Psychiatric Diagnoses in Children With CKD Compared to the General Population

Jessica L. Stahl, Aaron G. Wightman, Jennifer E. Flythe, Noel S. Weiss, Sangeeta R. Hingorani, and Ann Vander Stoep

Rationale & Objective: Children with chronic kidney disease (CKD) are subject to physical and psychosocial challenges, which may confer greater risk of developing psychiatric disorders. We sought to examine key psychiatric diagnoses in children with CKD compared with those in the general pediatric population and assess the correlation between parent-reported diagnosis and self-reported symptoms of depression.

Study Design: Cross-sectional.

Setting & Participants: Children ages 2-17 years receiving current medical care who participated in the Chronic Kidney Disease in Children Study (CKiD) or the National Survey of Children's Health.

Exposure: CKD.

Outcomes: Parent-reported diagnoses of depression, anxiety, or attention-deficit and hyperactivity disorder (ADHD).

Analytical Approach: Using Poisson regression, we determined the age, sex, and race-adjusted prevalence ratio comparing diagnoses between children with CKD and those in the general population overall and within subgroups of sex, race, maternal education status, and CKD stage. Secondarily, we examined the correlation between depression status using standardized

Children with chronic kidney disease (CKD) are subject to a myriad of disease-associated challenges which generate complex psychosocial effects, poor neurodevelopmental outcomes, and increased stressors in personal, peer, and familial domains.¹⁻⁴ Even mild CKD may

Editorial, XXXX

be associated with subtle physiologic changes that can lead to psychiatric disorders. Understanding the mental health of children with CKD across the range of illness severity is an important aspect of working within complex systems of care to promote optimal outcomes for this vulnerable group of patients.

Limited data suggest a prevalence of 60%-70%^{5,6} of any psychiatric diagnosis among children with CKD and up to 50% of those with a psychiatric diagnosis have multiple diagnoses.^{6,7} In comparison, the prevalence of any psychiatric diagnosis in population-based studies of children in the United States has been reported to be 50%.⁸ Available studies of children with CKD are limited

Kidney Med Vol 4 | Iss 6 | June 2022 | 100451

self-reported screening instrument scores and parent-reported diagnosis.

Results: Eight hundred seventy-five children with CKD and 72,699 children in the general population were included. Those with CKD had an adjusted prevalence ratio of 1.32 (95% Cl, 1.01-1.73) for depression, 0.72 (95% Cl, 0.52-0.99) for anxiety, and 1.03 (95% Cl, 0.86-1.25) for ADHD. The results were similar across subgroups of CKD stage, sex, race, or maternal education. The correlation between parent-reported diagnosis and instrument-detected depression was weak, r = 0.13 (95% Cl, 0.03-0.23).

Limitations: Retrospective parent- or self-reported data were used.

Conclusions: Children with CKD had a higher prevalence of parent-reported depression, equivalent prevalence of attention-deficit and hyperactivity disorder, and lower prevalence of anxiety diagnoses compared to other children. These findings are inconsistent with results of prior studies and suggest that baseline assessments used in CKiD may have limited utility in describing psychiatric disorders among children with CKD. Improved mental health assessment approaches in pediatric nephrology are needed.

> by small sample sizes,^{5,6,9-12} narrow representation of ethnic groups and geographic areas,^{5,6,9,12} and inconsistent definitions of psychiatric disorders as reflected in the use of a variety of symptom-based screening tools,^{7,9-12} all of which limit the clinical applicability, comparability, and generalizability of the findings. Parent-reported psychiatric diagnoses as collected in large research databases provide a potentially efficient method to close the knowledge gap surrounding psychiatric disorders and pediatric kidney disease; however, the validity of parent-reported diagnoses is unknown.

> To address this knowledge gap, we used data from the Chronic Kidney Disease in Children (CKiD) study¹³ and the National Survey of Children's Health (NSCH)¹⁴ to examine the relative prevalence of common psychiatric disorders in children with CKD and in the general pediatric population. We hypothesized that a relatively greater proportion of children with CKD would have diagnoses of depression, attention-deficit and hyperactivity disorder (ADHD), and anxiety, and that the prevalence would be

Visual Abstract included

Complete author and article information provided before references.

