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Recommendations for Kidney Health Monitoring in Neonatal Intensive Care Unit Graduates: A Modified Delphi Consensus Statement

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Neonatal Kidney Health Consensus Workshop Author List

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Abstract

Importance: Kidney disease is common in infants admitted to the Neonatal Intensive Care Unit (NICU). Despite the risk of chronic kidney disease (CKD) in infants discharged from the NICU, neither evidence- nor expert-based recommendations exist to guide clinical care after discharge.

Objective: To develop recommendations for risk stratification and kidney health monitoring among infants following discharge from the NICU.

Evidence Reviewed: At the National Institute of Health (NIH) supported "Consensus Workshop to Address Kidney Health in Neonatal Intensive Care Unit Graduates" meeting conducted in February 2024, a panel of 51 neonatal nephrology experts focused on three at-risk groups: (1) preterm infants, (2) critically ill infants with acute kidney injury (AKI), and (3) infants with critical cardiac disease. Using established modified Delphi processes, workgroups derived consensus recommendations.

Findings: In this modified Delphi consensus statement, the panel developed 10 consensus recommendations, identified gaps in knowledge, and prioritized areas of future research. Principal suggestions include risk stratification at time of hospital discharge, family and provider education and counseling for subsequent kidney health follow-up, and blood pressure assessment as part of outpatient care.

Conclusion and Relevance: Preterm infants, critically ill infants with AKI, and infants with critical cardiac disease are at increased risk of CKD. We recommend (1) risk assessment at the time of discharge, (2) provider and family education, and (3) kidney health assessments based on the degree of risk. Future work should focus on improved risk stratification, identification of early kidney dysfunction, and development of interventions to improve long-term kidney health.

Introduction:

Acute and chronic kidney complications are common among infants admitted to the neonatal intensive care unit (NICU).[1–4] Based on the existing literature, three groups are most vulnerable for poor long-term kidney health: (1) preterm infants, (2) critically ill infants with acute kidney injury (AKI), and (3) infants with critical cardiac disease.[5–14] Premature infants (<34 weeks of gestation) have a four-fold increase in chronic kidney disease (CKD) by adolescence.[5,14] AKI is a known risk factor for subsequent CKD.[4,7,15] Infants with critical cardiac disease have high rates of AKI and CKD during childhood.[16] The burden of CKD will likely continue to increase as more vulnerable infants survive into adulthood.

Despite increased CKD risk in infants discharged from the NICU, recommendations for kidney health monitoring during childhood do not exist.[17] Additionally, there are gaps in knowledge which must be addressed to optimize follow-up strategies and ultimately reduce the growing burden of CKD in these at-risk infant populations. To address these key

knowledge gaps, we convened a National Institute of Health (NIH)-supported workshop to develop expert-based follow-up recommendations based on existing evidence, highlight gaps in knowledge, and identify opportunities to improve care.

Methods:

The NIH-supported "Consensus Workshop to Address Kidney Health in Neonatal Intensive Care Unit Graduates" took place in Indianapolis, Indiana, February 27–28, 2024. The workshop followed the principles of the Acute Disease Quality Initiative (ADQI) consensus meetings.[18,19] We sought to combine interpretation of current knowledge with expert opinion to create recommendations for kidney health follow-up, describe gaps in knowledge, and establish research priorities.

Prior to the meeting, workgroups performed an objective scientific review and evaluation of the literature through December 2023 of kidney health outcomes in (1) preterm infants, (2) critically ill infants with AKI and (3) infants with critical cardiac disease. Infants ≥34 weeks' gestation were included in the critically ill infant subgroup to align with gestational age cutoffs in the literature. Infants were considered to have critical cardiac disease if admitted either before or after surgery for congenital heart defects, those with complications following cardiac surgery, or those with acute heart failure. Infants in each of the 3 groups were stratified as being at-risk or high-risk for CKD (Table 1).

The three workgroups were composed of neonatology, critical care, cardiology, and nephrology specialists, including trainees (Supplemental Table 1). The in-person meeting was conducted using mixed workgroups and large-group panel discussion formats. A family representative , a primary care provider, and an expert in equity and care delivery offered their perspectives, participated in the large-group panel discussions, and provided feedback as recommendations were developed. Work before and after the in-person meeting was completed virtually.

Using a modified Delphi method, each workgroup developed recommendations for follow-up supported by the representative literature or expert opinion when the evidence was scarce, and articulated research gaps and priorities.[18,19] These recommendations were presented iteratively to the panel to develop consensus and required at least 2/3 support for adoption (Table 2, Figure 1). These consensus recommendations were based on existing evidence and expert opinion; thus, institutional approval was not required. All panel members consented to their inclusion in this article. SQUIRE guidelines were followed whenever applicable.[20]

Results:

Overarching Recommendations

1. Preterm infants (<34 weeks' gestation), critically ill infants with AKI, and infants with critical cardiac disease are *at-risk* of CKD following NICU discharge. We recommend all *at-risk* infants have a discharge kidney health evaluation that includes a properly obtained blood pressure (BP), serum creatinine, and kidney health education in preparation for hospital discharge.

2. In infants with evidence of kidney disease at discharge (defined by a serum creatinine ≥0.5mg/dL, BP >95th percentile for age, hypertension treated with medications, nephrocalcinosis, or a congenital abnormality of the kidney or urinary tract (CAKUT)), we recommend follow-up with pediatric nephrology according to local guidance.

3. In all other *at-risk* infants that do not meet criteria for kidney disease at discharge, we recommend family- and provider-focused education and counseling for subsequent kidney health follow-up. We recommend BP assessment at all healthcare encounters. We encourage coordination of kidney-focused follow-up and ongoing risk assessment with subspecialty specific care models.

