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CKiD (CKD in Children) Prospective Cohort Study: A Review of Current Findings

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Abstract

Chronic kidney disease (CKD) is a life-long condition associated with substantial morbidity and premature death due to complications from progressive decline in kidney function. The incidence and prevalence of all stages of CKD in children continues to increase worldwide. Between 2000 and 2008, the kidney replacement therapy incidence rate among those 0–19 years of age rose 5.9% to 15 per million population, highlighting the importance of CKD research in children. Many comorbid conditions seen in adults with CKD, including cardiovascular disease and cognitive impairment, are also highly prevalent in children, implicitly demonstrating the crucial need for initiating therapy early to improve health outcomes in children with CKD.

The CKiD (Chronic Kidney Disease in Children) study is a prospective cohort study of 586 children aged 1–16 years with an estimated glomerular filtration rate (eGFR) between 30 and 90 ml/min/1.73 m^2. Since its inception, CKiD has identified risk factors for CKD progression and cardiovascular disease in children with CKD and has highlighted the effects of CKD on outcomes unique to children, including neurocognitive development and growth. This review summarizes findings to date, illustrating the spectrum of CKD-associated complications in children and emphasizing areas requiring further investigation. Taken in sum, these elements stress that initiating treatment at an early age is essential for reducing long term morbidity and mortality in children with CKD.

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Index words

Chronic kidney disease; children; CKD progression; neurodevelopment; cardiovascular disease; growth

Chronic kidney disease (CKD) is a growing worldwide public health issue. Various studies report a prevalence of CKD ranging from 15–74.7 cases per million children (5). Children with CKD are at risk for increased morbidity, mortality, and decreased quality of life, and a significant percentage of children with CKD will develop kidney failure by 20 years of age. Critically, the incidence and prevalence of all stages of CKD in children continues to increase worldwide, and, in the United States between from 2000 to 2008, the incidence of people 0–19 years of age initiating kidney replacement therapy rose 5.9% to 15 per million population (1). With the expected remaining lifetime for a child with end-stage renal disease (ESRD) treated with dialysis estimated to be approximately 18 years (5) and children requiring dialysis having mortality rates 30 to 150 times higher than the general pediatric population (5, 6), the early detection and management of CKD is crucial to delay or even prevent progression to ESRD.

The CKiD (Chronic Kidney Disease in Children) study was initiated to address the void in our knowledge of CKD in children. Enrolling 586children between the ages 1 and 16 years with an estimated glomerular filtration rate (eGFR) between 30 and 90 ml/min per 1.73 m^2, the CKiD study is the largest North American multicenter study of children with CKD. The observational cohort design and methods of the CKiD study have been described in detail previously (Box 2 and Table 1) (7). Children are followed longitudinally until they are 21 years of age, transplanted, or transferred to an adult center; the primary outcome is the rate of GFR decline with a secondary outcome of time to ESRD or a 50% decrease in GFR (7). CKiD enrolled a diverse cohort of children to explore risk factors for CKD progression and manifestations of CKD in this unique and important population (Table 2). Specific aims of CKiD include: (1) identifying and quantifying novel and traditional risk factors for progression of CKD; (2) characterizing CKD progression effects neurodevelopment, cognitive abilities, and behavior; (3) describing the prevalence of cardiovascular disease and associated risk factors; and (4) examining the effects of declining kidney function on growth in children with CKD. This review will summarize results from over 20 publications from the CKiD study (Box 4), placing these findings into the wider context of CKD in both children and adults worldwide.

Novel and traditional risk factors for GFR decline in CKD

The ability to assess CKD progression begins with defining kidney disease. In 2002, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) defined a five-stage classification system for severity of CKD based upon GFR and kidney damage markers (8). To apply this staging system optimally to children, CKiD first identified the necessary tools to validate creatinine measurements and then developed more accurate equations to estimate kidney function in children. Prior estimating equations for children were developed before the change in the standard methodology for creatinine measurement from Jaffe to enzymatic methods (9, 10). Accordingly, as a prerequisite to generating an estimating equation, CKiD investigators evaluated the use of iohexol clearance from plasma, with blood samples obtained at 120 and 300 minutes after iohexol infusion, as a means to measure GFR directly and to detect small changes in GFR (11), validating its use as an accurate method to obtain measured GFR (mGFR) (12–14). The relative ease of this technique is reflected by the fact that, of over 2000 iGFR assessments performed at over 48 CKiD sites, only 5–7% of measurements were unattainable.

Using iGFR data in conjunction with serum creatinine, serum urea nitrogen, serum cystatin C, sex, and height, CKiD developed more accurate equations to estimate GFR in children with CKD. The more complete estimating equation (Box 1) was highly correlated with iGFR (r=0.88; 95% confidence interval [CI] for difference between eGFR and mGFR, −17.1 to 12.7 mL/min/1.73 m2), with a small bias for eGFR values being lower (−2.23 ml/min/1.73 m^2) (15). A simpler "bedside formula" to estimate GFR in children with CKD was also derived (15).

Using the bedside CKiD equation, 79.4% of eGFR values were within 30% of the measured iGFRs. Critically, the new equations are based on enzymatic creatinine methodology; accordingly, they result in eGFR values 25% lower than values determined by the initial Schwartz equation, an equation derived from Jaffe-based serum creatinine measurements (9). These CKiD eGFR formulas are accurate in children aged 1 to 16 years with eGFR levels from 15 to 75 ml/min/1.73 m^2. Since these formulas have not been validated in children with higher GFR levels, additional studies in children and adolescents with normal kidney function and earlier stages of CKD are ongoing (15).

In addition to eGFR, the diagnosis of CKD is based upon the presence of structural and/or functional kidney damage, defined as the presence of proteinuria, abnormal urine sediment, and/or abnormal kidney imaging or pathology present for 3 months or longer. Proteinuria, defined as a urine protein to creatinine ratio (UPCR) >0.2 g/g and/or urine microalbumin-creatinine ratio >30 mg/g, is a urinary biomarker that has been strongly associated with the presence and progression of CKD.