Correspondence to J.L. Stahl (jessica_stahl@ med.unc.edu)

Kidney Med. 4(6):100451. Published online March 18, 2022.

doi: 10.1016/ j.xkme.2022.100451

© 2022 The Authors. Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. This is an open access article under the CC BY-NC-ND license (http:// creativecommons.org/ licenses/by-nc-nd/4.0/).



PLAIN-LANGUAGE SUMMARY

Children with chronic kidney disease (CKD) may be at the risk of developing psychiatric disorders compared with other children. We compared the parent-reported diagnoses of depression, anxiety, and attention-deficit and hyperactivity disorder (ADHD) in children with CKD with those in the general pediatric population using data from the Chronic Kidney Disease in Children Study and the National Survey of Children's Health. When age, race and ethnicity, and sex were accounted for, we found a 32% higher depression prevalence, 28% less anxiety prevalence, and similar ADHD prevalence in children with CKD compared with those in the other children. The correlation between parent-reported and instrument-detected depression was weak. In contrast to prior studies, condition prevalences were similar across CKD stages. Our results suggest that different methods to evaluate for psychiatric disorders are needed for children with kidney disease.

particularly high in those with more advanced stages of CKD.

METHODS

This study was determined to be exempted from review by the institutional review board of Seattle Children's Research Institute. Data from CKiD and NSCH are deidentified, publically available, and do not require additional informed consent.

Study Cohort

Using data obtained from children and adolescents across North America enrolled in the CKiD and NSCH studies, we performed a cross-sectional analysis comparing the histories of psychiatric diagnoses in children with CKD with those in the general pediatric population. Children and adolescents aged 2-17 years with CKD who participated in the CKiD study between 2005 and 2015, or in the 2007 NSCH were eligible for inclusion. We excluded NSCH participants who had not seen a health care provider within the last 12 months to ensure equivalence in opportunity for outcome assessment between the NSCH and CKiD comparator groups as all CKiD enrollees must have seen a medical provider within the last 12 months to enroll in the study.

Data Sources

CKiD

The CKiD study is a multicenter, longitudinal cohort study of children with CKD between the ages of 1 and 16 years recruited from 54 pediatric nephrology centers across North America. Study recruitment began in 2005, and data obtained at the time of entry into the study are available through 2015 from 891 participants in cohorts 1 and 2. Study participants completed a 2-part baseline assessment within 24 months of study enrollment and were subsequently followed annually using clinician, laboratory, and survey evaluations until transplantation, dialysis initiation, or transfer of care to an adult center. CKiD excludes children with prior malignancy, transplant, or dialysis within 3 months of the baseline assessment. Additional details of the study design and objectives have been previously described.¹³

NSCH

The NSCH is a survey conducted in the United States that employs random digit dialing techniques. The NSCH evaluates childhood well-being including demographic, medical, social, and mental health aspects of child health across a nationally representative sample of children aged 0-17 years. In 2007, data were collected via household landline telephones with 91,642 completed interviews.¹⁴

Study Variables

We defined exposure status as presence of CKD based on participation in the CKiD study. The primary outcomes were parent-reported diagnoses of depression, anxiety, and ADHD. In CKiD, these outcomes were ascertained during the baseline interview from the question: "Has a doctor or any other health care professional ever told you that (name of child) has any of the following diseases?," including "attention-deficit disorder," "attention-deficit hyperactivity disorder," "depression," and "anxiety disorder." In the NSCH, these outcomes were ascertained from the parent response to the question "Has a doctor or other health care provider ever told you that [name] had...," followed by "attention-deficit disorder or attention-deficit hyperactive disorder (that is, ADD or ADHD)," "depression," or "anxiety" in the telephone interview. We adjusted for age, sex, and race and ethnicity as potential confounders. In stratified analyses of the association between CKD and psychiatric disorder diagnoses, we evaluated subgroups based on maternal education level, sex, and race and ethnicity.

As a part of the baseline assessment, CKiD participants aged 7-17 years were asked to complete the Children's Depression Inventory (CDI), a 27-question, self-reported survey that assesses severity of depression symptoms in that age group.¹⁵ Raw CDI scores are converted to T scores based on age- and sex-adjusted general population norms with higher scores reflecting greater reported symptoms of depression. A T score ≥ 65 is considered "clinically significant," which we used in this study as the threshold defining the presence of depression.