Rationale: Mounting research has uncovered a high prevalence of CKD in children previously cared for in the NICU.[4,5,7,14] Patients discharged from the NICU with a history of preterm birth, critical illness with AKI, or critical cardiac disease appear to be at the highest risk of CKD.[4–14,21,22] The addition of "second hit" risk factors during childhood such as additional episodes of AKI, hypertension (HTN), diabetes, obesity, and nephrotoxic medication use, further increase CKD risk.[2,5–14,21,22] We recommend that AKI is defined using neonatal Kidney Disease: Improving Global Outcomes (KDIGO) criteria, with attention paid to accurate diagnosis, documentation and communication at discharge.[19,23,24] Our at-risk group is aligned with the recent KDIGO statement listing prematurity, small for gestational age birthweight, and AKI as risk factors for CKD development.[25]

Children with moderate CKD lose approximately 1% of their kidney function each year.[12] Early recognition of abnormal kidney function and stratification of CKD progression risk is essential. Both preventative and interventional strategies (i.e. nephrotoxin avoidance, BP monitoring and renin-angiotensin inhibition) support kidney health and delay CKD progression.[26,27] Therefore, we recommend a discharge kidney health evaluation, including a serum creatinine and a properly obtained BP, to allow for risk stratification and counseling.[28,29] We recommend serum creatinine, using a threshold of ≥0.5 mg/dL, given availability, low cost, and ease of interpretation (Supplemental Table 2). We recommend serum creatinine ≥0.5 mg/dL, HTN, or other kidney conditions at hospital discharge requires evaluation with providers knowledgeable in the care of children with CKD (Figure 1).

In infants at-risk of CKD at hospital discharge, we recommend that outpatient kidney assessment is integrated with other care whenever possible. Recognition of kidney disease risk and outpatient monitoring and education can be aided by multi-modal approaches.[23,30,31] We strongly recommend kidney health education occurs longitudinally using existing structures and resources.[32,33] Education of both family members (focusing on the importance of kidney-focused follow-up, avoidance of nephrotoxic medications and future AKI) and providers (focusing on CKD risk and strategies to optimize kidney health at NICU discharge and throughout childhood) and is paramount.

We encourage incorporation of kidney specific follow-up within already established programs and recommend follow-up occur in a systematic manner for all at-risk NICU

graduates. Recommended follow-up may occur in a variety of clinical settings depending on the patient population, location, resources, and subspeciality access.[32,35] Outpatient kidney evaluation may occur in-person or via telehealth.[32–34] Accurate BP assessment at outpatient visits and kidney-focused follow-up may occur in partnership with local providers, particularly in resource-limited settings.[29] The panel recognizes challenges in pediatric subspeciality access and have attempted to provide stratified and multi-disciplinary recommendations for follow-up.[35]

For all at-risk patients, we recommend BP monitoring at all healthcare encounters. For those at high-risk of CKD, we recommend a comprehensive kidney health assessment at two years of age that includes serum creatinine and cystatin C to estimate glomerular filtration rate (eGFR), BP assessment, and urine albumin/creatinine. The two-year assessment was chosen as kidney maturation should be complete by this age.[36–38] We advocate for use of cystatin C in combination with creatinine as it is muscle mass independent and has improved sensitivity for early CKD detection.[25,39] We also recommend urine screening for persistent albuminuria, as this and abnormal eGFR have therapeutic options (Figure 1).

The panel recognizes the challenges posed by these recommendations, particularly with respect to BP assessment. Our recommendations are in concert with existing American Academy of Pediatrics (AAP) guidelines advocating for BP assessment in those less than three years of age after NICU discharge at well-child care visits.[29] Children in these at-risk groups may have more contact with subspecialists. Therefore, we recommend BP assessments at all healthcare encounters.[28,29] We recognize AAP guidelines are inconsistently followed due to a variety of barriers.[29,40] Work is needed to improve BP assessment in infants.[41]

Recommendations for Preterm Infants (<34 Weeks' Gestational Age)

4. We recommend at-risk preterm infants (28 to <34 weeks' gestation) have BP assessment and kidney health education at 2 years of age in conjunction with standard care. Providers should consider comprehensive kidney health assessment if there are significant exposures that modulate risk.

5. We recommend high-risk preterm infants (<28 weeks' gestation, birthweight <1,500 grams, or history of AKI or dialysis) have a comprehensive kidney health assessment in conjunction with standard care at 2 years of age, or sooner if there are significant exposures or events that modulate risk.

Rationale: Nephrogenesis is near completion by 34–36 weeks of gestation.[42–44] Exposure to extrauterine environmental factors likely disrupts nephron formation following preterm birth, resulting in abnormal and/or lower nephron numbers.[42,43,45] Ongoing hyperfiltration and further nephron loss contribute to subsequent CKD and HTN.[9,46] Prediction of CKD development following preterm birth is difficult due to wide variation in nephron number, the absence of longitudinal follow-up cohort studies, and the resulting inability to risk stratify infants for early CKD detection.[21,46]

Over the last decade, multiple studies have linked preterm birth to increased risk of CKD and HTN.[14,47,48] In a cohort of children born 24–28 weeks' gestation, signs of CKD were detectable in 53% of patients at 2 years of age.[3,5] Of those evaluated, 18% had eGFR <90ml/min/1.73m^2, 36% had albuminuria, and 44% had elevated diastolic BP. In a Swedish birth registry study, the adjusted hazard ratio (HR) for CKD by adulthood in those born <28 weeks' gestation was 3.01 (95%CI 1.67–5.45).[14] Thus, we recommend, in addition to kidney health education and BP assessment at every healthcare encounter, infants born <28 weeks' gestation have a two-year comprehensive kidney health assessment. Assessment may occur sooner if additional CKD risk factors or significant exposures are present.

Infants born 28–34 weeks' gestation also have increased risk of CKD and HTN. A Swedish birth registry study demonstrated a HR for CKD at 43 years was 1.94 (95%CI 1.74–2.16).[14] A recent meta-analysis found children born preterm had lower eGFR, higher BP, albuminuria and smaller kidneys.[48] Therefore, we recommend infants born 28–34 weeks' gestation have BP assessment at every healthcare encounter and kidney health education at 2 years of age. In those with exposures modulating CKD risk, a comprehensive kidney health assessment may be indicated at two years of age.

In preterm infants, intrauterine growth restriction (IUGR) is an additional risk factor for developing CKD and HTN.[49] Thus, we included infants <1,500 grams as high-risk, capturing infants <10th percentile at 33 weeks' gestation and <3rd percentile at 34 weeks' gestation. In pediatric patients, AKI is an independent risk for CKD development.[50] However, studies examining this relationship in preterm infants are mixed.[3,11,47,51,52] We recommend preterm infants (28–34 weeks' gestation) with AKI or born <1,500 grams are considered high-risk for CKD and undergo comprehensive kidney health assessment at 2 years of age in addition to BP assessment and kidney education.

Recommendations for Infants with AKI (Born ≥34 Weeks' Gestational Age)

6. We recommend at-risk infants born ≥34 weeks' gestation (Stage 1 AKI) have a comprehensive kidney health assessment at 2 years of age in conjunction with standard health maintenance.