To better understand the factors that contribute to proteinuria in children with CKD, the CKiD study examined the epidemiologic distribution of proteinuria in a cross-sectional analysis of 419 children (16). Results showed that 76% of the CKiD cohort had significant proteinuria (62% with UPCR between 0.2 and 2 g/g and 14% with UPCR > 2 g/g). Non-Caucasian children had 40% higher UPCR levels than Caucasian children. Adult studies report similar results, indicating that further investigation is needed to determine if proteinuria contributes to the higher burden of ESRD in non-Caucasian individuals (17). Also noteworthy was the finding that, regardless of GFR, children with a glomerular cause of CKD had UPCR values on average 140% greater than those with non-glomerular kidney diseases (16).

Among CKiD participants with significant proteinuria, over half (55%) were receiving a renin-angiotensin system (RAS) antagonist (16). An important finding from a therapeutic standpoint of managing proteinuria was that children with glomerular disease receiving RAS antagonistic therapy had lower UPCR (median = 0.93 g/g) versus those with glomerular disease not receiving RAS antagonistic therapy (median UPCR = 3.78 g/g) (16). Similar findings of reduced levels of proteinuria were not present in children with non-glomerular disorders receiving antagonistic therapy, but this may be due to their overall lower median baseline UPCR of 0.42 g/g for those who were receiving a RAS antagonist and 0.45 g/g for those who were not (16).

For each 10% reduction in iGFR, CKiD participants had on average a 14% greater UPCR (16). This finding is consistent with other studies, including results from the European GISEN adult group, the pediatric Ital Kid project, and the ESCAPE trial, all of which showed proteinuria to be a strong predictor for progressive decline in kidney function (2, 18–20). Further review of studies examining the effect of proteinuria in children with CKD suggests that the severity of proteinuria may play a larger role in progression of CKD than the effect of glomerular versus non-glomerular proteinuria on kidney function (18, 19, 21). Accordingly, determination of the impact of glomerular versus nonglomerular disease and

severity of proteinuria on CKD progression is a key CKiD study goal; these results will be assessed with longitudinal follow up of the CKiD cohort.

Cardiovascular disease risk factors in children with CKD

Hypertension

Complications of CKD, such as acidosis, hypervolemia, hypertension, dyslipidemia, and anemia, all increase a child's risk for cardiovascular disease, the leading cause of death in children with kidney failure (22). Given the role of hypertension as a cardiovascular disease risk factor, the prevalence and correlates of hypertension were studied in 432 CKiD participants (23). Elevated BP was defined as BP ≥ 90th percentile for age, sex, and height (24), and hypertension was defined as BP ≥ 95th percentile or a history of hypertension with current antihypertensive medication treatment (24). Analysis of casual BP measurements obtained using an aneroid sphygmomanometer revealed 54% (n=233) of children in the CKiD cohort had either baseline systolic or diastolic hypertension or a history of hypertension plus antihypertensive medication use (23). Characteristics associated with elevated systolic BP included black race, glomerular cause of CKD, shorter duration of CKD, obesity, and elevated serum potassium (23). Diastolic hypertension was associated with younger age, black race, shorter duration of CKD, and nephrotic range proteinuria (23).

Pediatric and adult studies have shown the beneficial effect of strict BP control on kidney survival (25, 26). Despite efforts to control BP, almost half (n=98 of 202) of the CKiD cohort who were diagnosed with elevated BP had uncontrolled hypertension, defined as a systolic or diastolic BP ≥ 90th percentile with current prescribed use of antihypertensive medication (23). Male sex, black race, shorter duration of CKD, and lower use of angiotensin-converting-enzyme (ACE) inhibitors or angiotensin II-receptor-blockers (ARB) characterized the children in CKiD with uncontrolled hypertension.

Adult studies have reported racial disparities in kidney disease related blood pressure status, with blacks having a higher prevalence of poorly controlled hypertension than whites (27–30). As mentioned above, black children enrolled in CKiD had a significantly greater risk of having elevated BP at study entry as well as uncontrolled BP; this discrepancy persisted after adjusting for age, cause and duration of CKD, iGFR, degree of proteinuria, obesity, and antihypertensive medication use (23). Further studies are needed to identify whether genetics, environmental exposures, socioeconomic status, and/or barriers to healthcare contribute to racial differences in BP control.

Notably, children with uncontrolled BP were less likely to have received an ACE inhibitor or ARB compared with children who had controlled BP (Table 3)(23). When viewed in the context of the ESCAPE trial, in which children with CKD who received therapy with an ACE inhibitor and achieved BP in the low range of normal had a 35% reduction in the relative risk of 50% kidney function decline or progressing to ESRD within 5 years of initiating therapy (25), ACE inhibitors and angiotensin receptor blockers may be an integral therapy for managing kidney disease in children. Ongoing longitudinal analyses within CKiD will help advance our understanding of this issue.

Masked Hypertension and Left Ventricular Hypertrophy

To further evaluate the impact of elevated BP in the CKiD cohort, baseline echocardiographic findings (n=366), casual BP measurements, 24-hour ambulatory blood pressure monitoring (ABPM) data (n=226), kidney function, and demographic and clinical characteristics of the participants were analyzed (31). Hypertension was more commonly detected by ABPM than by casual BP measurements alone. Eighteen percent of the CKiD cohort had confirmed hypertension (hypertension detected by both ABPM and casual BP

measurements) and 38% had masked systolic or diastolic hypertension (hypertension detected only by ABPM). A significant percentage of children not receiving any antihypertensive therapy had either masked or confirmed hypertension, 29% and 15%, respectively (31). These results identify a need to improve the detection of hypertension in these children and to provide adequate therapy. The high prevalence of masked hypertension supports the routine use of ABPM to detect elevated BP and to guide antihypertensive therapy in children with CKD. This is also important in light of recent data on the prognostic value of ABPM measurements in adults with CKD (32).

