ADQI 26 Figures

ADQI XXVI (pADQI) FIGURES

Figure 1: An Evolving Approach to AKI Epidemiology

The study of AKI epidemiology in children is at an inflection point. The development of a standard definition has helped build our current understanding of pediatric AKI, however, the existing approach yields only incremental knowledge, and the community needs to transition into a new stage of analysis. The need for this transition is driven by several existing factors. First, there are gaps in our understanding of the impact of AKI on longitudinal and emerging outcomes; long term functional outcomes, quality of care and life, and other healthcare metrics have become priorities. Second, while certain aspects of AKI have been well described, our global understanding of AKI remains limited; in particular, AKI in under resourced and non-critical care contexts remain inadequately studied. Third, the causal relationship between AKI and outcomes remains poorly understood. Finally, the development of AKI biomarkers will allow identification of AKI events at the point of injury rather than the point of dysfunction. The next stage in epidemiologic evaluation of AKI will be steered by providers and traditional stakeholders, the priorities of patients and families, and by the needs of care systems and contexts. While barriers to a more fundamental understanding of AKI epidemiology exist, cyclical evaluation will allow us to provide better support for clinical decision making and process implementation, to improve the quality and efficiency of care, and will lead to better kidney and non-kidney outcomes that are prioritized by both providers and patients.

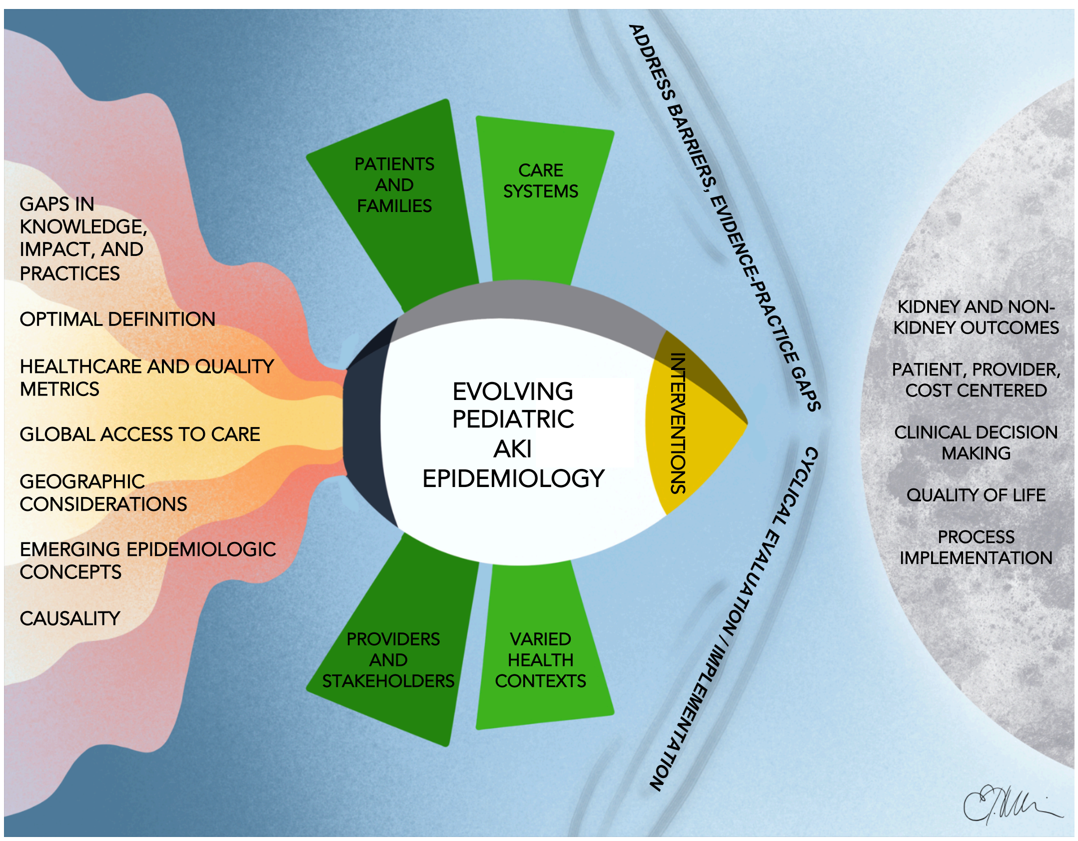

Figure 2. Acute kidney injury risk assessment and dynamic phenotyping. Panel A. Acute kidney injury (AKI) risk assessment. This should occur in children with any clinical changes or a planned kidney insult to stratify patients into those at standard or high risk for AKI such that kidney focused care can be implemented in high-risk children. **Panel B. Dynamic AKI Phenotyping.** Combined with individual susceptibility, multiple elements contribute to discernible AKI phenotypes in affected children which may have prognostic and therapeutic implications.