7. We recommend high-risk infants born ≥34 weeks' gestation (Stage 2/3 AKI, dialysis treatment, recurrent AKI, or AKI with severe non-renal comorbidities such as extracorporeal membrane oxygenation (ECMO), congenital diaphragmatic hernia (CDH), hypoxic-ischemic encephalopathy (HIE)) have a comprehensive kidney health assessment within 6 months of discharge. The frequency of subsequent assessments may vary based on clinical course but should include another assessment at two years of age.

8. If the 2-year comprehensive kidney health assessment is normal, infants ≥34 weeks' gestation with history of AKI may be discharged to routine well-child care, including annual BP assessment and ongoing kidney health education.

Rationale: Few studies evaluate CKD risk in infants ≥34 weeks' gestation with a history of AKI. A single center study assessing follow-up and early CKD detection in a cohort of infants from the Assessment of Worldwide Acute Kidney Injury Epidemiology (AWAKEN)

study found under-recognition of AKI in the NICU, insufficient follow-up, and lack of identification of long-term kidney sequelae.[1,53] A larger, long-term follow-up study suggests one-third of infants surviving an episode of AKI have CKD in childhood, but only half were ≥34 weeks' gestation.[54]

Several studies have examined CKD risk after AKI in the NICU in infants ≥ 34 weeks' gestation.[55–57] In children with a history of therapeutic hypothermia-treated HIE, one-third of survivors had decreased eGFR and albuminuria at 10 years of age, irrespective of AKI status.[55,56] In a follow-up study of children approximately 8 years after neonatal ECMO, 5% had mildly decreased eGFR (60–90 ml/min/1.73m^2), 12% had proteinuria, and 19% had HTN.[57] Children with AKI had 4.3 times higher odds of CKD or HTN than those without AKI (95%CI 1.6–12.1).[57] These studies, while limited in size and scope, informed our recommendations.

Studies in the pediatric population supplement the limited available evidence specific to neonatal AKI survivors. In a large prospective study examining long-term CKD risk in older critically ill children surviving AKI, 10% developed CKD within 3 years of AKI. Infants comprised nearly 40% of those who developed CKD.[15] These findings suggest critically ill infants with AKI are at-risk for CKD and HTN later in life. Thus, follow-up with a provider knowledgeable of these potential kidney sequelae is warranted, and should include assessments of BP, kidney function, and growth.

Given CKD and HTN have been documented in those with Stage 1 AKI, evaluations of BP and growth, along with ongoing kidney health education are recommended.[54] Infants with history of stage 2 or 3 AKI, dialysis treatment, recurrent AKI, or AKI in the setting of severe, non-renal comorbidities (i.e. ECMO, CDH, HIE, NEC, or CLD) are likely at higher risk to develop CKD or HTN; thus, follow-up beginning within 6 months of discharge is recommended, preferably with a pediatric nephrology provider. Consideration should be given to screening for HTN, proteinuria, and cystatin C measurement. We recommend ongoing follow-up with pediatric providers knowledgeable in the care of children with CKD and HTN until two years of age at which time those without kidney disease can continue regular BP monitoring and kidney health education with a primary care provider.

Recommendations for Infants with Critical Cardiac Disease

9. We recommend at-risk infants with critical cardiac disease have a comprehensive kidney health assessment at 2 years old or sooner if there are significant exposures or events that modulate risk.

10. We recommend in high-risk infants with critical cardiac disease plus an additional risk factor (Stage 2/3 AKI, single ventricle, heart transplant, HIE, preterm <34 weeks' gestation, ECMO, or daily nephrotoxic medication at discharge), a comprehensive kidney health assessment is performed at least every 6 months through 2 years of age coupled with annual nephrology follow-up.

Rationale: AKI is common in infants with critical cardiac disease. In a recent multicenter study of ~2,000 neonates with critical cardiac disease, AKI occurred in 54%.[16] Risk

factors for and incidence of AKI vary by population studied and definitions utilized.[16,58–60] Consequently, AKI associations with outcomes in infants with critical cardiac disease are heterogenous and inconsistent.[16,58–61] Existing data suggest AKI is important, but the current definitions of AKI may not fully capture meaningful kidney injury and future risks to kidney health.

Structured follow-up programs are common among children with critical cardiac disease. Despite this, data reflecting kidney-focused follow-up in these infants are limited, mostly single-center, and often include older children. Additionally, the timing and type of follow-up evaluation is variable. Further, CKD was not always associated with prior AKI, highlighting the challenge of identifying those who would benefit from follow-up and how often follow-up should occur.[6,62,63] Therefore, we recommend integration of kidney health assessments at regular intervals during structured cardiac-focused visits. For infants at high-risk of CKD, we recommend comprehensive kidney health assessments every six months. Further, we recommend ongoing assessment in at-risk infants to evaluate for significant exposures or events that may modulate risk.

Importantly, risk to long-term kidney health in infants with critical cardiac disease is not isolated to infancy. Survivors may have ongoing risk across their life, including continuing nephrotoxin exposure, cardiac-related HTN, and further surgical interventions. Recurrent AKI episodes may increase the risk of CKD development.[59] As such, we recommend follow-up occurs in infants at high-risk for long-term kidney disease, preferably with a pediatric nephrologist.

Research Gaps and Priorities

Despite the evidence presented which drives these consensus recommendations, crucial gaps in our understanding of the opportunities in neonatal nephrology research and clinical care remain. These include gaps in definitions of AKI, lack of experimental models, and absence of multicenter longitudinal cohort studies (Table 3).

Discussion:

Kidney disease affects approximately 37 million Americans and the societal cost is enormous.[25] Emerging research indicates a high prevalence of CKD among infants who have received care in the NICU. Preterm infants, critically ill term infants with AKI, and infants with critical cardiac disease are particularly vulnerable.

A cornerstone of pediatrics is the prevention of disease. Therefore, it is paramount to identify NICU graduates at the highest risk of kidney disease and intervene to prevent or halt progression of CKD. Our recommendations provide additional context to the recent KDIGO CKD evaluation guidelines, which highlight preterm birth, small for gestational age birthweight, and previous AKI as risk factors for CKD.[25] At-risk children receiving care in the NICU should have kidney health evaluation prior to hospital discharge. Those at high risk of long-term kidney disease should have kidney health assessment based on their degree of risk. AKI and other events which may modulate CKD risk must be well-communicated at time of discharge. Future research is needed to improve risk stratification, improve tools to

detect CKD, evaluate which clinical care models are best suited for different situations, and implement preventive strategies to decrease the prevalence and progression of CKD.