LVH is a common finding in adults with CKD, identifying individuals at additional risk for future CVD events (33, 34). Evaluation of the CKiD participants' echocardiography data from 1 year after they entered the study revealed that 17% (62 of 366) of these children had LVH (31). Eccentric LVH, characteristically associated with volume overload and anemia, was seen in 11%, while concentric LVH, typically considered to result from hypertension, was present in 6% of the children. Most importantly, a higher percentage of children with confirmed and masked hypertension had LVH (34% and 20%, respectively) compared to those with normal BPs (8%) (31). The presence of confirmed or masked hypertension was the strongest predictor for LVH (odds ratios of 4.3 and 4.1, respectively); these findings that strengthen the support of standard use of ABPM and echocardiography to help determine cardiovascular risk and to guide BP therapy in children with mild to moderate CKD (31).

Dyslipidemia

Adult and pediatric studies have shown dyslipidemia is due to disorders in lipoprotein metabolism and is often present in those with CKD(35). To determine the prevalence and pattern of dyslipidemia in children with CKD, a cross-sectional analysis of lipid measurements was performed in 391 CKiD participants (36). Forty-five percent of the children had dyslipidemia (defined as triglycerides >130 mg/dl, high-density lipoprotein [HDL] cholesterol <40 mg/dl, or non-HDL cholesterol >160 mg/dl) or combined dyslipidemia (defined as the presence of two or more lipid abnormalities) (36). Hypertriglyceridemia was present in 32% (n=126) of the CKiD cohort. Overweight or obese children had triglyceride levels on average 30% higher than those with a normal BMI ($p \leq 0.01$), and 61% of children with nephrotic-range proteinuria had hypertriglyceridemia. Other lipid abnormalities were also common in the CKiD cohort, with 16% having non-HDL-C levels greater than 160 mg/dL and 21% with low HDL-C levels less than 40 mg/dL; such abnoramlities were associated with increased age, obesity, and lower GFR (36).

An assessment of the relationship between GFR and the prevalence of dyslipidemia in the CKiD cohort revealed that children with a lower GFR (<30 versus >50 ml/min/1.73 m^2) had a significantly greater risk of having dyslipidemia and a nearly nine fold greater risk of combined dylipidemia (31). Increasing levels of proteinuria were also associated with an increased prevalence of dyslipidemia. Due to the high prevalence of dyslipidemia in children with CKD, these findings support recommendations to screen children with CKD for dyslipidemia so as to identify this risk factor early, to guide therapy, and ideally to improve cardiovascular health.

Anemia

Like traditional cardiovascular risk factors such as hypertension, LVH, and dyslipidemia, anemia also has been linked to poor cardiovascular outcomes and increased morbidity and mortality in children (37). Treatment of CKD-associated anemia has been associated with improvements in quality of life, neurocognitive function, and exercise tolerance (38, 39). To gain a better understanding of the relationship between hemoglobin levels and GFR, baseline hemoglobin values and iGFR were evaluated in 340 CKiD participants (40).

Anemia was defined by the 2006 NKF-KDOQI anemia guidelines as a hemoglobin level less than the fifth percentile of the reference range, (10.7–13.5 g/dL, based on NHANES III data) after adjusting for age and sex (41). Forty-five percent of the children in CKiD were anemic and hemoglobin levels were found to progressively decline when iGFR fell below 43 ml/min/1.73m^2 (40). Sixty percent of patients with anemia were not receiving erythropoiesis stimulating agents (ESA) and, of the children receiving an ESA, 14% had a hemoglobin level ≤11 g/dL. Results of this analysis emphasize the importance of recognizing the potential for hemoglobin decline and assessing the need for anemia treatment early in the course of CKD in children.

To evaluate racial disparities in anemia in children with CKD, hemoglobin differences by race were evaluated in 429 study participants (42). Results showed that African American race was associated with hemoglobin values that were on average 0.6 g/dL lower than their white counterparts, independent of GFR or cause of CKD. Fewer African American children had hemoglobin values greater than the 5th percentile for age and sex, and the disparity was even more marked at lower hemoglobin values (42). More studies are needed to evaluate whether early screening and initiation of therapy for anemia in African American children leads to improved outcomes and to explore if the definition of anemia should expand beyond age and sex to also include race (43).

Though the diagnosis of anemia in children differs with age and sex, the target hemoglobin levels that guide anemia therapy in children with CKD do not vary by age and sex. Furthermore, diagnostic and treatment guidelines are extrapolated mainly from adult references and influenced by findings from studies conducted in adults (44–46). Further investigation is needed to evaluate if current NKF-KDOQI hemoglobin target levels in children with anemia in CKD allow for optimal growth, development, and exercise tolerance, and to evaluate the effects of therapy on kidney function and cardiovascular disease risk (47).

Growth

Growth retardation is the most visible of all complications experienced by children with CKD. Historically, contributing factors for poor growth include abnormalities of the growth hormone IGF1 (insulin-like growth factor 1) axis, acidosis, malnutrition, and renal osteodystrophy (48).

To further examine the factors that contribute to poor growth in this patient population, the effect of abnormal birth history on growth outcomes was studied in 426 children enrolled in CKiD (49). This analysis revealed that a high prevalence (17%) of children with CKD were born with low birth weight (LBW; <2500 grams); this prevalence is substantially higher than the 7.4% to 8.2% prevalence of LBW seen in the United States (49a). Fourteen percent of the CKiD cohort was small for gestational age (SGA; birth weight less than 10th percentile for gestational age) and 40% of the cohort required neonatal intensive care immediately after birth (49). Noteworthy was the finding that children with a history of LBW or SGA had an additional negative effect on z-scores for both height (LBW: −0.43 ± 0.14, $p < 0.01$; SGA: −0.29 ± 0.16, $p = 0.07$) and weight (LBW: −0.37 ± 0.16, $p = 0.02$; SGA: −0.41 ± 0.19, $p = 0.03$), which suggests that abnormal birth weight may be associated with poor growth (49). These novel findings identify children with CKD and a history of LBW and SGA as having additional risk factors for abnormal growth independent of kidney function (49). In turn, these children may require earlier nutritional intervention and/or growth hormone therapy to optimize growth.

