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## Consensus-Based Recommendations on Priority Activities to Address Acute Kidney Injury in Children:

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## **Abstract**

**IMPORTANCE**—Increasing evidence indicates that acute kidney injury (AKI) occurs frequently in children and young adults and is associated with poor short-term and long-term outcomes. Guidance is required to focus efforts related to expansion of pediatric AKI knowledge.

**OBJECTIVE**—To develop expert-driven pediatric specific recommendations on needed AKI research, education, practice, and advocacy.

**EVIDENCE REVIEW**—At the 26th Acute Disease Quality Initiative meeting conducted in November 2021 by 47 multiprofessional international experts in general pediatrics, nephrology, and critical care, the panel focused on 6 areas: (1) epidemiology; (2) diagnostics; (3) fluid overload; (4) kidney support therapies; (5) biology, pharmacology, and nutrition; and (6) education and advocacy. An objective scientific review and distillation of literature through September 2021

was performed of (1) epidemiology, (2) risk assessment and diagnosis, (3) fluid assessment, (4) kidney support and extracorporeal therapies, (5) pathobiology, nutrition, and pharmacology, and (6) education and advocacy. Using an established modified Delphi process based on existing data, workgroups derived consensus statements with recommendations.

**FINDINGS**—The meeting developed 12 consensus statements and 29 research recommendations. Principal suggestions were to address gaps of knowledge by including data from varying socioeconomic groups, broadening definition of AKI phenotypes, adjudicating fluid balance by disease severity, integrating biopathology of child growth and development, and partnering with families and communities in AKI advocacy.

**CONCLUSIONS AND RELEVANCE**—Existing evidence across observational study supports further efforts to increase knowledge related to AKI in childhood. Significant gaps of knowledge may be addressed by focused efforts.

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## Introduction

The pediatric acute kidney injury (AKI) research field has expanded during the past decade with international epidemiologic studies, long-term AKI follow-up studies, validation of AKI prediction models, and continued investigation of novel AKI biomarkers.<sup>1–9</sup> The 26th Acute Disease Quality Initiative (ADQI XXVI) convened in Napa, California, in November 2021, the first Pediatric ADQI (pADQI) that specifically addressed the global burden of AKI in the child and young adult population, with focused attention paid to kidney development and AKI, prenatal or neonatal kidney physiology, dialysis devices engineered for children,<sup>10</sup> and the unique aspects of pediatric AKI epidemiology. The pADQI was assembled to mirror the global workforce in pediatrics and used a public and patient-facing approach. The primary aim of the pADQI was to identify the work priorities across the pediatric AKI landscape of care, education, research, and advocacy.

## Methods

The pADQI consensus meeting followed the established ADQI process, as previously described,<sup>11</sup> to provide expert-based statements and interpretation of current knowledge for use by clinicians according to professional judgment and identify evidence care gaps to establish research priorities. We performed an objective scientific review and distillation of literature through September 2021 of (1) epidemiology, (2) risk assessment and diagnosis, (3) fluid assessment, (4) kidney support and extracorporeal therapies, (5) pathobiology, nutrition, and pharmacology, and (6) education and advocacy. The 6 workgroups were composed of representatives from 5 continents of varying age (median: 43 years; range, 24–74 years), gender (23 male, 23 female) and professional discipline (physicians, nurses, pharmacists, and nutritionists). In addition, a pediatric patient survivor of AKI and an expert in equity and care delivery were included in the pADQI and assisted all workgroups. The in-person meeting was conducted using workgroups and large group in mixed in-person and virtual (72% in person) formats. Work following the in-person meeting was completed virtually.

Using a modified Delphi method, each workgroup determined key questions supported by representative literature, or professional opinion when evidence was scarce, and presented their drafts iteratively to develop consensus statements (target of 2–3 per group) (main document), and to articulate a research agenda with a more comprehensive background (Table; eBackground and eBox in the Supplement). The consensus statements were categorized as recommendations or suggestions. The work product was finalized and approved by the entire group in 2 follow-up web-based meetings. This summary statement was based on existing evidence in the literature, thus institutional approval was not required. All members of pADQI consented to their inclusion in this article. The statements are presented herein as direct quotations.

The age spectrum of patients receiving the care of pediatric specialists ranged from extremely low birthweight neonates to young adults. Throughout this manuscript, the terms *child*, *children*, and *pediatric* reflect the entire age spectrum, unless specifically noted.

## **Group 1: What Will Drive the Continuing Refinement and Evolution of AKI Epidemiology?**

### **Consensus Statement 1A (Recommendation)**

- AKI epidemiology related to short-term outcomes is well-described in critically ill neonates and children from high-income countries; however, further study is needed in other health care contexts, such as low-middle income countries and in non-ICU and ambulatory settings and for socioeconomic and long-term outcomes.