Limitations:

The recommendations of this Consensus Workshop are based on existing evidence and expert opinion; however, a systematic review of all individual studies was not performed. The expert opinions provided here focus on the first two years after birth. However, CKD risk is lifelong.[25] CKD screening should continue beyond two years of age as the risk likely increases with age and exposures. Screening for CKD should be strongly considered during periods of rapid growth (i.e. puberty). The frequency and intensity of assessment should be personalized and reflect shared decision making based on risk, screening results, and other individualized concerns.[25]

Conclusion:

As part of a NIH-sponsored Consensus Workshop, an expert panel developed consensus recommendations focusing on risk stratification at time of hospital discharge, family and provider education, counseling and timing of kidney health follow-up, and blood pressure assessment in at-risk neonatal populations. Implementing kidney assessments may aid in early recognition, intervention, and management of kidney disease in these vulnerable populations. Pragmatic clinical studies and multicenter collaborative work require a shared understanding of best practices to monitor kidney health. The recommendations put forth by this Consensus Workshop will set the foundation for future clinical care, greatly needed longitudinal follow-up studies, and research priorities in these vulnerable populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References:

1. Jetton JG, Boohaker LJ, Sethi SK, et al. Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study. Lancet Child Adolesc Health. Nov 2017;1(3):184–194. doi:10.1016/s2352-4642(17)30069-x [PubMed: 29732396]
2. Ameta P, Stoops C, Askenazi DJ. Risk of chronic kidney disease in children who developed acute kidney injury secondary to nephrotoxic medication exposure in infancy. Ren Fail. Dec 2023;45(1):2218486. doi:10.1080/0886022x.2023.2218486 [PubMed: 37254865]
3. Harer MW, Pope CF, Conaway MR, Charlton JR. Follow-up of Acute kidney injury in Neonates during Childhood Years (FANCY): a prospective cohort study. Pediatr Nephrol. Jun 2017;32(6):1067–1076. doi:10.1007/s00467-017-3603-x [PubMed: 28255805]
4. Starr MC, Charlton JR, Guillet R, et al. Advances in Neonatal Acute Kidney Injury. Pediatrics. Nov 2021;148(5)doi:10.1542/peds.2021-051220 [PubMed: 33781242]
5. Hingorani S, Schmicker R, Ahmad KA, et al. Prevalence and Risk Factors for Kidney Disease and Elevated BP in 2-Year-Old Children Born Extremely Premature. Clin J Am Soc Nephrol. Jul 19 2022;17(8):1129–38. doi:10.2215/cjn.15011121 [PubMed: 35853728]
6. Madsen NL, Goldstein SL, Frøslev T, Christiansen CF, Olsen M. Cardiac surgery in patients with congenital heart disease is associated with acute kidney injury and the risk of chronic kidney disease. Kidney Int. Sep 2017;92(3):751–756. doi:10.1016/j.kint.2017.02.021 [PubMed: 28412020]
7. Huynh L, Rodriguez-Lopez S, Benisty K, et al. Follow-up after neonatal heart disease repair: watch out for chronic kidney disease and hypertension! Pediatr Nephrol. Jun 4 2020;35(11):2137–2145. doi:10.1007/s00467-020-04621-4 [PubMed: 32500246]
8. Yu X, Yuan Z, Lu H, et al. Relationship between birth weight and chronic kidney disease: evidence from systematics review and two-sample Mendelian randomization analysis. Hum Mol Genet. Apr 24 2020;29(13):2261–2274. doi:10.1093/hmg/ddaa074 [PubMed: 32329512]
9. White SL, Perkovic V, Cass A, et al. Is low birth weight an antecedent of CKD in later life? A systematic review of observational studies. Am J Kidney Dis. Aug 2009;54(2):248–61. doi:10.1053/j.ajkd.2008.12.042 [PubMed: 19339091]
10. Selewski DT, Hyatt DM, Bennett KM, Charlton JR. Is acute kidney injury a harbinger for chronic kidney disease? Curr Opin Pediatr. Apr 2018;30(2):236–240. doi:10.1097/mop.0000000000000587 [PubMed: 29389682]
11. Maqsood S, Fung N, Chowdhary V, Raina R, Mhanna MJ. Outcome of extremely low birth weight infants with a history of neonatal acute kidney injury. Pediatr Nephrol. Jun 2017;32(6):1035–1043. doi:10.1007/s00467-017-3582-y [PubMed: 28194575]
12. Harer MW, Charlton JR, Tipple TE, Reidy KJ. Preterm birth and neonatal acute kidney injury: implications on adolescent and adult outcomes. J Perinatol. Apr 10 2020;40(9):1286–1295. doi:10.1038/s41372-020-0656-7 [PubMed: 32277164]
13. Eriksson JG, Salonen MK, Kajantie E, Osmond C. Prenatal Growth and CKD in Older Adults: Longitudinal Findings From the Helsinki Birth Cohort Study, 1924–1944. Am J Kidney Dis. Jan 2018;71(1):20–26. doi:10.1053/j.ajkd.2017.06.030 [PubMed: 28838764]
14. Crump C, Sundquist J, Winkleby MA, Sundquist K. Preterm birth and risk of chronic kidney disease from childhood into mid-adulthood: national cohort study. Bmj. May 1 2019;365:l1346. doi:10.1136/bmj.l1346 [PubMed: 31043374]

15. Mammen C, Al Abbas A, Skippen P, et al. Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: a prospective cohort study. Am J Kidney Dis. Apr 2012;59(4):523–30. doi:10.1053/j.ajkd.2011.10.048 [PubMed: 22206744]

16. Alten JA, Cooper DS, Blinder JJ, et al. Epidemiology of Acute Kidney Injury After Neonatal Cardiac Surgery: A Report From the Multicenter Neonatal and Pediatric Heart and Renal Outcomes Network. Crit Care Med. Oct 1 2021;49(10):e941–e951. doi:10.1097/ccm.0000000000005165 [PubMed: 34166288]

17. Feeney A, Slagle CL, Harer MW, et al. Approaches to neonatal acute kidney injury consultation and follow-up: results of a provider survey. J Perinatol. May 28 2024;doi:10.1038/s41372-024-02016-z

18. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. Aug 2004;8(4):R204–12. doi:10.1186/cc2872 [PubMed: 15312219]

