of seizures was related to more parent-reported internalizing symptoms. The study collected data on history of seizure, not epilepsy diagnosis; with that caveat in mind, the finding that those with seizure history have more internalizing symptoms is consistent with the pediatric epilepsy literature, which suggests increased risk of depression and anxiety for patients with epilepsy diagnosis [36–37]. Baseline IQ, family income, and maternal education were all protective factors, as was Hispanic ethnicity, for parent-reported attention problems. Not unexpectedly, parents rated boys as having more externalizing and fewer internalizing problems than girls.

This study has a number of limitations. Because this was the first longitudinal examination of emotional-behavioral functioning in this cohort, and we included a large number of predictors, our models should be considered exploratory and our results require replication. It is also important to note that literature regarding hypothesized mechanisms for the relationship between CKD and emotional-behavioral symptoms is lacking. It seems likely that both direct and indirect relationships exist between renal function and emotional-behavioral problems. Indirect effects may include the emotional burden of managing a chronic illness and its necessary medical and physical demands; its effects on caregiver and family functioning; comorbidities such as short stature; and the additional burden of neurocognitive difficulties. Direct links are more speculative in nature; biological factors inherent to progressive CKD, even at the mild to moderate levels of severity, likely also disrupt endocrine and neurological transmitters to influence mood and emotional functioning and may promote behavioral dysregulation. Future research should develop hypotheses and test potential mechanisms for the relationship between renal function and emotional-behavioral symptoms. Another limitation pertains to including only one measure of emotional-behavioral functioning. While many parent rating scales, including the BASC,

are well-validated, psychometrically sound measures of children's emotional-behavioral symptoms and are widely used in clinical practice, including structured interviews or child self-report would have produced a broader perspective. In addition, there is evidence that parents of children with CKD experience higher than normal rates of stress and fatigue, and are at risk for problems with adjustment [38–39], and we cannot account for the influence of possible parental psychopathology or stress-related dysfunction on parents' perceptions of their children's emotional and behavioral functioning. Interestingly, parent report has been found to be associated with both lower reported prevalence (anxiety) and higher reported prevalence (depression) of emotional-behavioral symptoms compared to diagnostic interview [27]. Lastly, this sample includes data from children with only mild to moderate CKD and, as per study protocol, did not follow children into renal replacement therapy. Certainly, there is a distinct need to follow children into the renal replacement phase of treatment to obtain a full picture of the trajectory of social and emotional-behavioral functioning in this population, and the recent continuation of the CKiD Study will permit such an examination in the future.

These results, in the context of other available investigations, suggest that although children with CKD generally have average emotional-behavioral parent ratings, there is a notable percentage of the population who may be at risk for problems with attention and adaptive behavior. These findings should encourage providers working with pediatric patients who have CKD to facilitate prompt, appropriate referrals for additional psychosocial assessment and evidence-based treatment when indicated. Future research should work toward better identification of when and how to screen children with CKD for emotional-behavioral disturbance, including development of evidence-based clinical guidelines for psychologists and nephrologists to use for the psychosocial care of their patients.

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Table 1.

Descriptive statistics for participant demographic characteristics and disease-related variables (n = 845).

Sample Characteristic	n (%) or median [IQR]
Baseline age in years	11.8 [8.2, 15.2]
Male Gender	519 (61%)
African-American race	187 (22%)
Hispanic ethnicity	120 (14%)
Maternal Education:	
High School or less	327 (40%)
Some College	228 (28%)
College or more	271 (33%)
Household income >$36K/year	497 (60%)
Full Scale IQ	97 [85, 107]
Glomerular Diagnosis	257 (30%)
Years since CKD onset	8.6 [4.1, 12.7]
eGFR	52 [39, 66]
Nephrotic Proteinuria	103 (13%)
HTN[a]	466 (55%)
Anemia[b]	273 (33%)
LBW or SGA	216 (27%)
Presence of Seizures[c]	100 (12%)

CKD Chronic kidney disease*; GFR* glomerular filtration rate*; HTN* Hypertension; *IQ* Intelligence Quotient*; LBW* low birth weight*; SGA* small for gestational age.