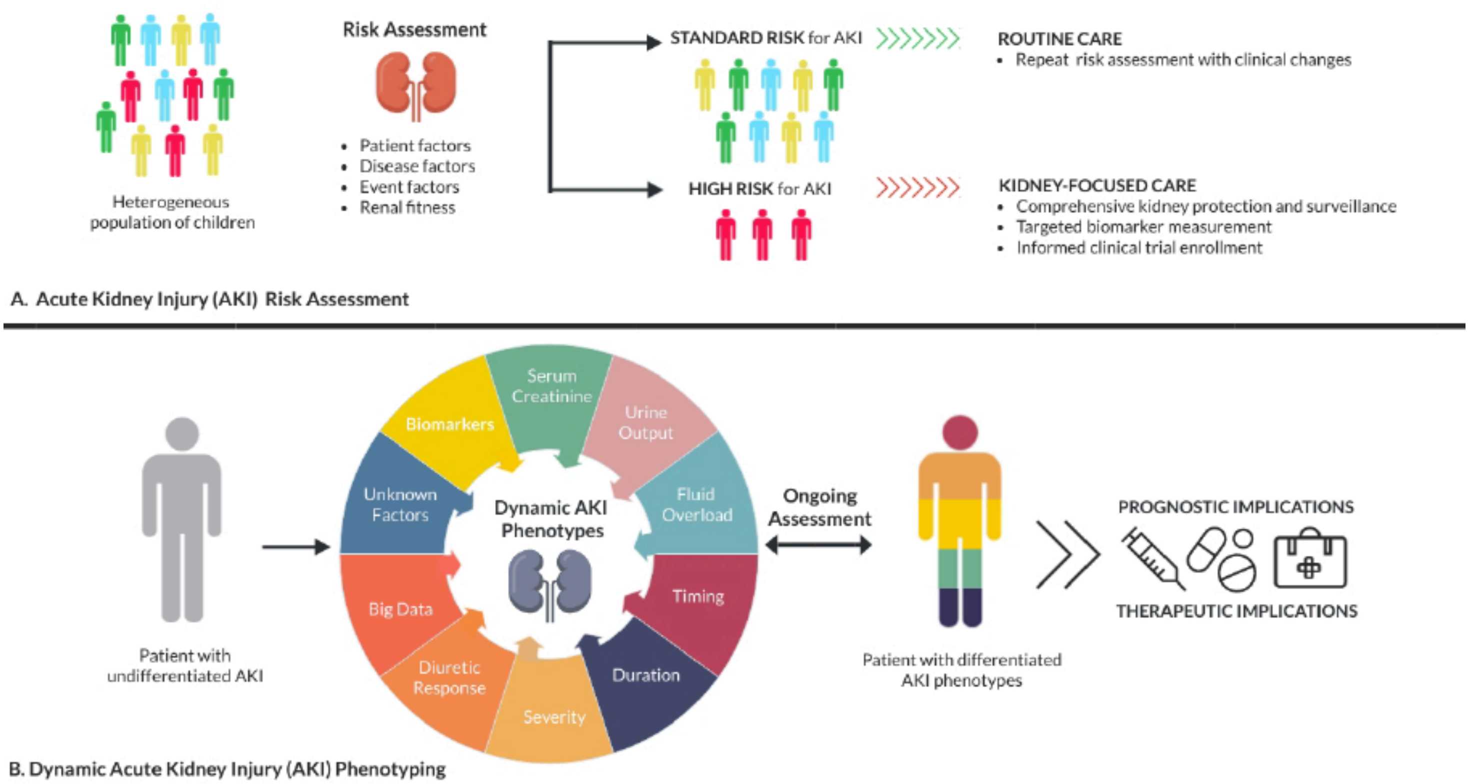

Figure 3.1: The Spectrum of Fluid Balance
There is a spectrum of fluid balance for the sick child that is a U-shaped curve. (A) This spectrum can swing between positive fluid balance (+FB) and negative fluid balance (-FB) with varying levels of clinical impact depending on the severity of the abnormal fluid balance. (B) Depending on the case-mix and/or resources available, the U-shaped curve may have more or less tolerance for a positive or negative fluid balance. These depict examples of different scenarios where a patient population may have greater or lesser tolerance of a +FB or -FB scenario. (C) For any given sick child, there are several factors (i.e., host factors, interventions, adverse outcomes) that may push them towards a greater +FB or -FB or pull them back towards a state of neutral fluid balance at the center. These may vary over the course of the hospitalization and can be constantly changing.