Longitudinal growth impairment is common in children with CKD and has been shown to adversely affect psychosocial development and quality of life in adults with child-onset of

CKD (50). Pediatric registry data has also shown increased mortality rates in children with poor growth (51–53). Longitudinal analysis of CKiD data will study the effects of declining kidney function on growth and evaluate the impact of growth failure on morbidity in children with kidney disease.

Health-Related Quality of Life

The health-related quality of life (HRQoL) of children with CKD is an important outcome measured in the CKiD study. Data from 402 children who completed the Pediatric Inventory of Quality of Life Core Scales (PedsQL) were analyzed and compared to PedsQL results in healthy children (54, 55). Children with CKD reported poorer overall HRQoL scores and poorer physical, school, emotional, and social domain scores compared to healthy children ($p<0.001$ for all parameters). Short stature (<5th percentile for height) was associated with significantly lower scores in the physical functioning domain (95% confidence interval [CI]: −10.9 to −0.6; P<.05) (54). Similar findings have been published in cross-sectional studies of children with CKD in Brazil and Canada; these results emphasize the importance of identifying decreased HRQoL in children with CKD and their families in order to provide appropriate support (49, 50).

In an effort to identify factors specifically impacting HRQoL of children with urologic disorders in CKiD, the prevalence and impact of urinary incontinence on HRQoL was examined in 329 children who were 5 years of age or older (56). Seventy-one percent (n=235) of the children were toilet trained, 23% (n=76) suffered frequent enuresis, and 6% (n=18) were incontinent. The diagnosis of obstructive uropathy was common (45.5%) in children who were incontinent. Children who were incontinent had significantly lower scores in the physical (−15, 95% CI, −29.8 to −1.9, p=0.03) and school (−15.3, 95% CI, −29.8 to −0.8, p=0.04) functioning scales, as well as a lower average total score (95% CI, −25.2 to −1.8, p=0.02) on the PedsQL child report compared to children who were toilet trained (56). These results highlight the importance of recognizing that urinary incontinence is common in children with CKD and that its presence has a substantial negative influence on the HRQoL of the affected children. Most importantly, inquiry and detection provide an opportunity to treat the problem.

Similarly, sleep disturbances and fatigue can adversely affect the HRQoL of children with CKD, along with their behavior, ability to learn and physical development (57). To further define the frequency and severity of sleep problems in children with CKD, data from 301 children enrolled in the CKiD study were analyzed (58). Adolescents (>14 years) with a lower iGFR (<50 ml/min per $1.73m^2$) reported falling asleep 2 to 3 times more often during the day compared to younger children with higher GFRs. Using an antidepressant or CNS-stimulating agent was associated with a greater frequency of trouble sleeping. Most noteworthy was the finding that a report of “often” or “almost always” having trouble sleeping from a parent or child was associated with lower PedsQL scores (58).

With sleep disturbances being common in children with CKD, the frequency and severity of fatigue symptoms was analyzed from CKiD data as well. Results showed that children with a iGFR <30 ml/min per $1.73m^2$ were almost four times more likely to report severe weakness than those with a mGFR ≥ 50 ml/min per $1.73m^2$ (58). Further analysis found that having “moderate” or “severe” weakness was significantly associated with a lower HRQoL (58). Results from this study identified the importance of detecting and managing sleep problems and daytime fatigue due to the potential positive impact therapy may have on HRQoL in addition to cognitive functioning, emotional regulation, and behavior in children with CKD (59).

Neurocognitive status

Previous studies of children with CKD suggest that toddlers and children with ESRD are at increased risk for delays in neurocognitive development; however, little information exists on this topic in children with mild to moderate CKD (4). A report of baseline neurocognitive function in the CKiD cohort revealed 21% to 40% of participants scored at least one standard deviation below normative data on measures of intelligence quotient, academic achievement, attention regulation, and executive functioning (60, 61), and children with nephrotic range proteinuria (UPCR >2 g/g) scored lower on verbal and full scale IQ and attention variability compared to those without significant proteinuria (60). In an accompanying analysis, CKiD cohort participants with hypertension scored lower on visual-spatial organization, planning, constructive abilities, and nonverbal reasoning (60). Results from these studies highlight the importance of recognizing neurocognitive dysfunction in children with CKD early because of the significant impact it may have on school performance and the opportunity it presents for prompt intervention.

Conclusion

CKD is an important condition in children. Cross-sectional analysis of baseline CKiD data has revealed valuable information that better defines the prevalence of comorbid conditions and associated risk factors, including hypertension, LVH, dyslipidemia, anemia, poor growth, and abnormal neurocognitive development, that accompany CKD. To date, CKiD data has facilitated the development of more accurate estimating equations for GFR, which will be valuable to monitor changes in kidney function of children over time and to identify risk factors associated with CKD progression. CKiD data also identified a high percentage of children with anemia, even at preserved eGFRs, prompting the need for further investigation to define the contributing factors. Further analysis of CKiD data will evaluate the impact of lower hemoglobin values on kidney function, cardiovascular health, growth, and neurocognitive development with the goal of helping define optimal hemoglobin targets based on clinical outcomes specifically for children that will guide therapy.

CKiD identified the prevalence of cardiovascular disease and associated risk factors and found hypertension and dyslipidemia to be commonly present in the CKiD cohort, with LVH present more often in children with hypertension or masked hypertension. These findings suggest that routine screening with ABPM and echocardiography may be beneficial to monitor the cardiovascular health of children with CKD. Longitudinal follow up of the cohort will provide valuable insights into the impact of progressive disease severity on neurocognitive development and growth experienced by this unique patient population. Tremendous work remains to be done, but CKiD has identified critical targets and developed important information to support intervention trails to address issues that issues that stem from CKD in children.