[a]HTN was defined as current systolic or diastolic blood pressure ≥90th percentile for age, sex, and height; OR self-reported HTN and current use of anti-hypertension medication.

[b]Hemoglobin <5th percentile for age and gender or taking an erythropoiesis-stimulating agent.

[c]Parent-reported history of seizures.

Table 2.

Median BASC-2 PRS *T*-scores, interquartile ranges, and percentage of participants with scores in the at-risk range from first visit with BASC ratings.

BASC-2 Composite Measures	Median[a] [IQR]	n (%) At-risk[b]
Behavioral Symptoms Index	50 [44, 57]	159 (19%)
Externalizing Problems	49 [43, 56]	124 (15%)
Internalizing Problems	51 [45, 59]	198 (24%)
Adaptive Skills	47 [40, 54]	212 (25%)
BASC 2 Clinical Scales		
Hyperactivity	50 [44, 57]	156 (19%)
Aggression	48 [43, 55]	125 (15%)
Conduct Problems	48 [42, 56]	91 (13%)
Anxiety	49 [42, 56]	149 (18%)
Depression	49 [43, 56]	154 (18%)
Somatization	53 [46, 63]	272 (32%)
Atypicality	49 [44, 57]	168 (20%)
Withdrawal	49 [42, 56]	160 (19%)
Attention Problems	53 [45, 60]	237 (28%)
BASC 2 Adaptive Scales		
Adaptability	49 [42, 57]	178 (21%)
Social Skills	48 [41, 56]	204 (24%)
Leadership	49 [40, 55]	184 (26%)
Activities of Daily Living	45 [39, 52]	259 (31%)
Functional Communication	48 [40, 55]	226 (27%)

BASC-2 PRS Behavior Assessment System for Children, Second Edition, Parent Report Scales.

[a] *T* scores have $M = 50$, $SD = 10$.

[b] At-risk is defined as a score ≥1 standard deviation above the mean (Behavioral Symptoms Index, Externalizing Problems, and Internalizing Problems composite scores and clinical scales) or ≥1 standard deviation below the mean (Adaptive Skills composite and adaptive scales).

Table 3.

Results of linear mixed models predicting CKiD participants' scores on the BASC-2 PRS composite scores.