### **Consensus Statement 1B (Suggestion)**

- An understanding of pediatric AKI epidemiology allows us to begin employing strategies to improve primary, secondary, and tertiary AKI prevention in at-risk patient groups.

Implementation of standardized criteria to define the presence and severity of AKI has facilitated a description of pediatric AKI epidemiology.<sup>11–14</sup> Prospective multicenter studies provide insight into the epidemiology of AKI in critically ill neonates and children.<sup>1,2</sup> Other studies describe AKI epidemiology in specific cohorts of children including sepsis,<sup>15</sup> those receiving nephrotoxins,<sup>16</sup> and cardiac surgical populations.<sup>17,18</sup> However, residual knowledge gaps remain regarding the accurate description of AKI epidemiology in other health care contexts as the most data come from high-income countries, and few studies have described AKI epidemiology outside critical care settings.

Pediatric literature has described AKI and morbidity, mortality, and health resource use in critically ill children with a gradient-response association between AKI severity and the risk of worse outcomes.<sup>1,19,20</sup> More recently, research has focused on assessing the medium and long-term sequelae of AKI, including longitudinal kidney function and its socioeconomic outcomes.<sup>16,21,22</sup>

A comprehensive description of pediatric AKI epidemiology reflects current practice and best available information (eFigure 1 in the Supplement). Given this, information should be up to date and readily available to clinicians and institutions in real time. A risk prediction study<sup>23</sup> and a randomized clinical trial<sup>24</sup> suggest a causal link between pediatric AKI and a limited scope of short-term outcomes, supporting prevention and mitigation of pediatric AKI and its complications as targets for improving outcomes. Pediatric AKI epidemiologic characteristics can be categorized as pre-event (eg, risk factors, key drivers, and predictors), peri-event (eg, demographic characteristics and etiology), and postevent (eg, outcomes and recovery). Studies of AKI epidemiology should explore the temporal nature of AKI, health contexts (eg, populations and locations) in which AKI has been inadequately described, and outcomes that are focused on patient, family, cost, and performance. Thus, by following epidemiologic trends, clinicians can help focus efforts to enhance public health surveillance, augment field investigations, clinical and preclinical studies, and further policy development to promote child health (eBox and eBackground in the Supplement).

## **Group 2: What Are the Unique Considerations for AKI Risk Stratification and Diagnosis in Children?**

### **Consensus Statement 2A (Recommendation)**

- Validated tools which incorporate patient characteristics and exposure and also interface with the local health care environment should be utilized to estimate AKI risk in children, including assessment of objective measures of kidney fitness in at-risk children prior to a predictable or planned intervention.

### **Consensus Statement 2B (Suggestion)**

- Unique AKI phenotypes in children may overlap and change over time. Differentiating AKI phenotype(s) informs prognosis and has the potential to guide therapeutics.

Previous studies<sup>1,25–28</sup> identified baseline patient characteristics and exposures that place children at increased risk for AKI, including but not limited to cancer therapy, cardiopulmonary bypass, extracorporeal membrane oxygenation, major surgical procedures, and a high nephrotoxic medication burden.<sup>1,26,29</sup> Integrating diagnostic resources may optimize AKI risk assessment for high-risk diagnoses (eg, by using point-of-care testing and automated algorithms) or exposures (eg, by using the electronic medical record) could be updated continuously in real time<sup>30</sup> (Figure 1A<sup>31</sup>).

Prior to a planned exposure associated with increased AKI risk, ascertainment of kidney fitness using traditional measures of kidney function and damage, including serum creatinine and cystatin C levels, and urine albumin or protein level can be used to direct comprehensive kidney protection and surveillance and prevent AKI development.<sup>32</sup> Preoperative values of candidate biomarkers may have utility in predicting AKI after cardiac surgery in adults and children.<sup>33–35</sup> Kidney functional reserve values can predict postoperative AKI in adults.<sup>36</sup> (Figure 1A<sup>31</sup>).

When available, biomarkers that indicate structural kidney injury may provide further insight into AKI risk and phenotype.<sup>37</sup> For example, structural biomarker concentration elevation in the absence of functional biomarker elevation may indicate early kidney injury that is not readily reversible. Conversely, functional biomarker elevation alone may be indicative of decreased effective circulating volume and direct care toward restoration of volume. The terms *functional AKI* and *structural AKI*, to supplant the terms *pre-renal AKI* and *intrinsic AKI* were first proposed by the ADQI X Consensus Conference.<sup>38</sup> Single center pediatric study and systematic reviews provide initial validation of these concepts, with structural AKI being associated with worse outcomes than functional AKI alone.<sup>39–41</sup>