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References

1. Collins AJ, Foley RN, Herzog C, Chavers B, Gilbertson D, Ishani A, et al. US Renal Data System 2010 Annual Data Report. Am J Kidney Dis. Jan; 57(1 Suppl 1):A8, e1–526. [PubMed: 21184928]

2. Wong H, Mylrea K, Feber J, Drukker A, Filler G. Prevalence of complications in children with chronic kidney disease according to KDOQI. Kidney Int. 2006 Aug; 70(3):585–90. [PubMed: 16788689]

3. Querfeld U. Undertreatment of cardiac risk factors in adolescents with renal failure. Perit Dial Int. 2001; 21(Suppl 3):S285–9. [PubMed: 11887837]

4. Gerson AC, Butler R, Moxey-Mims M, Wentz A, Shinnar S, Lande MB, et al. Neurocognitive outcomes in children with chronic kidney disease: Current findings and contemporary endeavors. Ment Retard Dev Disabil Res Rev. 2006; 12(3):208–15. [PubMed: 17061289]

5. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol. 2007 Dec; 22(12):1999–2009. [PubMed: 17310363]

6. McDonald SP, Craig JC. Long-term survival of children with end-stage renal disease. N Engl J Med. 2004 Jun 24; 350(26):2654–62. [PubMed: 15215481]

7. Furth SL, Cole SR, Moxey-Mims M, Kaskel F, Mak R, Schwartz G, et al. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Clin J Am Soc Nephrol. 2006 Sep; 1(5):1006–15. [PubMed: 17699320]

8. Nationa Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002 Feb; 39(2 Suppl 1):S1–266. [PubMed: 11904577]

9. Schwartz GJ, Haycock GB, Edelmann CM Jr, Spitzer A. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics. 1976 Aug; 58(2):259–63. [PubMed: 951142]

10. Schwartz GJ, Furth SL. Glomerular filtration rate measurement and estimation in chronic kidney disease. Pediatr Nephrol. 2007 Nov; 22(11):1839–48. [PubMed: 17216261]

11. Stake G, Monn E, Rootwelt K, Monclair T. The clearance of iohexol as a measure of the glomerular filtration rate in children with chronic renal failure. Scand J Clin Lab Invest. 1991 Dec; 51(8):729–34. [PubMed: 1806987]

12. Schwartz GJ, Furth S, Cole SR, Warady B, Munoz A. Glomerular filtration rate via plasma iohexol disappearance: pilot study for chronic kidney disease in children. Kidney Int. 2006 Jun; 69(11): 2070–7. [PubMed: 16612328]

13. Schwartz GJ, Abraham AG, Furth SL, Warady BA, Munoz A. Optimizing iohexol plasma disappearance curves to measure the glomerular filtration rate in children with chronic kidney disease. Kidney Int. Jan; 77(1):65–71. [PubMed: 19847157]

14. Ng DK, Schwartz GJ, Jacobson LP, Palella FJ, Margolick JB, Warady BA, et al. Universal GFR determination based on two time points during plasma iohexol disappearance. Kidney Int. Jun 8.

15. Schwartz GJ, Munoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009 Mar; 20(3):629–37. [PubMed: 19158356]

16. Wong CS, Pierce CB, Cole SR, Warady BA, Mak RH, Benador NM, et al. Association of proteinuria with race, cause of chronic kidney disease, and glomerular filtration rate in the chronic kidney disease in children study. Clin J Am Soc Nephrol. 2009 Apr; 4(4):812–9. [PubMed: 19297612]

17. Fischer MJ, Go AS, Lora CM, Ackerson L, Cohan J, Kusek JW, et al. CKD in Hispanics: Baseline characteristics from the CRIC (Chronic Renal Insufficiency Cohort) and Hispanic-CRIC Studies. Am J Kidney Dis. Aug; 58(2):214–27. [PubMed: 21705121]

18. Wuhl E, Mehls O, Schaefer F. Antihypertensive and antiproteinuric efficacy of ramipril in children with chronic renal failure. Kidney Int. 2004 Aug; 66(2):768–76. [PubMed: 15253732]

19. Ardissino G, Testa S, Dacco V, Vigano S, Taioli E, Claris-Appiani A, et al. Proteinuria as a predictor of disease progression in children with hypodysplastic nephropathy. Data from the Ital Kid Project. Pediatr Nephrol. 2004 Feb; 19(2):172–7. [PubMed: 14673629]

20. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia). Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. Lancet. 1997 Jun 28; 349(9069):1857–63. [PubMed: 9217756]