Data Analysis

We compared the histories of selected psychiatric diagnoses in the 2 samples using log-linear regression with

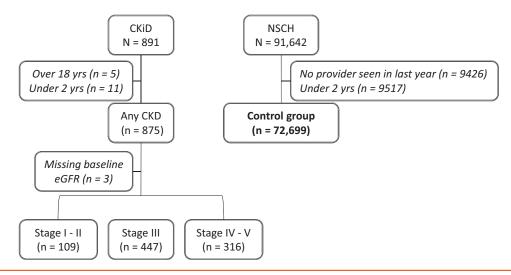


Figure 1. Consolidated Standards of Reporting Trials diagram. Abbreviations: CKD, chronic kidney disease; CKiD, Chronic Kidney Disease in Children Study; eGFR, estimated glomerular filtration rate; NSCH, National Survey of Children's Health.

Poisson distribution adjusted for age (continuous), sex (male and female), and race and ethnicity (Hispanic or Latino, non-Hispanic White, non-Hispanic Black, and non-Hispanic other). We conducted stratified analyses to assess differences in prevalence ratios (PRs) by sex, race and ethnicity, and maternal education status, as well as for differences by stage of CKD as determined by estimated glomerular filtration rate (eGFR) (mild: stage 1-2; moderate: stage 3; or severe: stage 4-5). We selected PR as the primary outcome to produce a reliable proportional comparison between children with CKD and the general pediatric population.

In secondary analyses, we examined pairwise correlations between parent-reported depression diagnosis and self-reported clinically significant (T score \geq 65) depressive symptoms using the CDI among CKiD participants who completed baseline CDI surveys. We did not evaluate anxiety and ADHD because other neurocognitive assessment tools used in CKiD, such as the Behavior Assessment System for Children, Second Edition and the Behavior Rating Inventory of Executive Function, are not correlated with specific diagnoses.

RESULTS

Characteristics of the Cohorts

A total of 72,699 children from NSCH and 875 children from CKiD met the inclusion criteria and were included in the analysis. For the stratified analysis by CKD stage, three CKiD participants had missing baseline eGFR data and were therefore excluded from the analysis. The remaining CKiD sample included 109 participants with mild kidney disease, 447 with moderate kidney disease, and 316 with severe kidney disease, as shown in Fig 1.

Demographic characteristics of the NSCH and CKiD samples are shown in Table 1. The non-CKD population

sample had approximately equal sex representation, whereas the CKiD population was predominantly male (48% vs 38% female, respectively). Higher proportions of Black (17%) and Hispanic (21%) groups were represented in the CKiD sample than in the NSCH sample (10% Black, 12% Hispanic). Maternal education beyond high school was seen in a larger portion of the NSCH sample (67%) than in the overall CKD (59%), mild CKD (44%), or moderate CKD (59%) samples, but was similar to the proportion of those with a maternal education beyond high school in the subset of children with severe CKD (64%). Mean ages were similar across all groups.

Prevalences of Depression, Anxiety, and ADHD

The crude prevalences and adjusted PRs of parent-reported diagnoses of depression, anxiety, ADHD, and multiple psychiatric diagnoses (ie, ≥ 2 of these diagnoses) comparing children with CKD to children in the general population are displayed in Table 2. In the adjusted model, a diagnosis of depression was 32% more prevalent in children with CKD than in the general pediatric population. A diagnosis of anxiety was 28% less prevalent in children with CKD, and ADHD was 3% more prevalent in those with CKD, as determined using the adjusted PR. The adjusted prevalence of multiple diagnoses was 32% lower in children with CKD than in those in the non-CKD sample. This pattern of results was broadly similar across strata of sex, race and ethnicity, and maternal education level (Table 3).

The adjusted PRs for depression, anxiety, and ADHD diagnoses in children with mild, moderate, and severe CKD are presented in Fig 2, with the aggregate CKD group adjusted PR shown for reference. There was a trend toward increased prevalence of depression with advancing CKD stage (adjusted PR: mild, 1.02; moderate, 1.42; severe, 1.82), though these differences are within the limits of

Table 1. Participant Characteristics Across the 2 cohorts, Overall and by Chronic Kidney Disease Stage (2005-2015)