Pediatric AKI is a heterogeneous disease with multiple etiologic factors, biochemical signatures, and clinical manifestations. Expert consensus and emerging data support the view that these elements combined with individual susceptibility contribute to unique, discernible AKI phenotypes in children with AKI (Figure 1B<sup>31</sup>). In particular, evidence supports the use of clinical features such as urine output,<sup>42,43</sup> severity and duration of creatinine elevation,<sup>44,45</sup> fluid overload,<sup>46</sup> response to loop diuretics,<sup>47,48</sup> and tubular injury biomarkers,<sup>39,41</sup> to refine AKI diagnosis and reveal unique phenotypes. The concept of *subclinical AKI* is defined by an elevation in a urine tubular injury biomarker without elevation in functional marker. Subclinical AKI is associated with worse outcomes in children without AKI or with functional AKI.<sup>39,41</sup> Although these studies examined static 1 or 2 factor-based AKI phenotypes, it is likely that more than 1 of these discernible phenotypes may be present in a child with AKI at a given time and that this unique phenotypic signature is dynamic (Figure 1B<sup>31</sup>). A dynamic diagnostic model to address a dynamic phenotype, akin to blood gas assessment in acute lung injury, may be required for AKI (eBox and eBackground in the Supplement).

### **Group 3: What Considerations Are Needed for Fluid Assessment in Sick Children?**

#### **Consensus Statement 3A (Recommendation)**

- Fluid balance is the difference between total input and output that can be expressed as “daily” and/or “cumulative” over a defined duration of time.

#### **Consensus Statement 3B (Suggestion)**

- Fluid overload denotes a pathologic state of positive fluid balance associated with a clinically observable event(s), which may vary by age, case-mix, acuity, and phase of illness. No specific threshold of positive fluid balance alone can define fluid overload across all sick children.

As with AKI diagnosis, consistent use of consensus terminology is essential to further our understanding of fluid management and outcomes. Many terms have been used imprecisely to assess the impact of fluid volume on outcomes in sick children, including fluid balance, fluid accumulation, and fluid overload. *Fluid overload* has been conflated to describe both the degree of positive fluid balance within a patient and its association with adverse outcomes.<sup>49–55</sup> Use of the term in this manner introduces bias into research and clinical



practice, as it presumes any degree of positive fluid balance is synonymous with fluid overload and is therefore detrimental. Moreover, such use presumes that net fluid removal and targeting negative fluid balance is beneficial. Fluid overload is a distinct pathologic state of positive fluid balance with adverse consequences. Fluid balance is an objective calculation using specific methods. We suggest that the term *percent cumulative fluid balance* be used to describe the previously referred term, *percent fluid overload*,<sup>56</sup> to separate the pathologic state from specific calculations. The terms *daily fluid balance*, *cumulative fluid balance*, and *percent cumulative fluid balance* describe fluid status of patients for purpose of clinical care and research (eTable 1 in the Supplement) more precisely.

The 2 methods most used to describe fluid balance are calculations from (1) cumulative fluid inputs and outputs and (2) changes in measured body weight.<sup>49–55,57–72</sup> The weight change method has certain advantages because it accounts for unmeasured insensible losses, does not require an invasive bladder catheter, and is less resource intensive. A weight-change method is preferred in neonates to estimate fluid balance.<sup>58,73–77</sup>

Sick children are a heterogenous cohort of patients, and fluid overload may vary according to patient-specific susceptibilities (eg, by patient age, case-mix, phase, or severity of illness). Thus, no specific threshold can be recommended uniformly to define fluid overload in sick children. Interventions to mitigate or treat fluid overload will need to be patient-specific and consider the pathophysiologic context, the dynamics of the patient's fluid balance, and the degree to which fluid balance affects the severity of the patient's fluid overload or volume depletion. eFigure 2 in the Supplement provides a visual model of this precision approach (eBox and eBackground in the Supplement).

## **Workgroup 4: How Can Use of Kidney Support and Extracorporeal Therapies in Children Be Advanced?**

### **Consensus Statement 4A (Recommendation)**

- A dedicated multidisciplinary team made up of kidney health care workers, patients, and families along with institutional investments of personnel, time, materials, and quality assurance/improvement systems are essential to a pediatric acute kidney support therapy (paKST) program.

### **Consensus Statement 4B (Suggestion)**

- Patient-centered goals of care, degree of kidney recovery, physiological stability, fluid balance, and global recovery and rehabilitation priorities inform decisions for de-escalation, liberation, transition, and follow-up to optimize hospital-based and lifelong outcomes.