21. Litwin M. Risk factors for renal failure in children with non-glomerular nephropathies. Pediatr Nephrol. 2004 Feb; 19(2):178–86. [PubMed: 14685838]
22. Mitsnefes MM. Cardiovascular morbidity and mortality in children with chronic kidney disease in North America: lessons from the USRDS and NAPRTCS databases. Perit Dial Int. 2005 Feb; 25(Suppl 3):S120–2. [PubMed: 16048275]
23. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, et al. Blood pressure in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children study. Hypertension. 2008 Oct; 52(4):631–7. [PubMed: 18725579]
24. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004 Aug; 114(2 Suppl):555–76. 4th Report. [PubMed: 15286277]
25. Wuhl E, Trivelli A, Picca S, Litwin M, Peco-Antic A, Zurowska A, et al. Strict blood-pressure control and progression of renal failure in children. N Engl J Med. 2009 Oct 22; 361(17):1639–50. [PubMed: 19846849]
26. Peralta CA, Norris KC, Li S, Chang TI, Tamura MK, Jolly SE, et al. Blood Pressure Components and End-stage Renal Disease in Persons With Chronic Kidney Disease: The Kidney Early Evaluation Program (KEEP). Arch Intern Med. Jan 9; 172(1):41–7. [PubMed: 22232147]
27. Collins AJ, Foley RN, Chavers B, Gilbertson D, Herzog C, Johansen K, et al. US Renal Data System 2011 Annual Data Report. Am J Kidney Dis. Jan.59(1 Suppl 1):A7. [PubMed: 22177944]
28. McClellan WM, Newsome BB, McClure LA, Howard G, Volkova N, Audhya P, et al. Poverty and racial disparities in kidney disease: the REGARDS study. Am J Nephrol. 32(1):38–46. [PubMed: 20516678]
29. Jolly SE, Burrows NR, Chen SC, Li S, Jurkovitz CT, Norris KC, et al. Racial and ethnic differences in mortality among individuals with chronic kidney disease: results from the Kidney Early Evaluation Program (KEEP). Clin J Am Soc Nephrol. Aug; 6(8):1858–65. [PubMed: 21784835]
30. Duru OK, Li S, Jurkovitz C, Bakris G, Brown W, Chen SC, et al. Race and sex differences in hypertension control in CKD: results from the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2008 Feb; 51(2):192–8. [PubMed: 18215697]
31. Mitsnefes M, Flynn J, Cohn S, Samuels J, Blydt-Hansen T, Saland J, et al. Masked hypertension associates with left ventricular hypertrophy in children with CKD. J Am Soc Nephrol. Jan; 21(1): 137–44. [PubMed: 19917781]
32. Minutolo R, Agarwal R, Borrelli S, Chiodini P, Bellizzi V, Nappi F, et al. Prognostic role of ambulatory blood pressure measurement in patients with nondialysis chronic kidney disease. Arch Intern Med. Jun 27; 171(12):1090–8. [PubMed: 21709109]
33. Matsumoto M, Io H, Furukawa M, Okumura K, Masuda A, Seto T, et al. Risk factors associated with increased left ventricular mass index in chronic kidney disease patients evaluated using echocardiography. J Nephrol. Jan 10.:0.
34. Cioffi G, Tarantini L, Frizzi R, Stefenelli C, Russo TE, Selmi A, et al. Chronic kidney disease elicits excessive increase in left ventricular mass growth in patients at increased risk for cardiovascular events. J Hypertens. Mar; 29(3):565–73. [PubMed: 21150636]
35. Saland JM, Ginsberg HN. Lipoprotein metabolism in chronic renal insufficiency. Pediatr Nephrol. 2007 Aug; 22(8):1095–112. [PubMed: 17390152]
36. Saland JM, Pierce CB, Mitsnefes MM, Flynn JT, Goebel J, Kupferman JC, et al. Dyslipidemia in children with chronic kidney disease. Kidney Int. Dec; 78(11):1154–63. [PubMed: 20736985]
37. Mitsnefes MM, Kimball TR, Kartal J, Witt SA, Glascock BJ, Khoury PR, et al. Progression of left ventricular hypertrophy in children with early chronic kidney disease: 2-year follow-up study. J Pediatr. 2006 Nov; 149(5):671–5. [PubMed: 17095341]
38. Montini G, Zacchello G, Baraldi E, Zanconato S, Suppiej A, Fabris F, et al. Benefits and risks of anemia correction with recombinant human erythropoietin in children maintained by hemodialysis. J Pediatr. 1990 Oct; 117(4):556–60. [PubMed: 2213378]
39. Akizawa T, Gejyo F, Nishi S, Iino Y, Watanabe Y, Suzuki M, et al. Positive outcomes of high hemoglobin target in patients with chronic kidney disease not on dialysis: a randomized controlled study. Ther Apher Dial. Oct; 15(5):431–40. [PubMed: 21974695]

40. Fadrowski JJ, Pierce CB, Cole SR, Moxey-Mims M, Warady BA, Furth SL. Hemoglobin decline in children with chronic kidney disease: baseline results from the chronic kidney disease in children prospective cohort study. Clin J Am Soc Nephrol. 2008 Mar; 3(2):457–62. [PubMed: 18235140]
41. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. Am J Kidney Dis. 2006 May; 47(5 Suppl 3):S11–145. [PubMed: 16678659]
42. Atkinson MA, Pierce CB, Zack RM, Barletta GM, Yadin O, Mentser M, et al. Hemoglobin differences by race in children with CKD. Am J Kidney Dis. Jun; 55(6):1009–17. [PubMed: 20418001]
43. Filler G, Huang SH, Sharma AP. Racial disparities in hemoglobin concentration in children with CKD. Am J Kidney Dis. Jun; 55(6):981–3. [PubMed: 20497835]
44. Drueke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006 Nov 16; 355(20):2071–84. [PubMed: 17108342]
45. Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006 Nov 16; 355(20):2085–98. [PubMed: 17108343]
46. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. American Journal of Kidney Diseases. 2007; 50(3):471–530. [PubMed: 17720528]
47. Filler G, Mylrea K, Feber J, Wong H. How to define anemia in children with chronic kidney disease? Pediatr Nephrol. 2007 May; 22(5):702–7. [PubMed: 17216248]
48. Mahesh S, Kaskel F. Growth hormone axis in chronic kidney disease. Pediatr Nephrol. 2008 Jan; 23(1):41–8. [PubMed: 17676425]
49. Greenbaum LA, Munoz A, Schneider MF, Kaskel FJ, Askenazi DJ, Jenkins R, et al. The association between abnormal birth history and growth in children with CKD. Clin J Am Soc Nephrol. Jan; 6(1):14–21. 49a. March of Dimes. [PubMed: 21030583]
50. Rosenkranz J, Reichwald-Klugger E, Oh J, Turzer M, Mehls O, Schaefer F. Psychosocial rehabilitation and satisfaction with life in adults with childhood-onset of end-stage renal disease. Pediatr Nephrol. 2005 Sep; 20(9):1288–94. [PubMed: 15942781]
51. Schaefer F, Wingen AM, Hennicke M, Rigden S, Mehls O. Growth charts for prepubertal children with chronic renal failure due to congenital renal disorders. European Study Group for Nutritional Treatment of Chronic Renal Failure in Childhood. Pediatr Nephrol. 1996 Jun; 10(3):288–93. [PubMed: 8792392]
52. Furth SL, Hwang W, Yang C, Neu AM, Fivush BA, Powe NR. Growth failure, risk of hospitalization and death for children with end-stage renal disease. Pediatr Nephrol. 2002 Jun; 17(6):450–5. [PubMed: 12107811]
53. Furth SL, Stablein D, Fine RN, Powe NR, Fivush BA. Adverse clinical outcomes associated with short stature at dialysis initiation: a report of the North American Pediatric Renal Transplant Cooperative Study. Pediatrics. 2002 May; 109(5):909–13. [PubMed: 11986455]
54. Gerson AC, Wentz A, Abraham AG, Mendley SR, Hooper SR, Butler RW, et al. Health-related quality of life of children with mild to moderate chronic kidney disease. Pediatrics. Feb; 125(2):e349–57. [PubMed: 20083528]
55. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr. 2003 Nov-Dec;3(6):329–41. [PubMed: 14616041]
56. Dodson JL, Cohn SE, Cox C, Hmiel PS, Wood E, Mattoo TK, et al. Urinary incontinence in the CKiD cohort and health related quality of life. J Urol. 2009 Oct; 182(4 Suppl):2007–14. [PubMed: 19695588]
57. Stores G. Children's sleep disorders: modern approaches, developmental effects, and children at special risk. Dev Med Child Neurol. 1999 Aug; 41(8):568–73. [PubMed: 10479046]
58. Roumelioti ME, Wentz A, Schneider MF, Gerson AC, Hooper S, Benfield M, et al. Sleep and fatigue symptoms in children and adolescents with CKD: a cross-sectional analysis from the