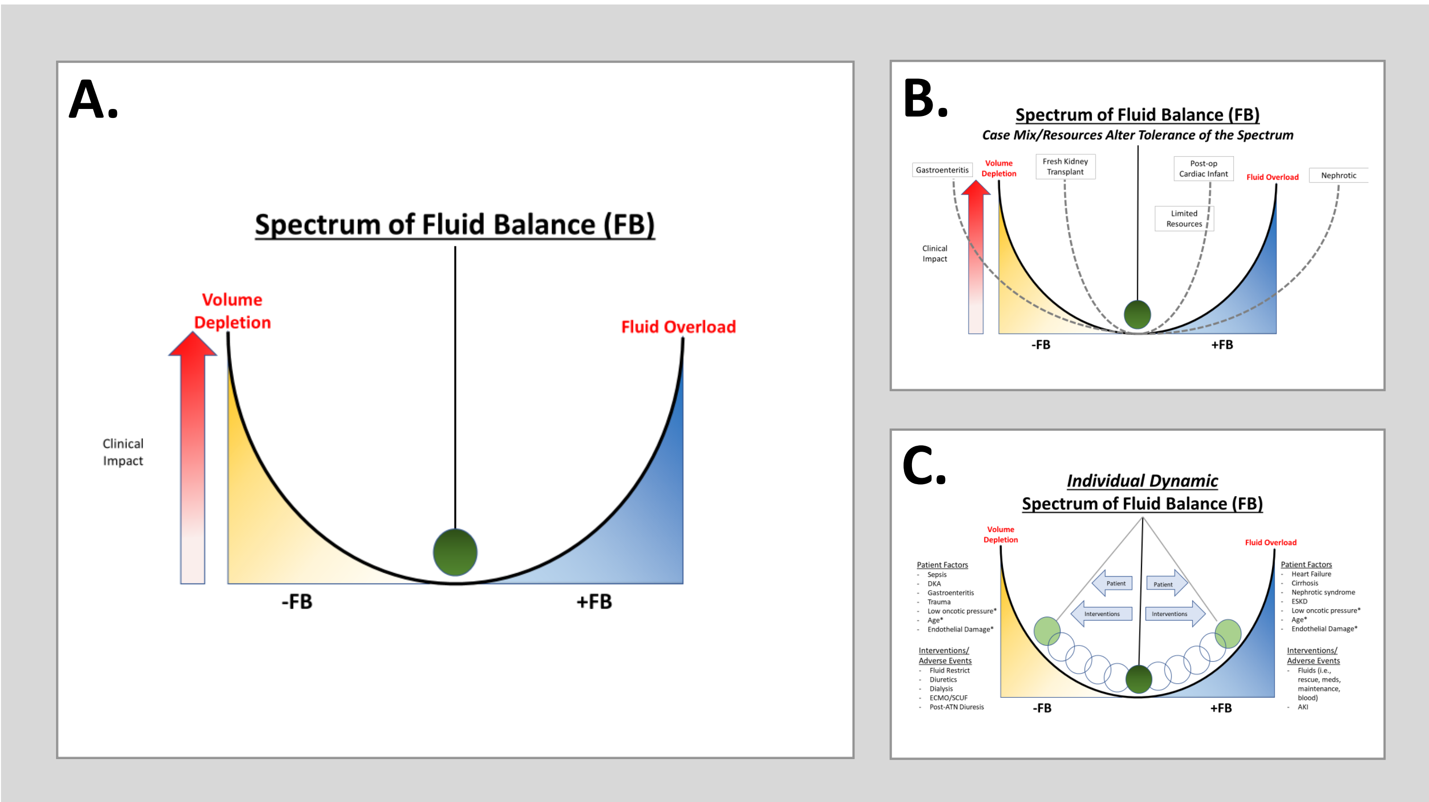

Figure 3.2 Complex Relationship of Fluid Overload and Mortality The directed acyclic graph (DAG) above is an example of the utilization of this tool to describe the complex relationship between fluid overload and mortality in sick children. Different DAGs would be necessary to evaluate positive or negative fluid balance or other fluid states and different outcomes. The variables depicted in this figure are likely not exhaustive and additional nuanced variables could be considered (e.g., genetics). The figure is meant to be as comprehensive as possible with current knowledge-to-date to demonstrate the complexity of the relationship and the importance that all factors are considered to minimize bias when trying to use observational studies to evaluate the fluid overload-mortality relationship and its potential for a causal pathway.
Legend: Arrows depict a known associated risk relationship (whether that is a positive or negative relationship) E=the primary exposure of interest (fluid overload in this example) O=the primary outcome of interest (mortality in this example) White circles = represent variables that are confounders in the primary exposure-outcome relationship and would be the required minimal adjustment variables to account for in order to get a fully adjusted analysis of the primary exposure-outcome relationship (i.e., the minimal adjustment set) Pink circles = represent additional variables that are also confounders but not necessary for a minimal adjustment set evaluating the primary exposure-outcome relationship. Orange circle = ancestor to primary exposure of interest

Complex Relationship of Fluid Overload and Mortality
(Directed Acyclic Graph, DAG)