		CKiD ^a			
	NSCH ^ь (n=72,605)	All (n=875)	Stage 1-2 (n=316)	Stage 3 (n=447)	Stage 4-5 (n=109)
Sex					
Female	34,939 (48%)	335 (38%)	124 (39%)	179 (40%)	31 (28%)
Race and ethnicity					
Black	7,510 (10%)	152 (17%)	58 (18%)	70 (16%)	22 (20%)
Hispanic or Latino	8,612 (12%)	185 (21%)	65 (21%)	94 (21%)	26 (24%)
Other	6,539 (9%)	51 (6%)	25 (8%)	22 (5%)	4 (4%)
White	48,842 (67%)	487 (56%)	168 (53%)	261 (58%)	57 (52%)
Missing	1,102 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Highest level of maternal education					
High school or less	18,226 (25%)	342 (39%)	108 (34%)	175 (39%)	58 (53%)
More than high school	48,794 (67%)	514 (59%)	202 (64%)	262 (59%)	48 (44%)
Missing	5,585 (8%)	19 (2%)	6 (2%)	10 (2%)	3 (3%)
Age in y					
Mean (SD)	10.1 (4.8)	10.9 (4.3)	10.8 (4.4)	10.9 (4.2)	11.5 (3.9)
Median [IQR]	10.0 [6.0-14.0]	11.0 [8.0-15.0]	11.0 [8.0-15.0]	11.0 [8.0-15.0]	12.0 [9.0-15.0]
Birth status					
Premature (<36 wk gestation)	NA	98 (11%)	38 (12%)	52 (12%)	7 (6%)
Missing	NA	34 (4%)	14 (4%)	16 (4%)	4 (4%)
Low birth weight (<2,500 g)	NA	152(19%)	56 (17%)	81 (18%)	14 (14%)
Missing	NA	52 (6%)	22 (7%)	23 (5%)	7 (6%)
Disease characteristics					
Glomerular diagnosis	NA	272 (31%)	138 (44%)	112 (25%)	22 (20%)
Hypertension	NA	412 (47%)	154 (49%)	204 (46%)	52 (48%)
Duration of CKD in y					
Mean (SD)	NA	8.1 (4.9)	7.0 (4.8)	8.4 (4.8)	10.0 (4.8)
Median [IQR]	NA	8.0 [3.8-12.3]	6.4 [2.8-10.7]	8.3 [4.2-12.5]	10.2 [5.9-14.2]
eGFR (mL/min/1.73 m²)					
Mean (SD)	NA	54.9 (22.7)	78.6 (17.5)	45.6 (8.6)	24.5 (3.8)
Median [IQR]	NA	52.5 [38.6-68.0]	74.8 [66.0-85.5]	46.3 [38.7-53.0]	25.1 [22.0-27.5]
Cohort entry year					
2005-2010	NA	574 (66%)	113 (36%)	351 (79%)	108 (99%)
2011-2015	NA	301 (34%)	203 (64%)	96 (21%)	1 (1%)

Abbreviations: CKD, chronic kidney disease; CKiD, Chronic Kidney Disease in Children Study; eGFR, estimated glomerular filtration rate; IQR, interquartile range; NA, not applicable; NSCH, National Survey of Children's Health; SD, standard deviation.

^aOf 875 total CKiD participants, 3 were missing stage of CKD data and were excluded from secondary analysis.

^bData on disease characteristics were not collected for NSCH participants. NSCH birth weight data are not included due to high missingness of >50%.

chance. There were no differences in prevalence of anxiety or ADHD diagnoses according to stage of CKD.

Table 2. Prevalence of Psychiatric Diagnoses in Children With Chronic Kidney Disease and in the General Pediatric Population

	Crude Prevalen	ice	Adjusted PR (95% Confidence	
Diagnosis	CKiD	NSCH	Interval) ^a	
Depression	5.7%	3.9%	1.32 (1.01-1.73)	
Anxiety	4.0%	5.4%	0.72 (0.52-0.99)	
ADHD	10.6%	9.2%	1.03 (0.86-1.25)	
≥2 of the above diagnoses	3.1%	4.2%	0.68 (0.47-0.99)	

Abbreviations: ADHD, attention-deficit and hyperactivity disorder; CKD, chronic kidney disease; CKiD, Chronic Kidney Disease in Children Study; NSCH, National Survey of Children's Health; PR, prevalence ratio. ^aAdjusted for age, sex, and race and ethnicity.