	Behavioral Symptoms Index (n = 1643)			Externalizing Problems (n = 1644)			Internalizing Problems (n = 1641)			Adaptive Skills (n = 1640)		
Predictor	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**
Baseline Age	−0.14	−0.36, 0.09	0.23	−0.22	−0.43, −0.01	0.04*	0.13	−0.11, 0.36	0.28	0.24	0.02, 0.47	0.03*
Male	1.42	0.04, 2.80	0.04*	2.43	1.11, 3.75	0.0003**	−2.99	−4.44, −1.54	<0.0001**	−3.27	−4.69, −1.86	<0.0001**
African-American	−0.51	−2.26, 1.23	0.56	−0.40	−2.06, 1.27	0.64	−0.29	−2.13, 1.54	0.75	1.22	−0.57, 3.00	0.18
Hispanic Ethnicity	−1.99	−3.97, −0.01	0.049*	−1.46	−3.34, 0.43	0.13	−1.09	−3.16, 0.99	0.30	1.49	−0.53, 3.52	0.15
Maternal Education												
Some college	1.22	−0.48, 2.92	0.16	0.12	−1.5, 1.74	0.88	0.87	−0.91, 2.65	0.34	0.59	−1.16, 2.34	0.51
College or more	−0.34	−2.12, 1.44	0.71	−0.98	−2.68, 0.71	0.26	−0.64	−2.51, 1.22	0.50	1.02	−0.81, 2.84	0.27
Household Income >$36K/year	−3.20	−4.78, −1.62	0.0001**	−1.90	−3.41, −0.40	0.01*	−2.43	−4.08, −0.78	0.004**	2.58	0.97, 4.20	0.00182**
Baseline FSIQ, per 5	−0.67	−0.90, −0.44	<0.0001**	−0.38	−0.60, −0.16	0.0008**	−0.41	−0.65, −0.17	0.001**	1.03	0.79, 1.27	<0.0001**
Glomerular Diagnosis	−0.80	−2.94, 1.34	0.46	0.25	−1.79, 2.28	0.81	−2.68	−4.93, −0.42	0.02*	0.00	−2.17, 2.18	>0.99
Time on Study	−0.44	−0.64, −0.24	<0.0001**	−0.31	−0.50, −0.13	0.001**	−0.51	−0.75, −0.27	<0.0001**	0.54	0.30, 0.78	<0.0001**
Baseline Duration with CKD	0.01	−0.20, 0.21	0.94	0.06	−0.14, 0.25	0.57	−0.19	−0.41, 0.03	0.08	−0.09	−0.3, 0.12	0.39
Baseline eGFR	−0.11	−0.51, 0.30	0.60	−0.30	−0.69, 0.08	0.12	−0.01	−0.44, 0.41	0.95	0.14	−0.26, 0.55	0.49
Change in eGFR	0.16	−0.31, 0.63	0.50	0.30	−0.14, 0.74	0.18	0.31	−0.23, 0.86	0.26	−0.03	−0.56, 0.49	0.90
LBW/SGA	−0.19	−1.70, 1.32	0.81	−0.81	−2.25, 0.63	0.27	−0.76	−2.34, 0.82	0.35	0.02	−1.52, 1.57	0.98
Seizures	0.49	−1.19, 2.16	0.57	0.49	−1.09, 2.06	0.54	2.18	0.25, 4.11	0.03*	−0.01	−1.74, 1.71	0.99
Proteinuria												
Persistent (vs. absent)	−0.77	−3.04, 1.50	0.51	−1.55	−3.72, 0.63	0.16	0.78	−1.64, 3.20	0.53	0.31	−1.95, 2.57	0.79
Acquired (vs. absent)	−0.33	−2.16, 1.50	0.73	−0.78	−2.49, 0.92	0.37	0.50	−1.64, 2.64	0.65	−1.11	−3.14, 0.91	0.28

	Behavioral Symptoms Index (n = 1643)			Externalizing Problems (n = 1644)			Internalizing Problems (n = 1641)			Adaptive Skills (n = 1640)		
Predictor	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**
Resolved (vs. persistent)	−0.02	−3.03, 2.98	0.99	−0.79	−3.60, 2.03	0.58	−1.04	−4.54, 2.45	0.56	0.67	−2.58, 3.93	0.68
Anemia												
Persistent (vs. absent)	0.19	−1.42, 1.81	0.82	0.43	−1.11, 1.96	0.59	0.80	−0.91, 2.51	0.36	−0.38	−2.01, 1.25	0.65
Acquired (vs. absent)	−0.86	−2.25, 0.52	0.22	−0.43	−1.73, 0.86	0.51	−0.84	−2.46, 0.79	0.31	0.42	−1.12, 1.95	0.59
Resolved (vs. persistent)	0.02	−1.77, 1.81	0.98	0.23	−1.44, 1.90	0.78	−0.71	−2.79, 1.37	0.50	0.94	−1.00, 2.88	0.34
HTN												
Persistent (vs. absent)	1.36	−0.01, 2.73	0.051	1.08	−0.23, 2.38	0.11	1.04	−0.41, 2.48	0.16	−0.95	−2.33, 0.44	0.18
Acquired (vs. absent)	0.05	−1.36, 1.47	0.94	−0.27	−1.59, 1.05	0.69	−0.41	−2.05, 1.23	0.62	−0.24	−1.82, 1.34	0.77
Resolved (vs. persistent)	−0.14	−1.50, 1.23	0.84	0.52	−0.76, 1.79	0.43	−0.44	−2.03, 1.15	0.59	0.23	−1.26, 1.73	0.76

BASC-2PRS Behavior Assessment System for Children, Second Edition, Parent Rating Scales; CKD Chronic kidney disease*; CKiD* Chronic Kidney Disease in Children cohort study; *GFR* glomerular filtration rate*; HTN* Hypertension; *FSIQ* Full-scale intelligence quotient*; LBW* low birth weight*; SGA* small for gestational age.