19. Goldstein SL, Akcan-Arikan A, Alobaidi R, et al. Consensus-Based Recommendations on Priority Activities to Address Acute Kidney Injury in Children: A Modified Delphi Consensus Statement. JAMA Netw Open. Sep 1 2022;5(9):e2229442. doi:10.1001/jamanetworkopen.2022.29442 [PubMed: 36178697]

20. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. Squire 2.0 (Standards for Quality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. Am J Crit Care. Nov 2015;24(6):466–73. doi:10.4037/ajcc2015455 [PubMed: 26523003]

21. Starr MC, Hingorani SR. Prematurity and future kidney health: the growing risk of chronic kidney disease. Curr Opin Pediatr. Apr 2018;30(2):228–235. doi:10.1097/mop.0000000000000607 [PubMed: 29432217]

22. Hirano D, Ishikura K, Uemura O, et al. Association between low birth weight and childhood-onset chronic kidney disease in Japan: a combined analysis of a nationwide survey for paediatric chronic kidney disease and the National Vital Statistics Report. Nephrol Dial Transplant. Nov 2016;31(11):1895–1900. doi:10.1093/ndt/gfv425 [PubMed: 26953592]

23. Chmielewski J, Chaudhry PM, Harer MW, et al. Documentation of acute kidney injury at discharge from the neonatal intensive care unit and role of nephrology consultation. J Perinatol. Jul 2022;42(7):930–936. doi:10.1038/s41372-022-01424-3 [PubMed: 35676535]

24. Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. Curr Opin Pediatr. Apr 2012;24(2):191–6. doi:10.1097/MOP.0b013e32834f62d5 [PubMed: 22227783]

25. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. Apr 2024;105(4s):S117–s314. doi:10.1016/j.kint.2023.10.018 [PubMed: 38490803]

26. van den Belt SM, Heerspink HJL, Gracchi V, de Zeeuw D, Wühl E, Schaefer F. Early Proteinuria Lowering by Angiotensin-Converting Enzyme Inhibition Predicts Renal Survival in Children with CKD. J Am Soc Nephrol. Aug 2018;29(8):2225–2233. doi:10.1681/asn.2018010036 [PubMed: 29930161]

27. Menon S, Kirkendall ES, Nguyen H, Goldstein SL. Acute kidney injury associated with high nephrotoxic medication exposure leads to chronic kidney disease after 6 months. J Pediatr. Sep 2014;165(3):522–7 e2. doi:10.1016/j.jpeds.2014.04.058 [PubMed: 24928698]

28. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. Pediatr Nephrol. Jan 2012;27(1):17–32. doi:10.1007/s00467-010-1755-z [PubMed: 21258818]

29. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics. Sep 2017;140(3)doi:10.1542/peds.2017-1904

30. Starr MC, Kula A, Lieberman J, et al. The impact of increased awareness of acute kidney injury in the Neonatal Intensive Care Unit on acute kidney injury incidence and reporting: results of a retrospective cohort study. J Perinatol. Sep 2020;40(9):1301–1307. doi:10.1038/s41372-020-0725-y [PubMed: 32681064]

31. Starr MC, Wallace S, Moore C, et al. Development of a Family-Centered Communication Tool for Kidney Health in Premature Infants: Qualitative Focus Group Study Using Human-Centered Design Methodology. J Particip Med. Jul 10 2023;15:e45316. doi:10.2196/45316 [PubMed: 37428553]
32. Brophy PD. Overview on the Challenges and Benefits of Using Telehealth Tools in a Pediatric Population. Adv Chronic Kidney Dis. Jan 2017;24(1):17–21. doi:10.1053/j.ackd.2016.12.003 [PubMed: 28224938]
33. Rohatgi R, Ross MJ, Majoni SW. Telenephrology: current perspectives and future directions. Kidney Int. Dec 2017;92(6):1328–1333. doi:10.1016/j.kint.2017.06.032 [PubMed: 28893419]
34. Clark SL, Begin B, De Souza HG, et al. Telehealth survey of providers and caregivers of children on peritoneal dialysis during the COVID-19 pandemic. Pediatr Nephrol. Jan 2023;38(1):203–210. doi:10.1007/s00467-022-05543-z [PubMed: 35425999]
35. Ashoor I, Weidemann D, Elenberg E, et al. The Pediatric Nephrology Workforce Crisis: A Call to Action. J Pediatr. Dec 2021;239:5–10.e4. doi:10.1016/j.jpeds.2021.03.033 [PubMed: 33798511]
36. Wu Y, Allegaert K, Flint RB, et al. When will the Glomerular Filtration Rate in Former Preterm Neonates Catch up with Their Term Peers? Pharm Res. Apr 2024;41(4):637–649. doi:10.1007/s11095-024-03677-3 [PubMed: 38472610]
37. Vanpée M, Blennow M, Linné T, Herin P, Aperia A. Renal function in very low birth weight infants: normal maturity reached during early childhood. J Pediatr. Nov 1992;121(5 Pt 1):784–8. doi:10.1016/s0022-3476(05)81916-x
38. Starr MC, Barreto E, Charlton J, et al. Advances in pediatric acute kidney injury pathobiology: a report from the 26th Acute Disease Quality Initiative (ADQI) conference. Pediatr Nephrol. Mar 2024;39(3):941–953. doi:10.1007/s00467-023-06154-y [PubMed: 37792076]
39. den Bakker E, Gemke R, Bökenkamp A. Endogenous markers for kidney function in children: a review. Crit Rev Clin Lab Sci. May 2018;55(3):163–183. doi:10.1080/10408363.2018.1427041 [PubMed: 29388463]
40. Shah L, Hossain J, Xie S, Zaritsky J. Poor adherence to early childhood blood pressure measurement guidelines in a large pediatric healthcare system. Pediatr Nephrol. Apr 2019;34(4):697–701. doi:10.1007/s00467-018-4132-y [PubMed: 30406366]
41. Flynn RS, Zedalis J, Denburg MR, Bernbaum JC, DeMauro SB. Improving Blood Pressure Screening in Neonatal Follow-up Clinic: A Quality Improvement Initiative. Pediatr Qual Saf. May-Jun 2022;7(3):e559. doi:10.1097/pq9.0000000000000559 [PubMed: 35720869]
42. Chevalier RL. Bioenergetic Evolution Explains Prevalence of Low Nephron Number at Birth: Risk Factor for CKD. Kidney360. 2020;1(8):863–879. doi:10.34067/kid.0002012020 [PubMed: 35372951]
43. Charlton JR, Baldelomar EJ, Hyatt DM, Bennett KM. Nephron number and its determinants: a 2020 update. Pediatr Nephrol. Apr 2021;36(4):797–807. doi:10.1007/s00467-020-04534-2 [PubMed: 32350665]
44. Perl AJ, Schuh MP, Kopan R. Regulation of nephron progenitor cell lifespan and nephron endowment. Nat Rev Nephrol. Nov 2022;18(11):683–695. doi:10.1038/s41581-022-00620-w [PubMed: 36104510]
45. Callaway DA, McGill-Vargas LL, Quinn A, et al. Prematurity disrupts glomeruli development, whereas prematurity and hyperglycemia lead to altered nephron maturation and increased oxidative stress in newborn baboons. Pediatr Res. Mar 2018;83(3):702–711. doi:10.1038/pr.2017.290 [PubMed: 29166383]
46. Carmody JB, Charlton JR. Short-term gestation, long-term risk: prematurity and chronic kidney disease. Pediatrics. Jun 2013;131(6):1168–79. doi:10.1542/peds.2013-0009 [PubMed: 23669525]
47. Hingorani S, Schmicker R, Ahmad KA, et al. Prevalence and Risk Factors for Kidney Disease and Elevated BP in 2-Year-Old Children Born Extremely Premature. Clin J Am Soc Nephrol. Aug 2022;17(8):1129–1138. doi:10.2215/cjn.15011121 [PubMed: 35853728]
48. Heo JS, Lee JM. The Long-Term Effect of Preterm Birth on Renal Function: A Meta-Analysis. Int J Environ Res Public Health. Mar 13 2021;18(6)doi:10.3390/ijerph18062951