Correlation of Parent-Reported and Self-Report Instrument-Identified Depression

Among the 346 CKiD participants who completed the CDI self-reported symptom screening instrument, 8 (2.3%) met the screening threshold for clinically significant depression symptoms, and 26 (7.5%) had a parent-reported depression diagnosis (Table 4). Only 2 patients were positive for depression by both criteria. Six patients met depression criteria according to the screening instrument, but did not have a parent-reported depression diagnosis. A total of 24 participants did not meet screening instrument criteria, but had a parent-reported diagnosis of depression. The CDI and parent-report pairwise Pearson correlation coefficient was 0.13 (95% confidence interval, 0.03-0.23).

Table 3. Adjusted Prev	alence and 95% Confidence	e Interval of Psychiatric	Diagnoses in Selected Strata ^a

	Adjusted PR (95% Confidence Interval) ^a			
	Depression	Anxiety	ADHD	
Sex				
Female	1.52 (1.03-2.26)	0.60 (0.34-1.08)	0.89 (0.57-1.40)	
Male	1.19 (0.82-1.72)	0.78 (0.53-1.15)	1.07 (0.87-1.32)	
Race and ethnicity				
Black	1.68 (0.91-3.11)	0.17 (0.02-1.25)	1.08 (0.71-1.63)	
Hispanic or Latino	1.13 (0.61-2.10)	0.66 (0.32-1.38)	1.33 (0.87-2.02)	
Other	0.60 (0.15-2.39)	0	0.66 (0.25-1.70)	
White	1.43 (1.00-2.04)	0.92 (0.64-1.32)	0.98 (0.76-1.27)	
Maternal education				
Lower than high school	1.30 (0.86-1.94)	0.63 (0.36-1.09)	0.76 (0.54-1.09)	
High school or higher	1.53 (1.06-2.20)	0.85 (0.57-1.26)	1.26 (1.00-1.59)	

Abbreviations: ADHD, attention-deficit and hyperactivity disorder; PR, prevalence ratio.

^aAdjusted for age, sex, and race and ethnicity.

DISCUSSION

In this analysis, children with CKD demonstrated a higher prevalence of parent-reported diagnoses of depression, equivalent prevalence of parent-reported ADHD, and lower prevalence of parent-reported anxiety as compared to a general pediatric population sample when adjusted for age, race and ethnicity, and sex. There was no evidence that the prevalence estimates differed between the categories of sex, race and ethnicity, maternal education level, or stage of CKD. Parent-reported diagnosis and CDI symptombased depression assessments were weakly correlated in children with CKD.

These results are unexpected as our findings are inconsistent with existing research of psychiatric diagnoses in pediatric patients with CKD. First, other studies have demonstrated higher prevalences of depression and anxiety in children with CKD compared to healthy controls.^{6,16-18} Second, in contrast to our failure to observe a progressive increase in diagnosis in patients with more severe kidney disease, other studies have shown higher prevalences in children with more advanced stages of CKD, including those with kidney failure and those who have undergone transplantation.^{5,6,16-18} While these studies were limited by small sample sizes, their use of semistructured interviews could be expected to provide robust information regarding both existing symptoms and lifetime psychiatric diagnoses.^{5,6,16} With regard to depression, the crude prevalence of 5.7% in children with CKD is similar to the proportion (5%) of CKiD participants from cohort 1 who screened positive for depression symptoms⁷ but is lower than other depression prevalence estimates in pediatric patients with CKD, which range from 7% to 35%.7.9-12 Our finding of equivalent prevalence of ADHD in children with CKD and in the general population is inconsistent with known effects of even mild CKD on attention and executive functioning seen in neurocognitive tests of children with CKD.^{2,1}

Direct comparisons with other studies are limited by methodologic differences, including variation in

psychiatric diagnosis definitions and ascertainment technique, and in study participant characteristics such as stage of CKD and age. One potential factor affecting our results is the caregiver relationship to the treatment team for those with CKD, which may differentially impact underreporting of parent-reported diagnoses by exacerbating social desirability bias. It is possible that the close relationship between families and their nephrology care team leads them to avoid reporting mental health concerns and diagnoses to the research team to avoid a perceived risk of stigmatization. In addition, there were some demographic differences between the CKiD participants and the general population including a lower proportion of female participants, those who self-identified as White, and those with mothers who completed high school. We would expect those differences to result in a lower risk of depression and a higher risk of ADHD in patients with CKD,²⁰ counter to our findings.