A paKST program requires thoughtful planning and synchronization across the health care enterprise (eFigure 3 in the Supplement).<sup>28,78</sup> Program development begins by identification of key stakeholders with a vested interest in paKST delivery and outcomes. A multidisciplinary team of kidney health care workers is responsible for fostering a culture of safety and transparency, navigating organizational barriers, facilitating shared decision-

making, providing education, maintaining equipment, developing and maintaining policies, procedures, and guidelines, and managing quality improvement data.<sup>28,78–84</sup> Patients and families are vital partners, identifying goals and advocating for effective and safe care. paKST device manufacturers and suppliers play an important role in working with pediatric paKST providers to design products that can be used safely and effectively in children, and to respond to the unique needs of a pediatric program. The care delivery model should be based on available resources with representation from multiple disciplines.<sup>28,78,79,82</sup> Multiple blood purification and extracorporeal treatment modalities have been developed (eTable 2 in the Supplement). Programs must define their standards of high-quality delivery for the procedures they provide. Most quality metrics proposed by the ADQI XXII conference are relevant for children.<sup>85</sup> If a program is unable to provide high-quality care in a particular area, the team must develop criteria and processes for transfer to an institution that provides such care, and should examine the components lacking in their program to see if they can be addressed. The education curriculum encompasses patient and team learning, is tailored to fit specific roles, and includes competency assessments.<sup>28,78,80,86,87</sup> Quality assurance or improvement systems should be integrated into clinical practice, recognizing that cost, varied definitions, and lack of agreed-on benchmarks are known barriers to implementation.<sup>28,78–80,82–84,88–92</sup> Previous work by Rewa et al<sup>80,89,90</sup> and the 22nd ADQI conference<sup>28,80</sup> has provided minimum programmatic standards that may be used for paKST.

While most children who require paKST for AKI will achieve liberation from dialysis, there is scant data to guide clinicians during kidney recovery.<sup>14,93–95</sup> Current practices use estimates of the ability to maintain euolemia and metabolic balance for decisions about timing of paKST liberation, transition, or de-escalation. Inability to execute timely transition from continuous paKST may negatively affect outcomes, especially in light of emerging data on effectiveness of the ICU Liberation Bundle.<sup>96–98</sup> After paKST liberation, children are at risk for lifelong morbidity, including chronic kidney disease, but guidance on optimal follow-up practices is lacking (eBox and eBackground in the Supplement).<sup>3,99–101</sup>

## **Workgroup 5: How Do the Unique Pathobiology, Nutrition, and Pharmacology of the Developing Child and AKI Need to Be Integrated?**

### **Consensus Statement 5A (Recommendation)**

- Successful pediatric translational AKI research programs include diverse teams using reverse translational approaches in partnership with clinical and epidemiological findings that prioritize development as a biologic variable. Sufficient support including pediatric specific government and industry funding along with meaningful partnerships among health professionals is necessary to understand and leverage the unique aspects of pediatric AKI to address kidney health and disease across the life course.

### **Consensus Statement 5B (Recommendation)**

- Patient centered outcomes such as functional status, quality of life, and optimal growth and development must drive the targeted nutritional interventions,

optimizing short- and long-term nutrition, and incorporate measures of acute and chronic changes of anthropometrics, body composition, physical function, and metabolic control.

Engagement of diverse stakeholders across the preclinical and translational research realms is needed to disseminate findings and transform care. Most translational AKI models do not account for the additional complexity of pediatric AKI including the concept of development as a biologic variable (DABV).<sup>102</sup> The association between premature birth and kidney function and maturation remain incompletely understood.<sup>103</sup> Furthermore, the associations between a single AKI episode during kidney development and short-term and long-term outcomes remain unclear.<sup>104</sup> Potential sex differences in AKI have prevented the inclusion of both males and females together in preclinical animal studies. In pediatrics, sex as a biologic variable is further confounded by DABV; hormone levels change throughout pubertal stages, and few clinical studies capture this information.<sup>105</sup> Animal models of AKI that consider sex hormones and sex chromosomes could inform clinical evaluations sensitive to sex as a biologic variable and DABV. The association between AKI and chronic kidney disease has been established, however, there is a paucity of data on the systemic long-term impact of AKI.<sup>106,107</sup> The potential associations between AKI with respect to DABV and long-term outcomes are unknown. Opportunities remain to use the unique aspects of pediatric patients, including but not limited to the lack of chronic comorbidities and ability to understand the impact of nephron endowment prior to nephron loss (Figure 2<sup>31</sup>).

Malnutrition and protein energy wasting are prevalent and independently associated with mortality in children hospitalized with AKI, especially those requiring paKST, with prevalence ranging from 30% to 55%.<sup>108–111</sup> Mortality is a crude end point to assess the importance of nutrition support in children with AKI. AKI survivors are at risk of worsened functional status, chronic ventilation, or dialysis after hospital discharge.<sup>111</sup> Nutrition support and mobilization offer opportunities to improve functional outcomes in survivors through attenuation of muscle loss and promotion of muscle protein synthesis in critically ill children.<sup>112</sup> The outcomes of malnutrition associated with somatic growth, body composition, development, immune function, metabolic derangements, and long-term physical and neurocognitive functioning require more precise measurement tools and targets.<sup>113</sup> Nutritional therapeutic interventions are nuanced and include changes in feeding modality, composition (macronutrient or micronutrient) and volume of nutrition-related fluids which intersects with medical AKI management and metabolic control, which can be further complicated by institution of paKST. Nutritional needs are further affected by DABV.

