Large study identifies risk factors in children with chronic kidney disease

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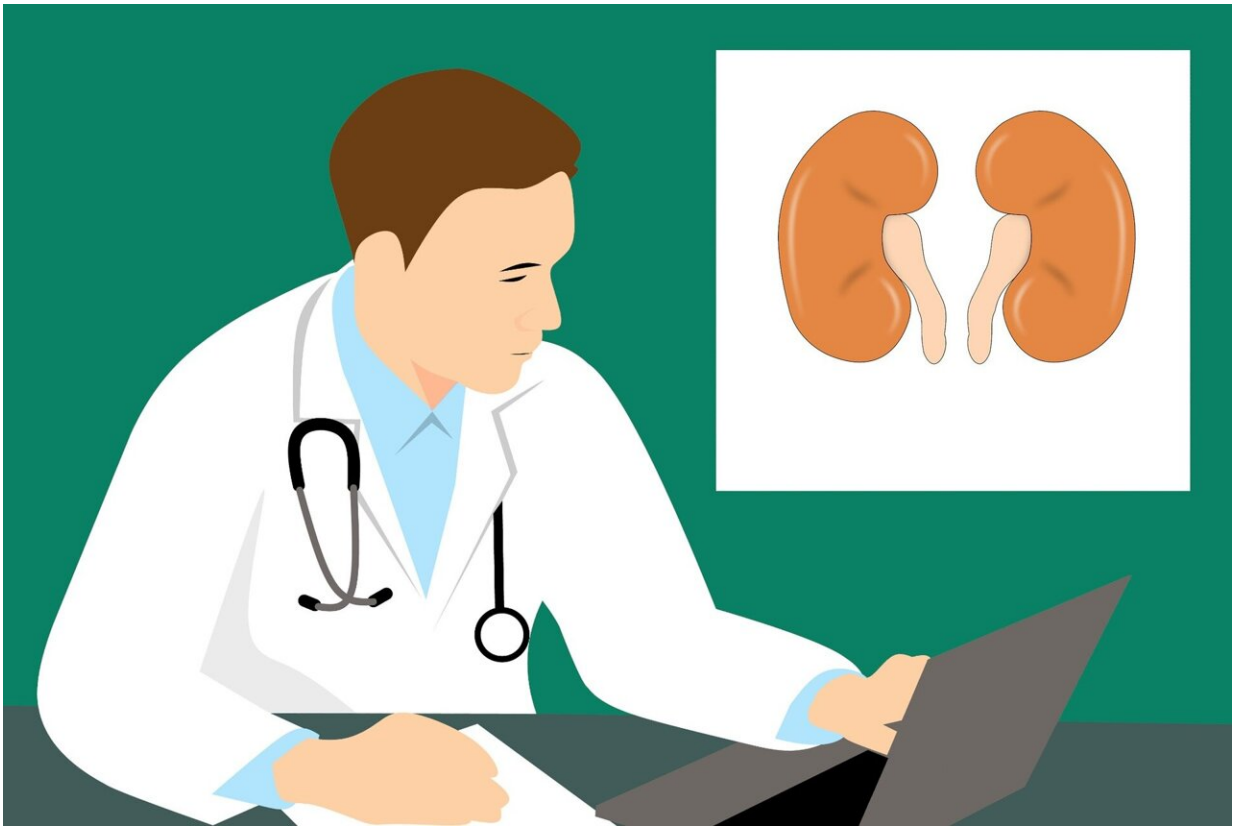

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Chronic kidney disease (CKD) in children is rare, which makes it difficult to study and leaves major gaps in the quantity and quality of evidence that informs the care of pediatric patients with the condition.

Even the largest prospective studies are limited in their usefulness, as they are constrained by selection bias and relatively small sample sizes for different causes and courses of the disease.

In a new study led by Children's Hospital of Philadelphia (CHOP) and Nemours Children's Health, researchers have overcome the obstacle of scale by analyzing electronic health record data from PEDSnet, a national multicenter pediatric network, to identify a large cohort of children with CKD, evaluate CKD progression, and examine clinical risk factors for kidney function decline. The findings were published in the *Clinical Journal of the American Society of Nephrology*.

"The overarching goal of this project was to demonstrate that real world EHR data can be used to model kidney function decline in children. Chronic kidney disease in children is rare and as such there are few high-quality studies that inform clinical decision making," said Caroline Gluck, MD, physician, Division of Nephrology at Nemours Children's Health, Delaware.

"In contrast to prospective cohort studies, this study represents an unbiased sample of the US source population and to our knowledge represents the largest cohort of children with CKD to date."

To better understand factors contributing to the decline in kidney function in patients with CKD, the researchers focused on children from six pediatric health systems in the PEDSnet database who were seen between January 1, 2009, to February 28, 2022. Of more than 7.1 million children, the researchers identified 11,240 (0.157%) with CKD.

They divided the group into subcohorts based on CKD type: glomerular, non-glomerular, and malignancy-associated. CKD progression was determined based on estimated glomerular filtration rate (eGFR), a calculated index of kidney function based on serum creatinine level that

determines the stage of kidney disease; the need for long-term dialysis; and the need for a kidney transplant.

The researchers found that the following attributes in children with CKD were associated with a more rapid decline in kidney function: disease of glomerular or malignancy-associated origins; high levels of protein in the urine (proteinuria); hypertension; younger age; more advanced CKD; male sex; and greater medical complexity at the start of follow-up care.

For example, over an average follow-up time of five years, 40% of patients with glomerular CKD required long-term dialysis or transplant or experienced more than a 50% reduction of eGFR, whereas the same was true of only 13% of patients with non-glomerular CKD.

Given the size of the population analyzed in the study—which also included children with cancer, who have a high burden of CKD but have been excluded from or underrepresented in prior studies—the findings can be applied more broadly to the pediatric CKD population.

"Children with the risk factors identified in our study are of particular concern for CKD progression and may be targeted for comparative effectiveness studies to preserve kidney function," said senior author Michelle Denburg, MD, MSCE, a nephrologist at Children's Hospital of Philadelphia and co-director of the CHOP Pediatric Center of Excellence in Nephrology and of the Penn-CHOP Kidney Innovation Center.

"The findings and methods in this study are foundational to future research in children with CKD, including the PRESERVE study I am co-leading with Dr. Christopher Forrest, Director of PEDSnet, which is leveraging EHR data from 16 pediatric health systems to analyze blood pressure management and preservation of kidney function in pediatric CKD. This study can also serve as a roadmap for use of EHR data

networks to adequately power the study of rare disease."

More information: Caroline A. Gluck et al, Evaluating Kidney Function Decline in Children with Chronic Kidney Disease Using a Multi-Institutional Electronic Health Record Database, *Clinical Journal of the American Society of Nephrology* (2023). DOI: 10.2215/CJN.0000000000000051

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