chronic kidney disease in children (CKiD) study. Am J Kidney Dis. Feb; 55(2):269–80. [PubMed: 20034719]

59. Owens LJ, France KG, Wiggs L. REVIEW ARTICLE: Behavioural and cognitive-behavioural interventions for sleep disorders in infants and children: A review. Sleep Med Rev. 1999 Dec; 3(4):281–302. [PubMed: 12531150]
60. Hooper SR, Gerson AC, Butler RW, Gipson DS, Mendley SR, Lande MB, et al. Neurocognitive Functioning of Children and Adolescents with Mild-to-Moderate Chronic Kidney Disease. Clin J Am Soc Nephrol. Jul 7.
61. Lande MB, Gerson AC, Hooper SR, Cox C, Matheson M, Mendley SR, et al. Casual Blood Pressure and Neurocognitive Function in Children with Chronic Kidney Disease: A Report of the Children with Chronic Kidney Disease Cohort Study. Clin J Am Soc Nephrol. Jun 23.

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Table 1

CKiD Study Measurements by Visit

Area	Measurement	Initial Visit	Follow-Up Visits		
			Every 3 to 6 mo	Years 1, 3, 5, 7	Years 2, 4, 6, 8
General	Physical exam/ medical history	X	X	X	X
	Medication use	X	X	X	X
	Symptom checklist	X	X	X	X
Kidney	mGFR **	X		X	
	Renal panel	X		X	X
	UPCR (first morning urine)	X		X	X
	Cystatin C-based eGFR	X		X	
	serum creatinine ***	X		X	X
	Local laboratory tests †	X		X	X
Cardiovascular	Echocardiogram			X	
	ABPM			X	
	Carotid IMT *			X	
	Lipid profile			X	
	Blood pressure	X	X	X	X
Neurocognitive	Pediatric Quality of Life survey		X	X	X
	Cognitive and development		X		X
	Behavioral assessment		X		X
	Magnetic resonance imaging *		X		X
	Neuropsychological assessment *		X		X
Growth and Nutrition	Height and length	X	X	X	X
	Weight	X	X	X	X
	Head and mid-arm circumference	X	X	X	X
	Tanner stage	X	X	X	X
	3-day diet record, food frequency		X	X	X

Area	Measurement	Initial Visit	Follow-Up Visits		
			Every 3 to 6 mo	Years 1, 3, 5, 7	Years 2, 4, 6, 8
	Physical activity		X	X	X
Inflammation	Wide-range C-reactive protein		X		X
Bone Health	Intact PTH		X		X
	Bone biopsy****		X		Year 2 only

† Included renal panel, complete blood count, and urine pregnancy test

* goal to do in 30 patients at select centers

** based on iohexol clearance

*** measured by high-performance liquid chromatography

**** goal to conduct 10.

Abbreviations: mGFR, measured glomerular filtration rate; UPCR, urine protein-creatinine ratio; eGFR, estimated glomuler filtration rate; ABPM, ambulatory blood pressure monitoring; IMT, intramedial thickness; PTH, parathyroid hormone.

Table 2

CKiD study Baseline patient characteristics

Characteristic[a]	Value
Age, y	11 [7,14]
Male sex	364 (62)
Race:	
Caucasian	384 (66)
Black	137 (23)
Multi-racial or Other	65 (11)
Hispanic ethnicity	84 (15)
Weight percentile	46 [18,79]
Weight z-score	−0.10 [−0.92,0.81]
Height percentile	24 [7,54]
Height z-score	−0.69 [−1.45,0.11]
BMI ≥ 90th percentile	134 (24)
BMI < 15th percentile	55 (10)
BMI percentile	65 [35,89]
Low birth weight, <2500 g	105 (19)
Premature birth, <36 wk	72 (13)
mGFR, ml/min/1.73 m^2	43.8 [32.8, 56.7]
Primary CKD diagnosis:	
Glomerular	129 (22)
Genitourinary, cystic, or hereditary	416 (71)
Other	41 (7)
Duration of CKD, y	6.4 [3.0,10.3]
Percent of life with CKD	92 [35,100]
Maternal education:	
High school or less/ <13 y	252 (43)
More than high school/13 to <16 y	164 (28)
4 years of college/≥16 y	170 (29)

Note: N = 586. continuous variables are given as median [25th, 75th percentile] or number (percentage).