These results and their limited comparability with other studies highlight the gap that exists in our understanding of psychiatric comorbidities in pediatric patients with CKD. Identifying methods of psychiatric assessment that allow efficient, accurate comparisons to the general population is crucial for advocating for and allocating resources to pediatric patients with CKD. The optimal method must balance time efficiency and accuracy. For example, symptom-based screening instruments are

Table 4. Parent-Reported Depression Diagnosis Compared to CDI Survey With Clinically Significant Depression Symptoms (T score \geq 65)

	CDI Depression Symptoms		
	Negative	Positive	
Parent-reported depression			
Negative	314	6	
Positive	24	2	

Abbreviation: CDI, Children's Depression Inventory.

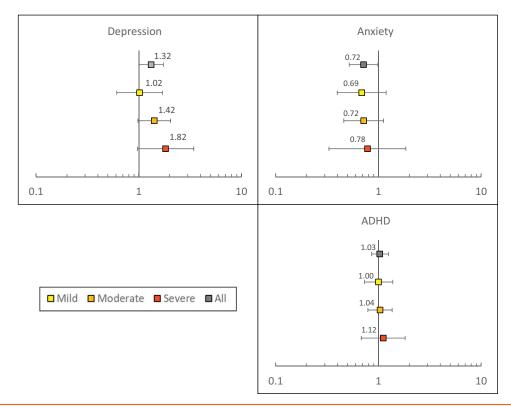


Figure 2. Prevalence ratios of psychiatric diagnoses in those with mild, moderate, and severe CKD compared to the general population sample. Abbreviation: ADHD, attention-deficit and hyperactivity disorder.

widely available and are relatively efficient; however, most instruments only identify current or recent symptoms of the diagnosis of interest. As such, diagnoses based on symptom-based screening instruments are not readily comparable to lifetime psychiatric diagnoses. This issue is underscored by the weak correlation between parentreported diagnosis and depression symptom self-report in our study. Additionally, caution is needed in using parent proxy reports in general to determine the mental health or psychiatric diagnosis status in children, as discordant parent and child reporting is common.²¹ This is a critical issue, as psychiatric symptoms may wax and wane over time, and the absence of recent symptoms is likely to result in misclassification with a high proportion of falsenegative diagnoses. The same is true of definitions that require active treatment, in addition to self-report or historical diagnosis. In the previous study of depression in CKiD cohort 1, which used such criteria, 14 participants reported a prior diagnosis of depression but did not screen positive for depression. Retrospective self- or parentreported diagnosis is an efficient method of ascertainment but, as seen here, is limited in providing precise estimates of psychiatric diagnoses.

Other studies have employed semistructured interviews which are resource intensive and time consuming, but can provide information regarding both current symptoms and lifetime psychiatric diagnoses.^{5,6,16} The gold standard for psychiatric diagnosis is assessment by a qualified mental

health professional; however, this is both time and resource intensive. Including more longitudinal assessments of mental health in research and in clinical care may maintain efficiency and could improve accuracy in identifying psychiatric diagnoses. This could be accomplished with repeated assessments, or by modifying current screening instruments to include historical in addition to recent symptoms. Integrated medical records with both behavioral and mental health information also play important roles, as does emphasis on the performance of regular mental health screening and assessment starting at the time of CKD diagnosis. Instituting standardized comprehensive methods of assessment and disease definitions for psychiatric disorders would greatly improve our collective ability to study and to derive meaning from evaluations of mental health status in this vulnerable population.

Strengths of this study include the robust sample size for both CKD and comparison groups and similar methodology for data collection, which increases comparability between those groups. In particular, the similarities in psychiatric diagnosis assessment between the CKiD and NSCH samples act to minimize bias in comparing outcomes.

We are limited by the ascertainment of outcomes via parent recall of health care provider communication, which may result in underreporting of psychiatric disorders in both the CKD and general population samples. Additionally, legislation regarding mental health privacy rights of children

and adolescents differs between states, such that there may be underreporting of psychiatric diagnoses by the caregiver respondent in cases in which the child has been diagnosed, but has not disclosed, their diagnosis to the caregiver. Social desirability bias may also result in underreporting of psychiatric disorders in both the survey-based samples, though the degree of the bias may differ. In children with CKD, intensive, longitudinal monitoring associated with the CKiD study and their existing relationship with the nephrology team may lead to lower referral, recruitment, and enrollment of those with comorbid psychiatric disorders. Differences in psychiatric diagnostic practices and patterns at different centers and by different providers may induce misclassification in both CKD and general pediatric groups; however, such a bias would likely be nondifferential. It is possible that while both groups have been seen by care providers, the children with CKD may use their nephrology team as primary care practitioners and may be less likely to undergo standard pediatric psychosocial screening compared with children who are seen in primary care settings and are not referred for psychiatric evaluation. Further, we are unable to make causal inferences regarding CKD and the assessed psychiatric diagnoses, as information regarding the timing of psychiatric symptoms and diagnosis relative to the onset and duration of CKD is unavailable.