Identifying and measuring appropriate outcome variables represent the first step to define the phenotypic nutritional morbidities in pediatric AKI, and thereby enable evaluation of nutritional intervention efficacy.<sup>114,115</sup> We recommend program-based focused nutrition support for children with AKI and transitioning through acute kidney disease.<sup>116</sup> Such a program would use evidence-based nutrition therapy adjusted in response to changes in objectively measured nutrition-related outcomes characterized by mitigating functional

decline, a return to metabolic homeostasis, and facilitation of long-term physical and neurocognitive rehabilitative processes.

Physiologic derangement in acute illness, with susceptibility factors of DABV render kidney-eliminated and nephrotoxic medication use uniquely complex in sick children. High-value medications can be selected for detailed pharmacokinetic/pharmacodynamic/pharmacogenomics characterization to inform drug disposition, dosing, and monitoring decisions at the bedside for AKI and paKST (eBox and eBackground in the Supplement).<sup>117,118</sup>

## **Workgroup 6: Who Are the Key Stakeholders and What Is Required to Promote Education and Advocacy for AKI in Children?**

### **Consensus Statement 6A (Recommendation)**

- Given the adverse immediate and lifelong outcomes for children with AKI, education and advocacy are essential, starting with the patient and family and expanding across health care teams, systems, and communities.

### **Consensus Statement 6B (Suggestion)**

- Customized AKI education and advocacy require a comprehensive, multidisciplinary, and patient/family centered focus, with AKI champions embedded at every level, embracing the complexities of diverse settings and individuals, which need to evolve over the pediatric life span.

Education may address the widespread gaps in AKI recognition.<sup>119</sup> Lack of AKI awareness may be associated with disparities in AKI outcomes.<sup>120</sup> Extending education to all stakeholders can reduce the risk of missing AKI or delaying care.<sup>121</sup> Because delayed changes in clinical markers (serum creatinine level, urine output) may delay recognition of kidney injury, education requires awareness of risk factors. Education must be delivered in varied settings, different backgrounds of health care workers, and available resources with a flexible approach adjusted for the scenario and depth of knowledge needed (Figure 3<sup>31</sup>).

Education must include recognition of AKI risk, prevention and treatment of volume depletion, careful attention to fluid balance, avoidance or limitation of nephrotoxic medications, and blood pressure monitoring. Checklists, standardized screening and care protocols (care bundles), adapted to and used across varied settings, can enhance identification of patients with or at risk for AKI.<sup>122</sup> Successful education programs also require strong advocacy efforts to engage different constituents, including patients and families, community members, physicians, allied health care professionals, industry affiliates, and governmental and nongovernmental organizations (eTable 3 in the Supplement). Education must be tailored to all members of the health care team, including patients and family, and should occur on micro (individual learners, training program curriculum, teaching modules, and alert systems for providers) and macro (health care system, communitywide educational programs, and governmental policy) levels.

AKI education must be an integral part of the curriculum of foundational and advanced education for all health care professionals, with continuing medical education for all practitioners. Programs should view AKI as a core competency metric.<sup>121,123</sup> Specialists in AKI (including educators, researchers, and advocates) must use educational methods for those who access online free open-access medical education,<sup>124</sup> available globally 24 hours per day. Patients and families may be unaware of the AKI episode or of the potential for long-term adverse outcomes. AKI education may help empower them to participate in healthy lifestyle modification and may improve follow-up, which has the potential to improve long-term outcomes.<sup>125,126</sup> Adaptable and multifaceted educational tools, available in a variety of primary languages and for varying levels of health literacy, should support comprehensive care from admission through discharge, follow-up and potentially, readmission. Connectivity between patient and family with clinician may be essential in the AKI care continuum.

AKI diagnosis remains a significant challenge across areas with varying resource availability (low-income, war zones, and disaster areas), with the lack of appropriate laboratory supplies, adequate medical infrastructure, and personnel. A recent survey emphasized the importance of involving and educating governments about the implications of AKI.<sup>127</sup> Fostering partnerships with industry and the international medical community will also be beneficial. Public-private partnerships and programs may have established platforms that can be used for earlier diagnosis of AKI (eBox and eBackground in the Supplement).<sup>128</sup>

## Discussion

The pADQI consensus statements are expert-derived landscape definitions of the multifaceted and multidisciplinary approach needed to improve prediction, diagnosis, management, and follow-up care for AKI in children. The AKI story requires partnerships between patients and providers, across the medical landscape and across the ages of children. We have provided recommendations for current efforts and identified opportunities to address knowledge gaps (eBox in the Supplement).

## Limitations

This study has limitations. The recommendations of the pADQI are based on existing evidence and consensus but a systematic review on all individual studies and pieces of data was not performed. We also acknowledge recent studies on AKI epidemiology, biomarkers, fluid accumulation, kidney support therapy, nutrition, pharmacology, and education are in progress or have been completed since the completion of pADQI and we could not account for their findings in our recommendations.