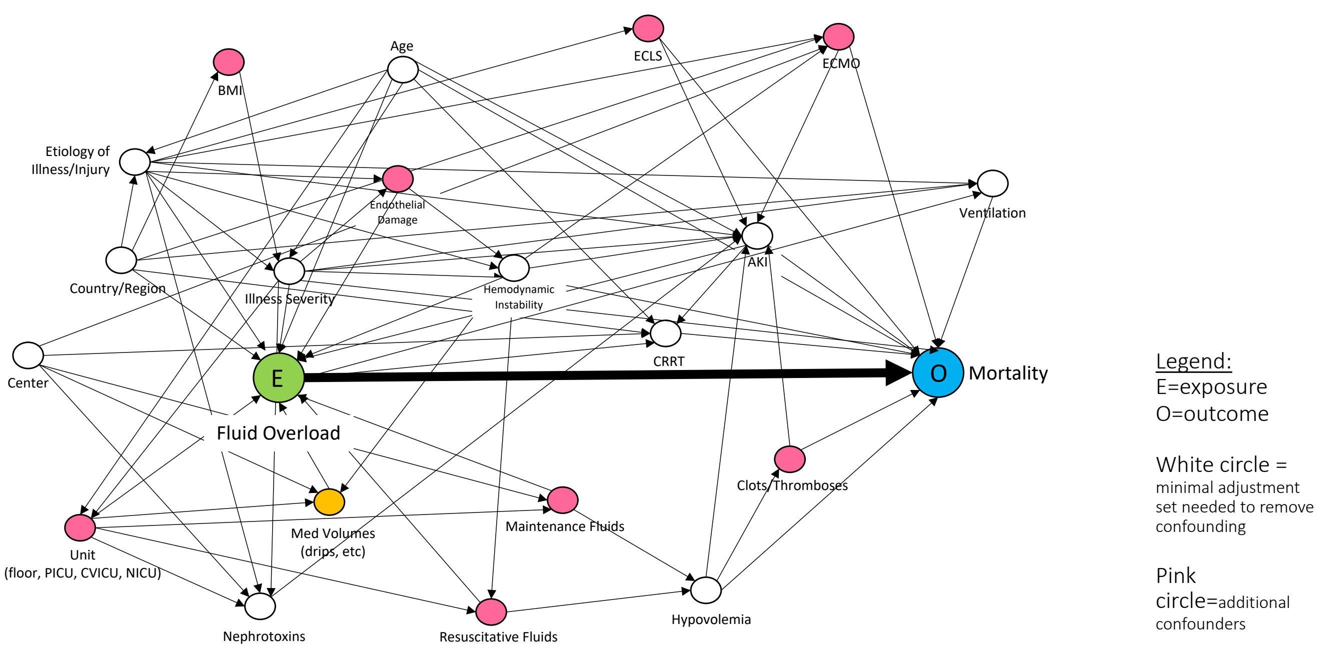

Figure 4. Pediatric acute kidney support therapy (paKST)
Improving hospital-based and lifelong outcomes among children with severe AKI requiring paKST requires a multi-pronged approach. Establishing an experienced and well-trained health care team, fully integrating the patient and family, and pursuing ongoing quality improvement initiatives are foundational to a strong paKST program. Understanding and implementing various paKST components is also critical to providing safe and effective therapy for kidney and non-kidney indications. Equally essential is the ability to execute timely de-escalation of paKST with a plan for appropriate follow-up for these children.

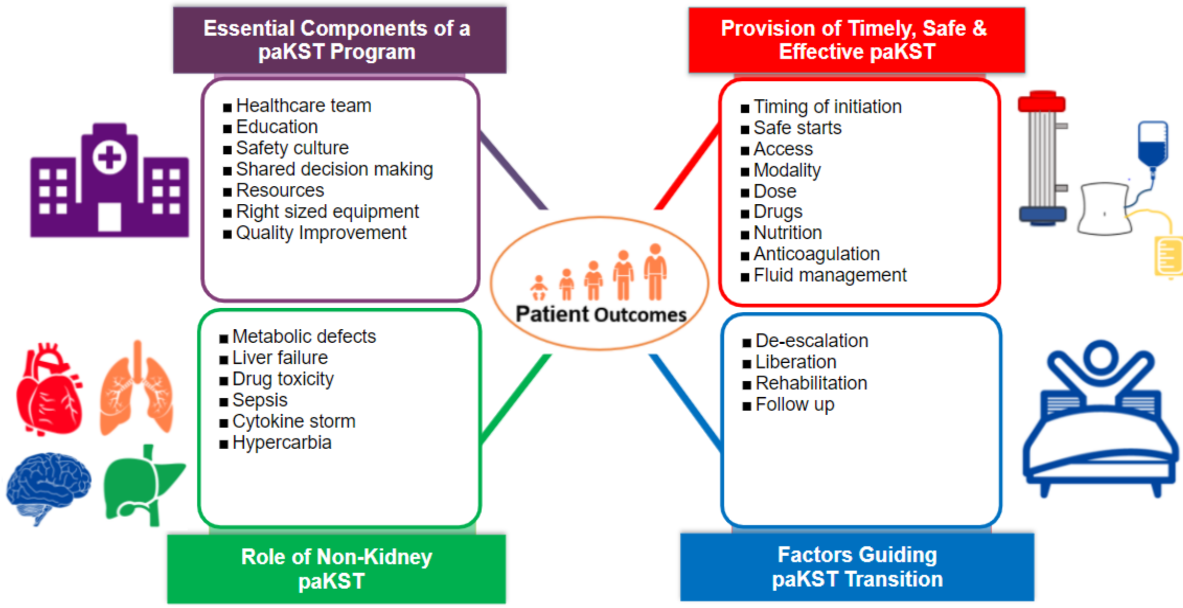

Figure 5.1 Development as a Biologic Variable in Pediatric Kidney Function and Recovery. The left slope highlights many of the important developmental stages that are critical to reach optimal kidney function. Within these phases of normal development, many questions remain unanswered. For example, the factors that influence nephron endowment, challenges of *ex utero* nephrogenesis, developmental regulation of transporters within the kidney, and role of sex as a biologic variable remain incompletely understood. The slope on the right represents the normal aged-related decline of kidney function. Acute kidney injury can occur at any phase along the developmental trajectory resulting in early kidney compromise and potentially accelerated nephron loss. The timing and degree of pediatric AKI likely influence the trajectory either to recovery of normal kidney functional development or persistently decreased function. Highlighted by the rock climber, research efforts must focus on uncovering and capitalizing on the ways to improve the outlook of an injured pediatric kidney. These efforts may include optimization of nutrition, limiting further injury and novel therapeutics. As illustrated by the patient on dialysis, there are also factors that accelerate nephron loss and the trajectory towards 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 may impact the recovery or decline of kidney function after pediatric AKI.