49. Gjerde A, Lillås BS, Marti HP, Reisæter AV, Vikse BE. Intrauterine growth restriction, preterm birth and risk of end-stage renal disease during the first 50 years of life. Nephrol Dial Transplant. Jul 1 2020;35(7):1157–1163. doi:10.1093/ndt/gfaa001 [PubMed: 32040151]
50. Sigurjonsdottir VK, Chaturvedi S, Mammen C, Sutherland SM. Pediatric acute kidney injury and the subsequent risk for chronic kidney disease: is there cause for alarm? Pediatr Nephrol. Nov 2018;33(11):2047–2055. doi:10.1007/s00467-017-3870-6 [PubMed: 29374316]
51. Bruel A, Rozé J-C, Quere M-P, et al. Renal outcome in children born preterm with neonatal acute renal failure: IRENEO—a prospective controlled study. Pediatr Nephrol. 2016:1–9. doi:10.1007/s00467-016-3444-z
52. Pulju M, Pruitt C, Reid-Adam J, et al. Renal insufficiency in children born preterm: examining the role of neonatal acute kidney injury. J Perinatol. Jun 2021;41(6):1432–1440. doi:10.1038/s41372-021-01097-4 [PubMed: 34035456]
53. Roy JP, Goldstein SL, Schuh MP. Under-Recognition of Neonatal Acute Kidney Injury and Lack of Follow-Up. Am J Perinatol. Apr 2022;39(5):526–531. doi:10.1055/s-0040-1716841 [PubMed: 32971562]
54. Akkoc G, Duzova A, Korkmaz A, Oguz B, Yigit S, Yurdakok M. Long-term follow-up of patients after acute kidney injury in the neonatal period: abnormal ambulatory blood pressure findings. BMC Nephrol. Mar 23 2022;23(1):116. doi:10.1186/s12882-022-02735-5 [PubMed: 35321692]
55. Robertsson Grossmann K, Bárány P, Blennow M, Chromek M. Acute kidney injury in infants with hypothermia-treated hypoxic-ischaemic encephalopathy: An observational population-based study. Acta Paediatr. Jan 2022;111(1):86–92. doi:10.1111/apa.16078 [PubMed: 34431538]
56. Robertsson Grossmann K, Vishnevskaya L, Diaz Ruiz S, et al. Kidney outcomes in early adolescence following perinatal asphyxia and hypothermia-treated hypoxic-ischaemic encephalopathy. Pediatr Nephrol. Apr 2023;38(4):1205–1214. doi:10.1007/s00467-022-05705-z [PubMed: 35976440]
57. Zwiers AJ, IJsselstijn H, van Rosmalen J, et al. CKD and hypertension during long-term follow-up in children and adolescents previously treated with extracorporeal membrane oxygenation. Clin J Am Soc Nephrol. Dec 05 2014;9(12):2070–8. doi:10.2215/CJN.02890314 [PubMed: 25278545]
58. Van den Eynde J, Delpire B, Jacquemyn X, et al. Risk factors for acute kidney injury after pediatric cardiac surgery: a meta-analysis. Pediatr Nephrol. Mar 2022;37(3):509–519. doi:10.1007/s00467-021-05297-0 [PubMed: 34595570]
59. Hasson DC, Alten JA, Bertrandt RA, et al. Persistent acute kidney injury and fluid accumulation with outcomes after the Norwood procedure: report from NEPHRON. Pediatr Nephrol. May 2024;39(5):1627–1637. doi:10.1007/s00467-023-06235-y [PubMed: 38057432]
60. Sasaki J, Rodriguez Z, Alten JA, et al. Epidemiology of Neonatal Acute Kidney Injury After Cardiac Surgery Without Cardiopulmonary Bypass. Ann Thorac Surg. Nov 2022;114(5):1786–1792. doi:10.1016/j.athoracsur.2021.09.032 [PubMed: 34678277]
61. Blinder JJ, Goldstein SL, Lee VV, et al. Congenital heart surgery in infants: effects of acute kidney injury on outcomes. J Thorac Cardiovasc Surg. Feb 2012;143(2):368–74. doi:10.1016/j.jtcvs.2011.06.021 [PubMed: 21798562]
62. Greenberg JH, Zappitelli M, Devarajan P, et al. Kidney Outcomes 5 Years After Pediatric Cardiac Surgery: The TRIBE-AKI Study. JAMA Pediatr. Nov 1 2016;170(11):1071–1078. doi:10.1001/jamapediatrics.2016.1532 [PubMed: 27618162]
63. Sethi SK, Sharma R, Gupta A, et al. Long-Term Renal Outcomes in Children With Acute Kidney Injury Post Cardiac Surgery. Kidney Int Rep. Jul 2021;6(7):1850–1857. doi:10.1016/j.ekir.2021.04.018 [PubMed: 34307979]
64. Schwartz GJ, Muñoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. Mar 2009;20(3):629–37. doi:10.1681/asn.2008030287 [PubMed: 19158356]
65. Cai T, Karlaftis V, Hearps S, et al. Reference intervals for serum cystatin C in neonates and children 30 days to 18 years old. Pediatr Nephrol. Oct 2020;35(10):1959–1966. doi:10.1007/s00467-020-04612-5 [PubMed: 32447504]