* p<.05

** p<.01.

Table 4.

Results of linear mixed models predicting CKiD participants' scores on selected BASC-2 PRS clinical scales.

	Depression (n = 1646)			Attention Problems (n = 1650)		
Predictor	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**
Baseline Age	0.06	−0.15, 0.28	0.57	−0.18	−0.40, 0.04	0.11
Male	−1.16	−2.50, 0.18	0.09	3.81	2.44, 5.17	<0.0001 **
African-American	−0.77	−2.46, 0.92	0.37	−0.47	−2.19, 1.25	0.59
Hispanic Ethnicity	−0.85	−2.77, 1.07	0.38	−2.31	−4.26, −0.36	0.02 *
Maternal Education						
Some college	0.80	−0.84, 2.44	0.34	0.93	−0.74, 2.61	0.27
College or more	−0.32	−2.04, 1.40	0.72	−0.01	−1.76, 1.75	0.99
Household Income >$36K/year	−2.96	−4.48, −1.44	0.0001 **	−2.13	−3.68, −0.57	0.007 **
Baseline FSIQ, per 5	−0.36	−0.59, −0.14	0.002 **	−0.84	−1.07, −0.61	<0.0001 **
Glomerular Diagnosis	−1.90	−3.98, 0.19	0.08	−0.73	−2.83, 1.37	0.49
Time on Study	−0.41	−0.64, −0.18	0.0004 **	−0.32	−0.54, −0.09	0.006 **
Baseline Duration with CKD	−0.15	−0.35, 0.05	0.14	0.05	−0.15, 0.25	0.63
Baseline eGFR	−0.04	−0.44, 0.35	0.84	−0.01	−0.40, 0.39	0.98
Change in eGFR	0.32	−0.19, 0.82	0.22	−0.06	−0.58, 0.46	0.82
LBW/SGA	−0.62	−2.09, 0.84	0.40	1.31	−0.17, 2.80	0.08
Seizures	0.95	−0.88, 2.77	0.31	−0.02	−1.80, 1.77	0.98
Proteinuria						
Persistent (vs. absent)	−1.03	−3.28, 1.23	0.37	0.67	−1.57, 2.91	0.56
Acquired (vs. absent)	0.73	−1.27, 2.74	0.47	0.29	−1.74, 2.32	0.78

	Depression (n = 1646)			Attention Problems (n = 1650)		
Predictor	**Est.**	**CI (95%)**	**p**	**Est.**	**CI (95%)**	**p**
Resolved (vs. persistent)	0.28	−3.00, 3.56	0.87	−3.48	−6.79, −0.17	0.04 *
Anemia						
Persistent (vs. absent)	1.36	−0.22, 2.95	0.09	0.22	−1.37, 1.81	0.79
Acquired (vs. absent)	−0.67	−2.19, 0.85	0.39	−1.31	−2.84, 0.23	0.10
Resolved (vs. persistent)	−1.40	−3.34, 0.54	0.16	−0.29	−2.25, 1.67	0.77
HTN						
Persistent (vs. absent)	1.03	−0.30, 2.37	0.13	1.59	0.24, 2.94	0.02 *
Acquired (vs. absent)	0.22	−1.32, 1.76	0.78	0.24	−1.32, 1.80	0.76
Resolved (vs. persistent)	−0.11	−1.59, 1.38	0.89	0.25	−1.26, 1.75	0.75

BASC-2PRS Behavior Assessment System for Children, Second Edition, Parent Rating Scales; CKD Chronic kidney disease*; CKiD* Chronic Kidney Disease in Children cohort study; *GFR* glomerular filtration rate*; HTN* Hypertension; *FSIQ* Full-scale intelligence quotient*; LBW* low birth weight*; SGA* small for gestational age.

* p<.05

** p<.01.