Clinical Research

Economic burden and healthcare costs of congenital anomalies of the kidney and urinary tract: a systematic review

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ABSTRACT

BACKGROUND Congenital anomalies of the kidney and urinary tract (CAKUT) cause significant morbidity and economic burden worldwide, highlighting the needs to understand its associated costs. This study aimed to assess the economic burden of CAKUT management.

METHODS A systematic review was conducted across 5 databases, including PubMed, ScienceDirect, ProQuest, Nature, and Google Scholar, for studies published up to September 11, 2024, focusing on both direct (e.g., hospitalizations, surgeries, and treatments) and indirect (e.g., lost work time and complications management) healthcare costs related to CAKUT and published in English. Non-economic studies, reviews, editorials, abstracts, animal/*in vitro* studies, and duplicates were excluded. Methodological quality was assessed using the Risk Of Bias In Non-randomized Studies - of Interventions tool. Narrative synthesis and descriptive statistics were applied. Cost-effectiveness analysis followed Joanna Briggs Institute guidelines.

RESULTS 8 studies met the inclusion criteria, revealing wide variations in CAKUT-related healthcare costs across countries and interventions. These studies focused on reviewing both direct and indirect costs, along with interventions that reduce overall healthcare expenditure. Key findings include: (1) In the USA, bilateral renal agenesis costs averaged USD 26,032; (2) In Australia, early whole exome sequencing reduced diagnostic costs by 20% in genetic kidney disease cases; (3) Robotic surgery demonstrated long-term cost-effectiveness despite higher inpatient costs; (4) Other cost-saving strategies include the early renal ultrasound algorithm and genomic testing for CAKUT.

CONCLUSIONS CAKUT imposes a significant and variable economic burden globally. Identifying cost-effective interventions is crucial for optimizing care and reducing the financial impact. Further research on cost management strategies is needed to improve outcomes and efficiency.

KEYWORDS cost effectiveness, economic burden, health care costs, health expenditures, urogenital abnormalities

Congenital anomalies of the kidney and urinary tract (CAKUT) are developmental defects of the kidneys, ureters, bladder, and urethra that occur during embryonic development. They affect approximately 3–6 per 1,000 live births and account for 23% of all congenital anomalies. They are a leading cause of chronic kidney disease (CKD), contributing to 34–59% of CKD cases and 40–50% of kidney failure in children.[1,2] In Europe, CAKUT is the third most common congenital anomaly found in Europe after congenital heart diseases and limb malformations. Early detection through antenatal ultrasound screening plays an essential role in early detection.[3]

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Management of CAKUT is complex and must be tailored to specific anomalies. Early intervention helps prevent renal damage; however, surgical timing must consider tissue maturation. The risks associated with CAKUT include infections, bleeding, and anesthesia-related complications. Long-term management focuses on treatment efficacy, disease progression, and preservation of renal function.[4,5] In severe cases that progress to end-stage renal disease, dialysis, kidney transplantation, and long-term immunosuppressive therapy are crucial. Transplant patients with CAKUT face challenges in graft survival, with 10-year survival rates ranging from 70–76%.[5,6]

Despite the clinical burden of CAKUT, its economic impact has not been well characterized. Most studies have largely focused on medical outcomes, with limited data quantifying direct (e.g., hospitalizations, surgeries, and treatments) and indirect (e.g., lost productivity and long-term care) costs. The lack of economic evidence hinders effective healthcare planning and policy development. This study aimed to fill this gap by synthesizing existing data on both the direct and indirect costs of CAKUT management. We examined the financial burden associated with interventions for CAKUT, including dialysis, transplantation, surgical procedures, and genetic testing and identified cost-effective strategies to alleviate the overall burden on patients, families, and healthcare systems.

METHODS

In accordance with the for Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines,[7] we conducted a systematic literature review following a rigorous and comprehensive approach to identify relevant studies. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews under registration No. CRD420250656573 and was developed prior to the study in alignment with established PRISMA standards to enhance transparency and reproducibility.