## Conclusions

Nearly 2 decades of work in critical care nephrology has delivered a robust foundation on which to frame future AKI education, advocacy, research, and clinical practice. AKI in children is unique and is associated with long-lasting consequences. Improved outcomes in patients will require a comprehensive and cross-discipline approach requiring stakeholders across medicine, community, and government to partner with children and their families.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Key Points**

**Question**

What are the clinical care, education, research and advocacy-based priorities for acute kidney injury (AKI) in children and young adults?

**Findings**

In this consensus statement, a panel of 46 global experts developed pediatric AKI specific consensus statements regarding epidemiology, diagnostics, mechanical support, educational goals, and biologic and physiologic development of the growing child. In addition gaps in knowledge and areas for further research were identified.

**Meaning**

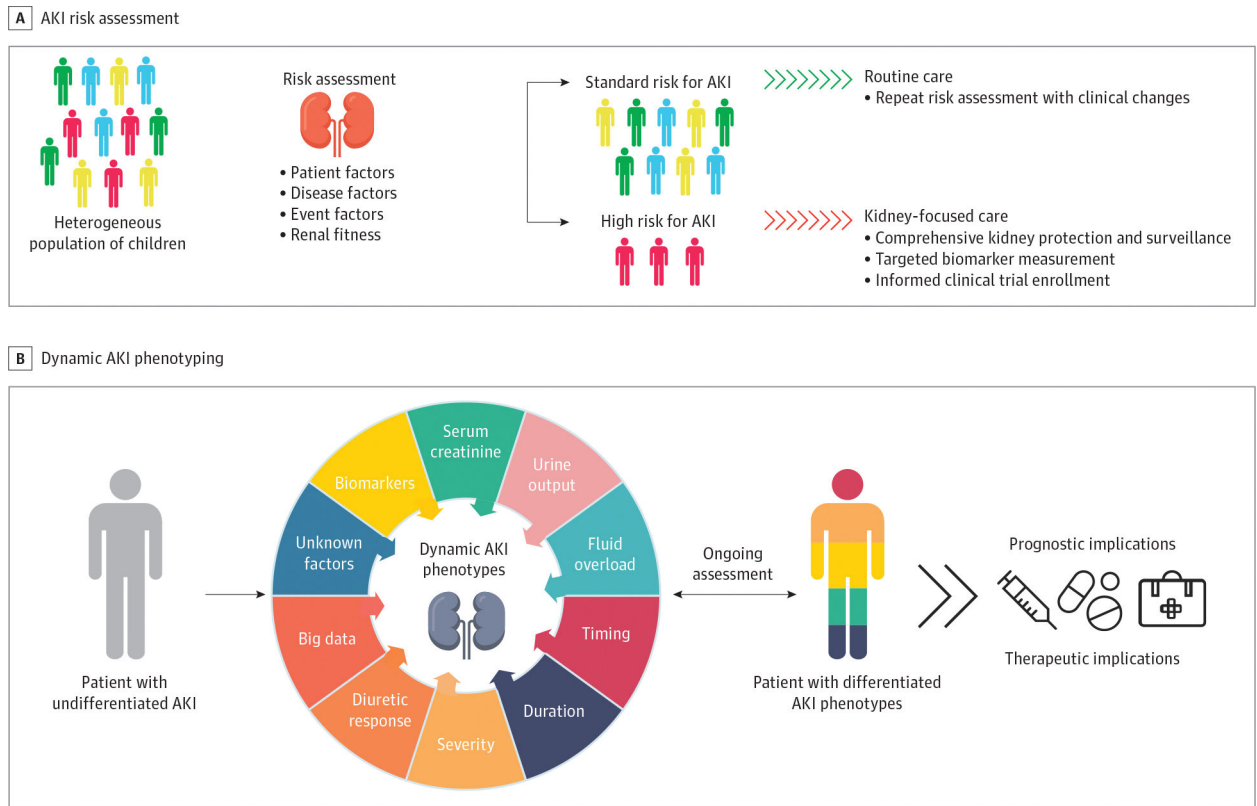
Focused and coordinated efforts, integrating AKI specialists and researchers with the general medical community and population, may improve short-term and long-term outcomes for children and young adults with AKI in the areas of disease awareness, diagnostics, recognition, management, and follow-up.

