



# Application of the updated international IgA nephropathy prediction tool in pediatric patients

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## ABSTRACT

The International IgA Nephropathy Prediction Tool (IgAN-PT) aims to provide individualized risk assessments for patients diagnosed with primary IgAN, which is a prevalent cause of kidney disease, especially among young adults. This tool helps clinicians to understand the risk for worsening kidney function over a period of 5-7 years post-diagnosis. This scoring can be conducted by the physician at the time of diagnosis, while it requires only routine clinical data, laboratory results, and biopsy findings. This system also is applicable to adults and pediatrics of all ethnicities.

### *Implication for health policy/practice/research/medical education:*

The International IgA Nephropathy Prediction Tool (IgAN-PT) is a noteworthy development to assess the risk of IgA nephropathy development. This tool developed in 2018 and was designed to predict the likelihood of a 50% decline in renal function or progression to renal insufficiency based on clinical and histopathological markers at the time of kidney biopsy. The impact of this tool extends beyond mere risk prediction; since it serves as a pivotal resource for clinicians striving to personalize treatment and management strategies in IgAN too.

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## Introduction

IgA nephropathy (IgAN) is recognized as the most common form of glomerulonephritis worldwide and serves as a significant contributor to chronic kidney disease and end-stage renal disease (ESRD) (1). Annually, it affects approximately 200,000 to 350,000 individuals globally (2). The prevalence of IgAN varies significantly by region, with it accounting for about 40% of glomerulonephritis in Asia (1,3). This regional discrepancy may be influenced by genetic and racial factors (1,3). The clinical progression of IgAN can range from persistent, asymptomatic microscopic hematuria to rapid deterioration leading to renal insufficiency (4). The risk of progressive deterioration in renal function is highly variable; studies indicate that the incidence of end-stage kidney disease can range from 5% to 60% within a decade following diagnosis (4, 5). This variability underscores the challenge in

predicting individual patient outcomes (5). For example, a previous systematic review and meta-analysis by Duan et al, indicates that older age increases the incidence of ESRD by approximately 1.95 times, emphasizing age as a critical risk factor for disease progression (6). In 2018, the International IgA Nephropathy Prediction Tool (IgAN-PT) was introduced as a pivotal instrument to assess the individual risk of disease progression in patients suffering from primary IgAN. This innovative tool named as IgAN-PT, incorporates both clinical and histopathological markers collected at the time of renal biopsy, thereby enabling the prediction of a 50% decrease in glomerular filtration rate (GFR) or the onset of renal insufficiency in affected individuals. Notably, the tool has undergone modifications to cater specifically to the pediatric population, allowing for risk assessments at both one and two years following the kidney biopsy (7,8). The initial

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model was derived from a multiethnic cohort involving 2781 patients and validated in an additional 1146 patients (4). It incorporates several clinical indicators including age, eGFR, proteinuria, blood pressure, and histological findings defined by the Oxford classification (MEST score) (4,9). These variables are recognized for their association with the severity of renal impairment and are essential in stratifying patient risk (9). However, recent studies have updated the prediction tool for use one- or two-years post-biopsy. This updated model showed improved calibration and predictive performance compared to the original version when applied after one year. The updated tool also demonstrated a higher concordance statistic for four-year predictions, indicating better accuracy in risk stratification (8,10,11).

### Search strategy

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different keywords like; IgA nephropathy, glomerular filtration rate, kidney failure progression and Oxford classification.

### Performance of IgAN-PT over time

The IgAN-PT shows excellent discriminatory ability for predicting outcomes within the first five years post-diagnosis, achieving an area under the curve (AUC) of 0.90. This indicates a high level of accuracy in identifying patients at risk of a 50% decline in renal function or progression to end-stage kidney failure during this period. As time progresses, the predictive accuracy of the IgAN-PT remains strong but shows a slight decline. For instance, the AUC is reported at 0.83 for predictions extending up to 20 years. This gradual decrease suggests that while the tool is highly effective in the short term, its predictive power may diminish slightly over longer durations (12).

### IgAN-PT in children

The IgAN-PT is designed with two distinct models—one that accounts for ethnicity and one that does not. This tool is pioneering in its ability to forecast the risk of a 30% reduction in kidney function or the onset of renal disturbance in pediatrics at the time of biopsy. It utilizes specific clinical risk factors combined with the Oxford MEST histology scores for its predictions (10,13). Recently, the tool underwent an update using a diverse international cohort of 947 children diagnosed with IgAN, where 38% of participants were monitored into adults. This updated prediction model, applicable one-year post-biopsy, demonstrated better model fit compared to its original version. Barbour et al, at this study, recommend applying the original pediatric prediction tool at the time of biopsy for children, while the updated version should be utilized to reassess risk levels one or 2 years following the renal biopsy (10,13,14).

### Conclusion

The IgAN-PT represents a significant advancement in the prediction and management of IgAN, a common form of glomerulonephritis that can lead to kidney failure if left untreated. This tool is instrumental for nephrologists in assessing the risk of disease progression based on a variety of clinical and histological parameters. An understanding of its development, validation, and clinical applications is pivotal for physicians dealing with this condition. Looking forward, the continuous refinement of this tool is essential. Future studies should explore the predictive power of the model across different populations, focusing on ethnic and genetic variations that may influence disease severity and progression. Additionally, adaptations of the tool could enhance its applicability in various healthcare settings, ensuring that it remains a relevant and dynamic resource in nephrology.

### Conflicts of interest

The author declares that she has no competing interests.

### Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author utilized **Perplexity** to refine grammar points and language style in writing. Subsequently, the author thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

### Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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