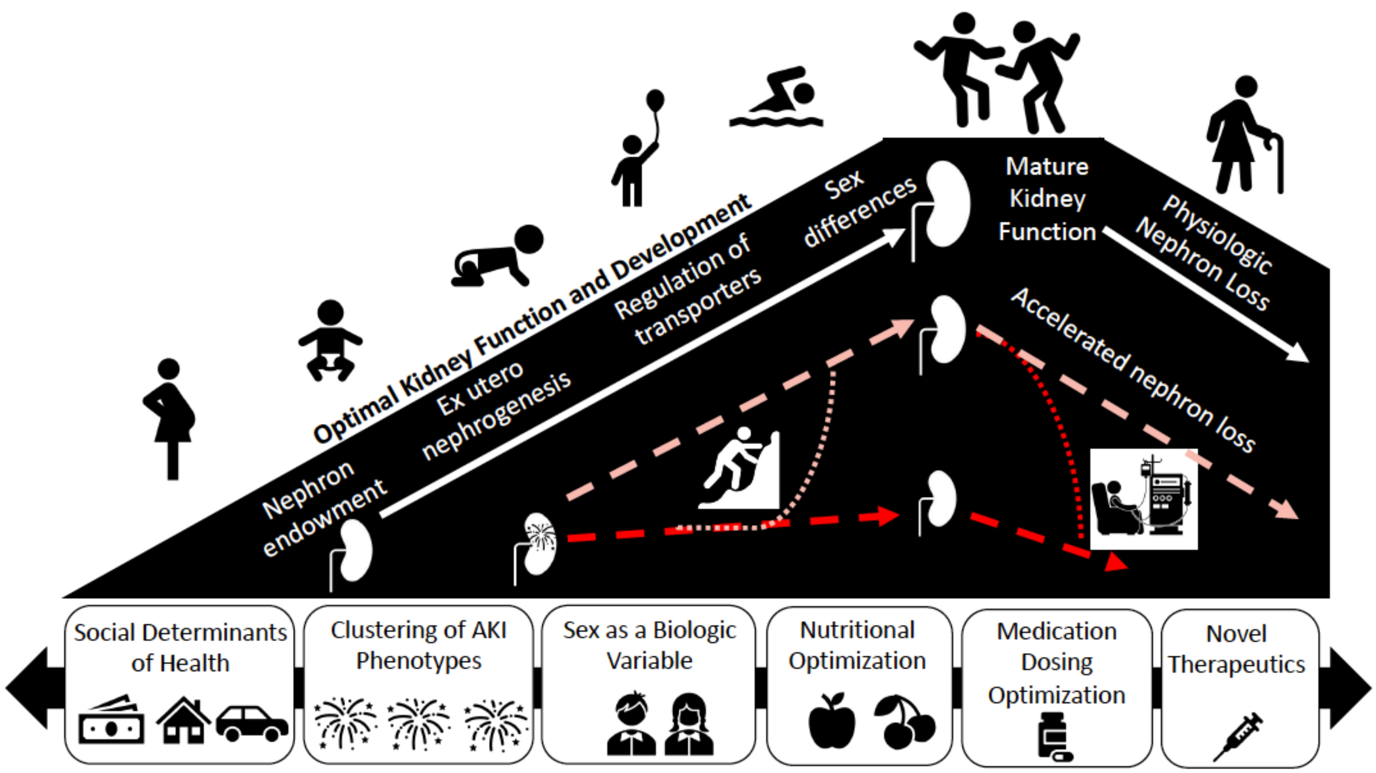

Figure 5.2 Development as a Biologic Variable.
The left slope of figure highlights many of the important developmental stages that are critical to reach optimal kidney function. Within these phases of normal development, many questions remain unanswered. For example, the factors that influence nephron endowment, challenges of ex utero nephrogenesis, developmental regulation of transporters within the kidney, and role of sex as a biologic variable remain incompletely understood. The right-handed slope represents the normal aged-related decline of kidney function. Acute kidney injury 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 influence the trajectory either to recovery of normal kidney function or persistently decreased function. Highlighted by the rock climber, 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. As illustrated by the patient on dialysis, there are also factors that accelerate nephron loss and the trajectory towards 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 impact the recovery or decline of kidney function after AKI.