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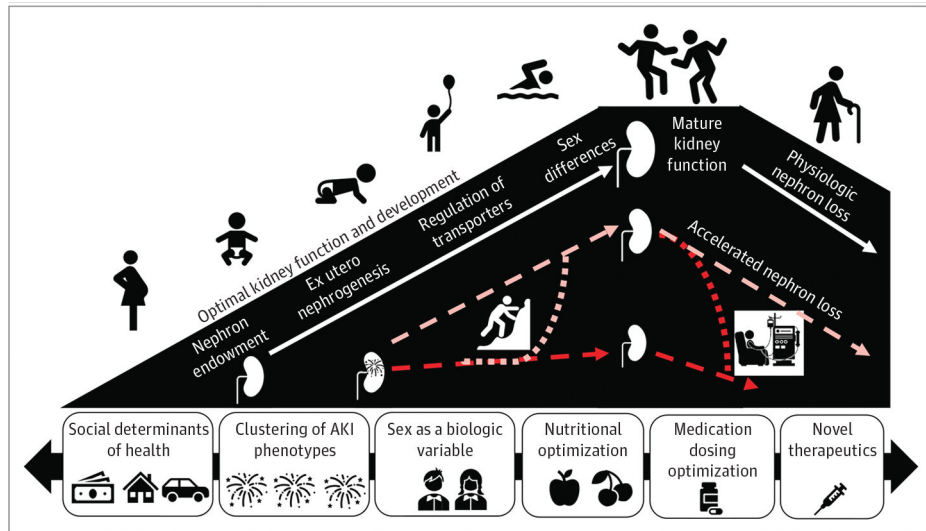
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**Figure 1. Acute Kidney Injury (AKI) Risk Assessment and Dynamic Phenotyping**

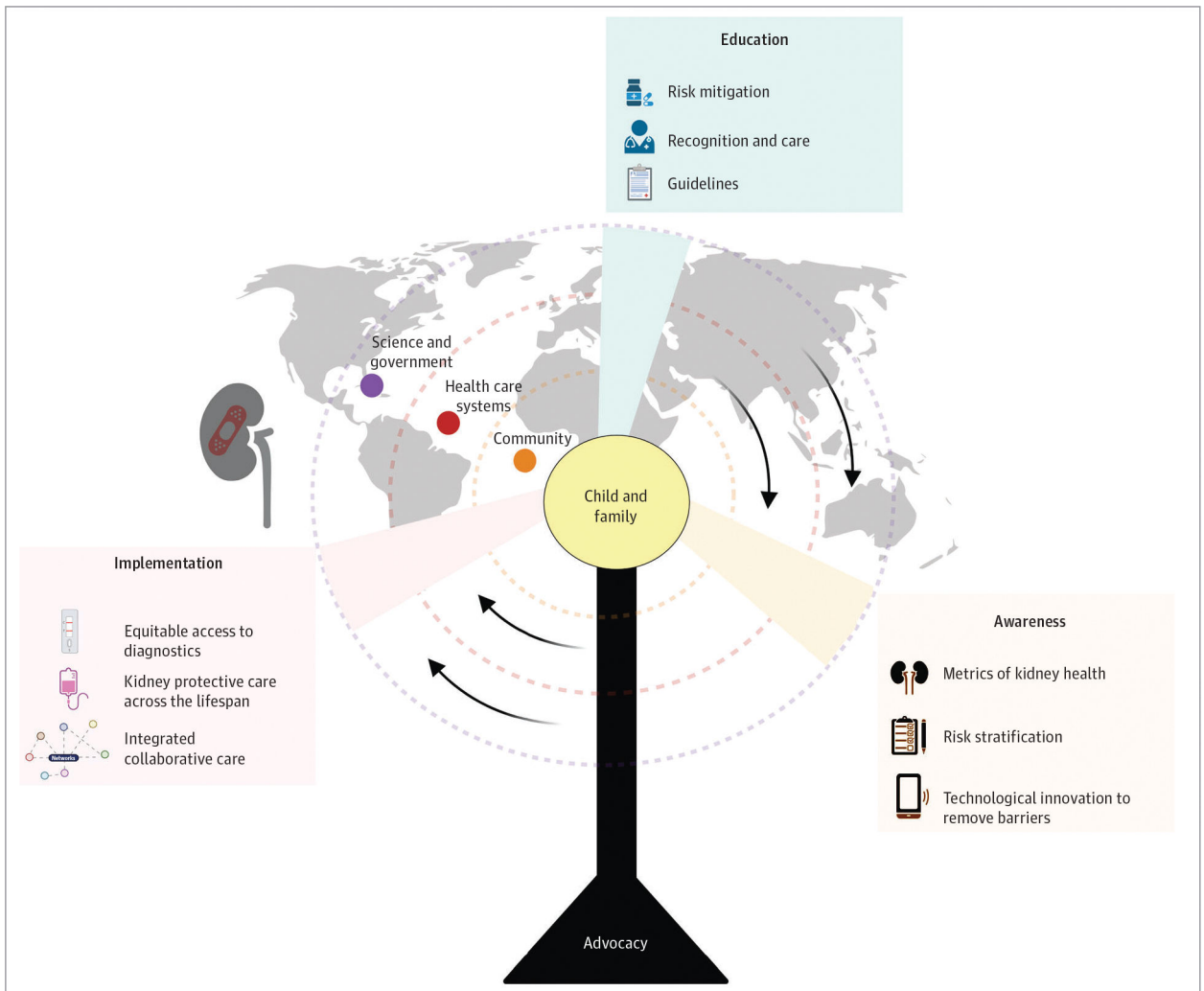
A, AKI risk assessment should occur in children with a potential kidney insult or any clinical changes to stratify patients into those at standard or high risk for AKI such that kidney-focused care can be implemented. B, Combined with individual susceptibility, multiple elements contribute to discernible AKI phenotypes in affected children that may have prognostic and therapeutic implications. Adapted from the 26th Acute Disease Quality Initiative<sup>31</sup> with permission. These are open access images distributed under the terms of the Creative Commons Attribution License.