To our knowledge, this is the largest study to date of psychiatric diagnoses in the pediatric population with CKD and the first to utilize a direct comparison of a population with CKD to a nationwide population sample. Despite highly comparable CKiD and NSCH data, the inconsistencies between our results and those of previous studies suggest that isolated use of the baseline parentreport assessments from the CKiD database may have limited utility in evaluating a history of psychiatric disorders among children with CKD. Improved diagnostic classification is a critical first step toward better understanding the relationship between CKD and mental illness to guide our development of targeted interventions to address and prevent the development of psychiatric disorders in this population.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Jessica L. Stahl, MD, MS, Aaron G. Wightman, MD, MA, Jennifer E. Flythe, MD, MPH, Noel S. Weiss, MD, DrPH, Sangeeta R. Hingorani, MD, MPH, and Ann Vander Stoep, PhD

Authors' Affiliations: Division of Nephrology and Hypertension, Department of Medicine, UNC School of Medicine, University of North Carolina Kidney Center (JLS, JEF), and Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, NC (JLS, JEF); Department of Pediatrics (AGW, SRH), Department of Epidemiology (NSW, AVS), and Department of Psychiatry and Behavioral Sciences, University of Washington (AVS), and Division of Nephrology, Seattle Children's Hospital, Seattle, WA (AGW, SRH)

Address for Correspondence: Jessica Stahl, MD, MS, 7025 Burnett Womack Building; Chapel Hill, NC 27599-7155. Email: jessica_stahl@med.unc.edu Authors' Contributions: Research idea and study design: JLS, AGW, SRH, NSW, AVS; data acquisition: JLS; data analysis/ interpretation: JLS, JEF, AGW, SRH, NSW, AVS; statistical analysis: JLS; supervision or mentorship: AGW, JEF, SRH, NSW, AVS. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Support: Dr Stahl was supported by the National Institutes of Health T32 Pediatric Nephrology Training Program grant [5T32 DK007662-28]. Dr Flythe is supported by R01 HL152034 awarded by the National Heart, Lung, and Blood Institute of the National Institutes of Health. The above funding contributors had no role in the study design, analysis, interpretation, or report.

Financial Disclosure: In the last 3 years, Dr Flythe has received speaking honoraria from the American Society of Nephrology and multiple universities, as well as investigator-initiated research funding unrelated to this project from the Renal Research Institute, a subsidiary of Fresenius Kidney Care, North America. She serves on a medical advisory board for Fresenius Kidney Care, North America and a scientific advisory board and Data and Safety Monitoring Committee for National Institute of Diabetes and Digestive and Kidney Care, North America and AstraZeneca. The remaining authors declare that they have no relevant financial interests.

Acknowledgments: Data in this manuscript were collected by the Chronic Kidney Disease in Children 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, and Derek Ng, PhD) at Johns Hopkins Bloomberg School of Public Health. CKiD is supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases, with additional funding from Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Heart, Lung, and Blood Institute (U01 DK066143, U01 DK066174, U24 DK082194, U24 DK066116). The CKiD website is located at https://statepi.jhsph. edu/ckid.

Peer Review: Received September 13, 2021. Evaluated by 3 external peer reviewers, with direct editorial input from the Statistical Editor and the Editor-in-Chief. Accepted in revised form January 23, 2022.

REFERENCES

- Massengill SF, Ferris M. Chronic kidney disease in children and adolescents. *Pediatr Rev.* 2014;35(1):16-29. doi:10.1542/pir. 35-1-16
- Hooper SR, Gerson AC, Butler RW, et al. Neurocognitive functioning of children and adolescents with mild-to-moderate chronic kidney disease. *Clin J Am Soc Nephrol.* 2011;6(8):1824-1830. doi:10.2215/CJN. 09751110
- Hooper SR, Duquette PJ, Icard P, Wetherington CE, Harrell W, Gipson DS. Social-behavioural functioning in paediatric chronic kidney disease. *Child Care Health Dev.* 2009;35(6): 832-840. doi:10.1111/j.1365-2214.2009.00992.x
- Ruebner RL, Laney N, Kim JY, et al. Neurocognitive dysfunction in children, adolescents, and young adults with CKD. *Am J Kidney Dis.* 2016;67(4):567-575. doi:10.1053/j.ajkd.2015.08.025