66. Hidayati EL, Utami MD, Rohsiswatmo R, Tridjaja B. Cystatin C compared to serum creatinine as a marker of acute kidney injury in critically ill neonates. Pediatr Nephrol. Jan 2021;36(1):181–186. doi:10.1007/s00467-020-04668-3 [PubMed: 32594242]

67. Pierce CB, Muñoz A, Ng DK, Warady BA, Furth SL, Schwartz GJ. Age- and sex-dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease. Kidney Int. Apr 2021;99(4):948–956. doi:10.1016/j.kint.2020.10.047 [PubMed: 33301749]

68. Askenazi DJ, Heagerty PJ, Schmicker RH, et al. Prevalence of acute kidney injury (AKI) in extremely low gestational age neonates (ELGAN). Pediatr Nephrol. Sep 2020;35(9):1737–1748. doi:10.1007/s00467-020-04563-x [PubMed: 32488672]

Key Points

Question:

What are the (1) evidence-based expert recommendations for kidney health follow-up in infants after neonatal discharge, and (2) most important research questions that need to be answered to improve the health of infants at risk of chronic kidney disease during childhood?

Findings:

In this modified Delphi consensus statement, a panel of 51 neonatal nephrology experts developed 10 consensus recommendations regarding the follow-up of infants at risk of chronic kidney disease during childhood. The panel also identified critical gaps in knowledge and determined research priorities.

Meaning:

Specific subpopulations of infants discharged from the neonatal intensive care unit, including those born preterm, critically ill infants with acute kidney injury and infants with critical cardiac disease, are at increased risk for developing chronic kidney disease during childhood. Key recommendations include risk assessment at time of hospital discharge, provider and family education, and risk stratified longitudinal follow-up.

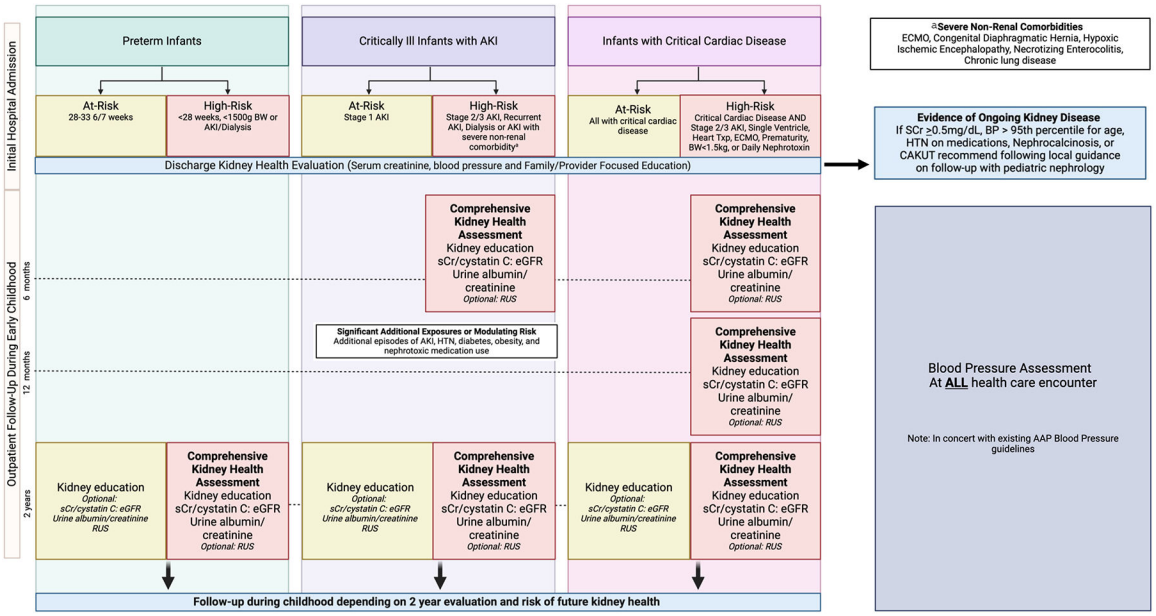

Figure 1.

Consensus recommendations for outpatient kidney health follow-up for infants at risk of kidney disease during childhood.

Table 1.

Risk Stratification Scheme Relevant to Kidney Monitoring and Follow-Up Recommendations

Patient and Risk Factors	
At-Risk	• 28–33 6/7 weeks' gestation • ≥34 weeks' gestation and Stage 1 AKI • Critical Cardiac Disease[a] (see definition below)
High-Risk	• Preterm Infants – <28 weeks' gestation OR – BW <1500 grams OR – AKI/Dialysis • Critically Ill Infants with history of AKI and: – Stage 2/3 AKI or dialysis treatment – Recurrent AKI – AKI with severe non-renal comorbidity (ECMO, CDH, HIE, NEC, CLD) • Infants with Critical Cardiac Disease and: – Stage 2/3 AKI – Single Ventricle – Heart Transplant – HIE – Preterm <34 weeks' gestation or BW <1500 grams – ECMO – Daily nephrotoxic medications at discharge

AKI, acute kidney injury; BW, birth weight; ECMO, extracorporeal membrane oxygenation, CDH, congenital diaphragmatic hernia; HIE, hypoxic ischemic encephalopathy; NEC, necrotizing enterocolitis; CLD, chronic lung disease.

[a]Critical Cardiac Disease: A group of serious heart defects that are present from birth. Infants were considered to have critical cardiac disease if they were admitted either before or after corrective/palliative surgery for congenital heart defects, experienced complications following neonatal cardiac surgery such as sepsis, or developed myocardial failure (acute) from a variety of etiologies, including but not limited to acute myocarditis, idiopathic cardiomyopathy or genetic abnormalities.

Table 2.