[a]Missing data: n=8 missing Hispanic ethnicity; n=16 missing height percentile; n=28 missing BMI percentile ≥ 90th percentile; n=28 missing BMI percentile < 15th percentile; n=31 missing height velocity; n=16 missing height < 3rd percentile

Abbreviations: BMI, body mass index; mGFR, measured glomerular filtration rate, CKD, chronic kidney disease; CKiD, CKD in Children.

Table 3

Controlled and Uncontrolled Blood Pressure in CKiD*

Characteristic	Uncontrolled BP (n=96)	Controlled BP (n=104)	p-value
Male sex	67 (68)	53 (51)	0.01
Black Race	22 (22)	10 (10)	0.02
CKD duration, y	6 ± 4	8 ± 4	<0.01
Antihypertensive medication use:			
ACEi/ARB	74 (76)	92 (88)	0.02
CCB	32 (33)	17 (16)	<0.01
Other medications:	34 (35)	22 (21)	0.03

N=202 receiving antihypertensive medications. .

*Seventy-three children with SBP and DBP <90th percentile receiving antihypertensive medications but not reporting a diagnosis of high BP were excluded from analysis. Data from Flynn et al.[23]

Abbreviations: BP, blood pressure; ACEi: angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease

Box 1

CKiD Estimating Equations

Complete estimating equation

$eGFR\ (ml/min/1.73m^2) = 39.1[height\ (m)/SCr\ (mg/dl)]^{0.516} * [1.8/SCysC\ (mg/L)]^{0.294} * [30/SUN\ (mg/dl\ )]^{0.169} \times [1.099]^{male} \times [height\ (m)/1.4]^{0.188}$

Bedside formula

$eGFR\ (ml/min/1.73\ m^2) = [0.413 * Height\ (cm)] / [SCr\ (mg/dl)]$

Abbreviations: CKiD, CKD in Children; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; SCysC, serum cystatin C; SUN, serum urea nitrogen

Box 2

CKiD Study Participants Inclusion and Exclusion Criteria

Inclusion Criteria

- Age 1 to 16 yr
- eGFR * 30 to 90 ml/min/1.73 m^2
- Informed consent (from parent or guardian)

Exclusion Criteria

- Solid organ, bone marrow, or stem cell transplant
- Dialysis within last 3 months
- Cancer or HIV diagnosis within last 12 months
- Inability to complete major data collection procedures
- Current enrollment in randomized clinical trial with unknown specific treatment
- Plans to relocate away from any CKiD site
- History of structural heart disease
- Genetic syndromes involving central nervous system
- History of profound mental retardation (IQ <40, significant impairment in adaptive function, and/or inability to independently execute self-care skills)

* eGFR estimated via the Schwartz equation using height and two measurements of serum creatinine obtained 18 mo before enrollment.

Abbreviations: eGFR, estimated glomerular filtration rate; HIV, human immunodeficiency virus; IQ, intelligence quotient; CKiD, CKD in Children.

Box 3

Summary of Novel Findings from CKiD study

1. Identify novel and traditional risk factors for the progression of CKD

- New bedside CKiD formula to estimate GFR in children age 1–16 years with GFR from 15 to 75 ml/min/1.73m^2 (see Box 1).
- New GFR estimating formula using enzymatic creatinine shows 25% reduction in eGFR from Schwartz equation based on the Jaffe method for measuring serum creatinine.
- Race, lower iGFR, and glomerular cause of CKD are independently associated with level of proteinuria.
- More than 30% of the children met the NKF-KDOQI definition for anemia in pediatric patients, hemoglobin concentration < 5th percentile of normal when adjusted for age and sex.
- Hemoglobin level declines in a linear manner below a threshold iGFR of 43 ml/min/1.73m^2, independent of age, race, sex, and underlying diagnosis.
- African American children with CKD have lower hemoglobin levels and a higher prevalence of anemia than Caucasian children despite no difference in erythropoietin or iron therapy.

2. Characterize the impact of a decline in kidney function on neurodevelopment, cognitive abilities, and behavior

- At study entry, 21% to 40% of children with CKD scored more than 1 SD below norm on a variety of neurocognitive tests.
- Children with proteinuria (UPCR >2) scored lower on verbal IQ, full-scale IQ, and attention variability compared to those without elevated proteinuria.
- High blood pressure (SBP and/or DBP ≥ 90th percentile) is independently associated with lower scores on performance IQ, which tests visual-spatial organization and construction, and non-verbal reasoning.
- HRQoL is adversely affected compared to healthy controls early in the course of CKD.
- Urinary incontinence occurs in almost 30% of children with CKD and is associated with impaired HRQoL.
- Sleep and fatigue problems in children with CKD are associated with decreased HRQoL.

3. Identify the prevalence and the evolution of cardiovascular disease risk factors in children with CKD

- Nephrotic range proteinuria is significantly associated with elevated DBP.
- African American children had a higher risk of having elevated blood pressures at entry into the CKiD study.
- Children with hypertension not receiving ACE inhibitor and/or ARB medication have an increased prevalence of uncontrolled BP.
- Use of calcium channel blockers is more common in children with uncontrolled BP.
- Strong association between the presence of hypertension and LVH.
- Likelihood of LVH was 4 times higher in children with masked hypertension compared to normotensive children.

4. Examine the effects of declining GFR on growth and assess the consequences of growth failure on morbidity in children with CKD

- Low birth weight and being small for gestational age at birth are novel risk factors for short stature in children with CKD.
- Short stature in children with CKD is associated with lower scores in the physical functioning domain of the PedsQL.

Abbreviations: ACE: angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; LVH, left ventricular hypertrophy; HRQoL, health-related quality of life; PedsQL, Pediatric Inventory of Quality of Life Core Scales; DBP, diastolic blood pressure; SBP, systolic blood pressure; IQ, intelligence quotient; SD, standard deviation; iGFR, iohexol-based glomerular filtration rate; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; CKD, chronic kidney disease; CKiD, CKD in Children. NKF-KDOQI, National Kidney Foundation's Kidney Disease Outcomes Quality Initiative.