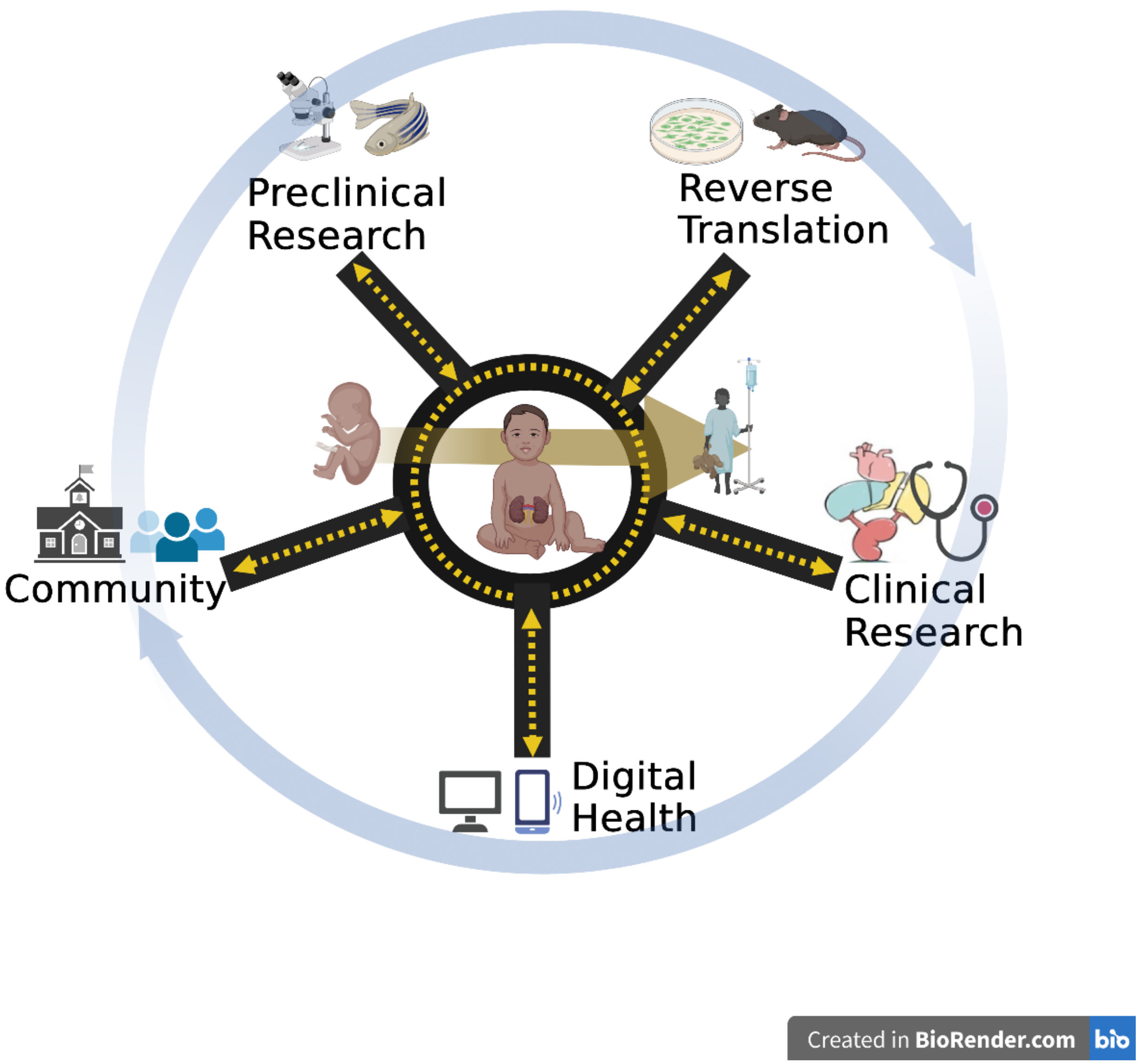

Figure 6. The role of education and advocacy in pediatric acute kidney injury (AKI). Education to improve AKI awareness and recognition in children rests on the pillar of advocacy and must engage key stakeholders in developing multi-disciplinary, context-appropriate, and customized approaches to improve AKI care globally and across all resource settings. Effective AKI education programs center the child and family (yellow circle at center), and expand across health care teams, systems, and communities with champions embedded at every level (Community (orange), Healthcare Systems (red), Science & Government (purple)). AKI education must be a core competency for healthcare providers 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 multi-disciplinary collaborative care, and recognizes the unique impact of AKI in children on long-term health outcomes across the lifespan.