Consensus recommendations for outpatient kidney health follow-up for infants

Consensus Recommendations	Level of Evidence[a]
Overarching Recommendation	
1.Preterm infants (<34 weeks' gestation), critically ill infants with AKI, and infants with critical cardiac disease are at-risk of CKD following NICU discharge. We recommend all at-risk infants have a discharge kidney health evaluation that includes a properly obtained BP, serum creatinine, and kidney health education in preparation for hospital discharge.	**3**
2.In infants with evidence of kidney disease at discharge (defined by a serum creatinine ≥0.5mg/dL, BP >95th percentile for age, hypertension treated with medications, nephrocalcinosis, or CAKUT), we recommend follow-up with pediatric nephrology according to local guidance.	**5**
3.In all other at-risk infants who do not meet criteria for kidney disease at discharge, we recommend family- and provider-focused education and counseling for subsequent kidney health follow-up. We recommend BP assessment at all healthcare encounters. We encourage coordination of kidney-focused follow-up and ongoing risk assessment with subspeciality specific care models.	**5**
Preterm Infants (<34 Weeks' Gestational Age)	
4. We recommend at-risk preterm infants (28 to <34 weeks' gestation) have BP assessment and kidney health education at 2 years of age in conjunction with standard care. Providers should consider a comprehensive kidney health assessment if there are significant exposures that modulate risk.	**3**
5. We recommend high-risk preterm infants (<28 weeks' gestation, birthweight <1,500 grams, or history of AKI or dialysis) have a comprehensive kidney health assessment in conjunction with standard care at 2 years of age, or sooner if there are significant exposures or events that modulate risk.	**3**
Critically Ill Infants with AKI (Born ≥34 Weeks' Gestational Age)	
6. We recommend at-risk infants born ≥34 weeks' gestation (Stage 1 AKI) have a comprehensive kidney health assessment at 2 years of age in conjunction with standard health maintenance.	**3**
7. We recommend high-risk infants born ≥34 weeks' gestation (Stage 2/3 AKI, dialysis treatment, recurrent AKI, or AKI with severe non-renal comorbidities such as receipt of ECMO, CDH, HIE, NEC, CLD) have a comprehensive kidney health assessment within 6 months of discharge. The frequency of subsequent assessments may vary based on clinical course but should include another assessment at 2 years of age.	**3**
8.If the 2-year comprehensive kidney health assessment is normal, infants ≥34 weeks' gestation with history of AKI may be discharged to routine well-child care, including annual BP assessment and ongoing kidney health education.	**5**
Infants with Critical Cardiac Disease	
9. We recommend at-risk infants with critical cardiac disease have a comprehensive kidney health assessment at 2 years old or sooner if there are significant exposures or events that modulate risk.	**3**
10. We recommend in high-risk infants with critical cardiac disease (Stage 2/3 AKI, single ventricle, heart transplant, HIE, preterm <34 weeks' gestation, ECMO, or daily nephrotoxic medication at discharge) a comprehensive kidney health assessment is performed at least every 6 months through 2 years of age coupled with annual nephrology follow-up.	**3**

AKI, acute kidney injury; CKD, chronic kidney disease; NICU, neonatal intensive care unit; BP, blood pressure; CAKUT, congenital anomaly of kidney or urinary tract; ECMO, extracorporeal membrane oxygenation; CDH, congenital diaphragmatic hernia; HIE, hypoxic ischemic encephalopathy; NEC, necrotizing enterocolitis; CLD, chronic lung disease.

[a]Quality Rating Scheme for Studies and Other Evidence modified from Oxford Center for Evidence-based medicine per journal standards with ratings from 1 (Properly powered and conducted randomized clinical trial; systematic review with meta-analysis) to 5 (Opinion of respected authorities; case reports)

Table 3.

Consensus identification of priority gaps and research opportunities

Groups	Priority Gaps	Opportunities and Potential Next Steps
Overarching	• AKI definition in infants (accuracy, biomarker incorporation, fluid adjusted, rate of decline, urine output thresholds) • NICU discharge assessment and risk stratification • Family engagement (empowerment, perspective, educational materials) • Role of experimental models of neonatal AKI to identify novel biomarkers and tools to screen for reduced functional renal reserve • Use of traditional and novel biomarkers to inform post-AKI risk-stratification, prognostication, treatment, and screening • Discharge planning strategies to improve outpatient kidney health follow-up	• Multicenter studies to better understand risk for progression to CKD in NICU graduates • Harmonize existing quality improvement and research registry platforms to improve our understanding of outcomes • Develop key areas for short- and long-term outcomes to measure and modulate AKI risk • Develop a database of follow-up data in NICU graduates, including information such as serum creatinine at discharge • Engage patient and caregivers to improve the care of neonates with AKI who are at risk for CKD • Determine the ideal timing and cadence of follow-up for high and at-risk infants • Perform studies of high-risk events and collect all data surrounding episodes of AKI with ongoing follow-up • Study strategies to optimize long-term kidney health in at -risk neonates
Preterm Infants	• Postnatal environment effect on *ex utero* nephrogenesis • Standardizing methods to assess kidney health outcomes (accurate GFR and estimating GFR equations, nephron endowment, renal reserve, ultrasound volumes) • Experimental models during ongoing nephrogenesis of AKI to address gaps in our understanding of biomarkers, reduced functional renal reserve, damage and adaptive repair processes and interventions to optimize kidney growth	• Develop estimating equations for GFR prior to and after hospital discharge using measured GFR in neonates and infants born preterm • Compare measured GFR to estimated GFR in 2-year-old children born preterm • Develop methods to determine when nephrogenesis in complete in humans
Critically Ill Infants with AKI	• Understanding how specific etiologies and severities of neonatal AKI impact long-term kidney health and risk for CKD progression • Role of risk stratification, monitoring and treatment strategies to improve morbidity and mortality and long-term CKD	• Risk stratification tools for the development and progression of CKD • Development of optimal model for identification of neonates at risk for CKD and arrangement of dedicated, outpatient nephrology follow-up
Infants with Critical Cardiac Disease	• Identification of diagnostic criteria that integrate biomarkers to delineate cardiac specific AKI sub-phenotypes • Determination of perioperative best practices that decrease the development, severity, and impact of AKI • Optimal cadence and duration of kidney-focused follow-up in infants with critical cardiac disease	• Identify and test perioperative risk stratification tools for CKD development • Develop strategies to reduce CKD prevalence and progression in those with AKI • Prospective multicenter investigations evaluating the risk of progression to CKD

AKI, acute kidney injury; NICU, neonatal intensive care unit; CKD, chronic kidney disease; GFR, glomerular filtration rate.