- Bakr A, Amr M, Sarhan A, et al. Psychiatric disorders in children with chronic renal failure. *Pediatr Nephrol.* 2007;22(1):128-131. doi:10.1007/s00467-006-0298-9
- Berney-Martinet S, Key F, Bell L, Lépine S, Clermont MJ, Fombonne E. Psychological profile of adolescents with a kidney transplant. *Pediatr Transplant*. 2009;13(6):701-710. doi:10. 1111/j.1399-3046.2008.01053.x
- Kogon AJ, Matheson MB, Flynn JT, et al. Depressive symptoms in children with chronic kidney disease. J Pediatr. 2016;168(Jan):164-170. doi:10.1016/j.jpeds.2015.09.040
- Merikangas KR, He JP, Burstein M, et al. Lifetime prevalence of mental disorders in U.S. adolescents: results from the national comorbidity survey replication-adolescent supplement (NCS-A). J Am Acad Child Adolesc Psychiatry. 2010;49(10):980-989. doi:10.1016/j.jaac.2010.05.017
- Reynolds JM, Garralda ME, Postlethwaite RJ, Goh D. Changes in psychosocial adjustment after renal transplantation. *Arch Dis Child*. 1991;66(4):508-513. doi:10. 1136/adc.66.4.508
- Kogon AJ, Vander Stoep A, Weiss NS, Smith J, Flynn JT, McCauley E. Depression and its associated factors in pediatric chronic kidney disease. *Pediatr Nephrol.* 2013;28(9):1855-1861. doi:10.1007/s00467-013-2497-5
- Kogon AJ, Kim JY, Laney N, et al. Depression and neurocognitive dysfunction in pediatric and young adult chronic kidney disease. *Pediatr Nephrol.* 2019;34(9):1575-1582. doi: 10.1007/s00467-019-04265-z
- Moreira JM, Bouissou Morais Soares CM, Teixeira AL, Simões e Silva AC, Kummer AM. Anxiety, depression, resilience and quality of life in children and adolescents with pre-dialysis chronic kidney disease. *Pediatr Nephrol.* 2015;30(12):2153-2162. doi:10.1007/s00467-015-3159-6

- Furth SL, Cole SR, Moxey-Mims M, et al. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. *Clin J Am Soc Nephrol.* 2006;1(5):1006-1015. doi:10.2215/CJN.01941205
- 14. Blumberg SJ, Foster EB, Frasier AM, et al. Design and operation of the National Survey of Children's Health, 2007. *Vital Health Stat 1*. 2012;1(55):1-149.
- 15. Kovacs M. Children's Depression Inventory CDI Manual. New York Multi-Health Syst; 1992:1-800.
- Dinc GS, Cak T, Kultur EC, Bilginer Y, Kul M, Topaloglu R. Psychiatric morbidity and different treatment modalities in children with chronic kidney disease. *Arch Pediatr.* 2019;26(5): 263-267. doi:10.1016/j.arcped.2019.05.013
- Marciano RC, Soares CM, Diniz JS, et al. Mental disorders and quality of life in pediatric patients with chronic kidney disease. *J Bras Nefrol.* 2010;32(3):316-322. doi:10.1590/S0101-28002010000300014
- Marciano RC, Soares CM, Diniz JS, et al. Behavioral disorders and low quality of life in children and adolescents with chronic kidney disease. *Pediatr Nephrol.* 2011;26(2):281-290. doi:10. 1007/s00467-010-1683-y
- Mendley SR, Matheson MB, Shinnar S, et al. Duration of chronic kidney disease reduces attention and executive function in pediatric patients. *Kidney Int.* 2015;87(4):800-806. doi: 10.1038/ki.2014.323
- Avenevoli S, Baio J, Bitsko RH, et al. Mental health surveillance among children—United States, 2005-2011. *MMWR Suppl.* 2013;62(2):1-35.
- De Los Reyes A, Augenstein TM, Wang M, et al. The validity of the multi-informant approach to assessing child and adolescent mental health. *Psychol Bull.* 2015;141(4):858-900. doi:10. 1037/a0038498