**Figure 2. Development as a Biologic Variable Related to Acute Kidney Injury**

The left slope highlights important developmental stages critical to reach optimal kidney function. The right slope represents the normal age-related decrease of kidney function. Acute kidney injury (AKI) can occur at any phase along the developmental trajectory resulting in early kidney compromise and potentially accelerated nephron loss. The timing and degree of AKI likely affect the trajectory to recovery of normal kidney function or persistently decreased function. Research efforts must focus on uncovering and capitalizing on the ways to improve the outlook of an injured kidney. These efforts may include optimization of nutrition, limiting further injury, and novel therapeutics. There are factors that accelerate nephron loss and the trajectory toward kidney failure. The social determinants of health, the types or clusters of AKI, sex as a biologic variable, nutritional factors, and medication dosing are all components that affect the recovery or decrease of kidney function after AKI. Adapted from the 26th Acute Disease Quality Initiative<sup>31</sup> with permission. These are open access images distributed under the terms of the Creative Commons Attribution License.





**Figure 3. The Role of Education and Advocacy in Pediatric Acute Kidney Injury (AKI)** Education to improve AKI awareness and recognition in children rests on the pillar of advocacy and must engage key stakeholders in developing multidisciplinary context-appropriate customized approaches to improve AKI care globally and across all resource settings. Effective AKI education programs center the child and family, and expand across health care teams, systems, and communities with champions embedded at every level, health care systems, science, and government. AKI education must be a core competency for health care clinicians to ensure that AKI risk mitigation measures are in place to reduce AKI in community and hospital settings, to facilitate early recognition of AKI through technological innovation, and to appropriately manage AKI using context-specific guidelines that recognize the need for continuity of care and clinical follow-up. Implementation of an effective AKI education and advocacy program assures equitable access to diagnostics, emphasizes integrated multidisciplinary collaborative care, and recognizes the unique long-term health outcomes of AKI in children across the life span. Adapted from the 26th Acute Disease Quality Initiative<sup>31</sup> with permission. These are open access images distributed under the terms of the Creative Commons Attribution License.

**Table.**

### Consensus-Derived Considerations to Address Knowledge Gaps for Children and Young Adults With Acute Kidney Injury

Paradigm	Consensus	Knowledge gap and needed work
Epidemiology	<ul style="list-style-type: none"> <li>Stratified understanding of high risk: Neonates, heart disease, chronic kidney disease, sepsis, cystic fibrosis, transplant history, oncologic history, chronic liver disease</li> </ul>	<ul style="list-style-type: none"> <li>Middle- and low-income populations</li> <li>Expanded AKI phenotypes</li> </ul>
Diagnostics	<ul style="list-style-type: none"> <li>Biomarker-based delineation of standard vs high risk</li> </ul>	<ul style="list-style-type: none"> <li>Integration of concurrent diagnostics</li> <li>Differentiation of diagnostics over time</li> </ul>
Fluid balance	<ul style="list-style-type: none"> <li>Use of percent fluid balance and anchor weight (ICU admission weight)</li> </ul>	<ul style="list-style-type: none"> <li>Adjudicate “fluid overload” by illness state</li> </ul>
KST	<ul style="list-style-type: none"> <li>Institute benchmarks and components of KST team</li> <li>Need for pediatric specific extracorporeal therapies</li> </ul>	<ul style="list-style-type: none"> <li>KST team, quality, and cost optimization</li> <li>KST integration of tandem therapies</li> </ul>
Biopathology	<ul style="list-style-type: none"> <li>Pediatrics incorporated into research efforts</li> <li>Importance of nephrotoxin stewardship programs</li> <li>Promoting bench-bedside collaboration between preclinical, epidemiological and clinical trial researchers</li> </ul>	<ul style="list-style-type: none"> <li>Determination of sex as a biological variable related to AKI</li> <li>Characterize medications affected by AKI across developmental spectrum</li> <li>Identify the optimal nutritional interventions by age for AKI</li> </ul>
Education and advocacy	<ul style="list-style-type: none"> <li>Differential approach based on national resources</li> <li>Integration of electronic medical record/checklists</li> </ul>	<ul style="list-style-type: none"> <li>Governmental and community partnerships</li> <li>Cross-discipline health care training</li> </ul>

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; KST, kidney support therapy.