PubMed, ScienceDirect, ProQuest, Nature, and Google Scholar were searched for studies published before September 11, 2024. The search strategy used a combination of keywords and Medical Subject Heading terms and was designed to capture all relevant articles related to the economic burden and healthcare costs associated with CAKUT. The search strategy was refined as follows: ("Economic Burden" OR "Financial Burden" OR "Economic Impact" OR "Healthcare Expenses" OR "Cost Burden" OR "Socioeconomic Impact") OR ("Healthcare Costs" OR "Medical Costs" OR "Healthcare Expenditure" OR "Treatment Costs" OR "Cost of Care" OR "Cost Effectiveness") AND ("Congenital Anomalies of the Kidney and Urinary Tract" OR "Congenital Kidney Anomalies" OR "Congenital Urinary Tract Anomalies" OR "CAKUT" OR "Urinary Tract Congenital Disorders" OR "Paediatric Kidney Malformations").

For Google Scholar, a structured search using Boolean operators was applied, and the first 200 results sorted by relevance were manually screened to ensure the inclusion of grey literature and economic analyses that were not indexed in the traditional databases.

Eligibility criteria

We included studies that examined the economic burden and healthcare costs associated with CAKUT in individuals of any age who required medical care. The inclusion criteria were original research articles and studies reporting healthcare costs related to CAKUT, including hospitalizations, surgeries, treatments, or complications; studies reporting on cost-effectiveness or socioeconomic impact; and articles published in English. We also included studies that compared CAKUT with other congenital anomalies to assess the relative cost burdens. Reviews, editorials, and conference abstracts without full data; studies not reporting any economic outcomes; animal or *in vitro* studies; and duplicate publications were excluded.

Study selection and data extraction

All studies were screened for eligibility by two independent reviewers (AMA and PARR) in two stages: an initial screening of titles and abstracts, followed by a full-text review. Disagreements were resolved by consensus or consultation with a third reviewer (RF). A standardized data extraction form was developed, piloted, and used to collect the information: author(s), year of publication, country, study design, sample size, population characteristics, types of CAKUT, cost components (direct and indirect), cost-effectiveness outcomes, and statistical methods used. In cases where the sample size was not directly reported, estimates were derived from available data, such as patient registries, hospital discharge databases, or population surveys.

Ethical considerations

This review was conducted in compliance with the highest standards of research integrity. Because the analysis involved secondary data from published studies, formal ethical approval was not required. However, all included studies were reviewed to ensure that appropriate ethical approval and informed consent had been obtained, as documented in the respective publications. Moreover, the review process maintained strict confidentiality and anonymity regarding the study data and adhered to ethical guidelines concerning the handling of information in systematic reviews. Transparency and avoidance of data manipulation were prioritized to preserve the accuracy and reliability of these findings, thereby upholding ethical research principles.

Currency conversion

All cost data were converted to United States dollar (USD), the most widely recognized global reserve currency.[8] The cost data were converted to USD 2024 using the Campbell and Cochrane Economics Methods Group Evidence for Policy and Practice Information and Coordination Center cost converter.[9]

Quality assessment

The methodological quality of the included studies was assessed using the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I).[10] Each study was evaluated based on key criteria, including study design, sample size, cost measurement methods, and risk of bias in outcomes. Any discrepancies in the selection or extraction processes were resolved through discussion with a third reviewer (RF).

The included studies were critically appraised for methodological quality by using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist. The key domains of assessment included clarity of objectives, rigor in methods, defined population and timeframe, data integrity, and transparency in reporting economic outcomes. This standardized evaluation provided a robust quality framework, ensuring reliable insights into the economic burden and healthcare costs associated with CAKUT in Italy, Colombia, the USA, and Australia.

Data analysis

A narrative synthesis was conducted due to the heterogeneity in study designs and outcome measures. Descriptive statistics, including mean, median, standard deviation, and interquartile range, were used to summarize cost data. Cost-effectiveness ratios were reported where available. Cost-effectiveness analysis was conducted in line with the Joanna Briggs Institute reviewer's manual for systematic reviews of economic evaluations,[11] incorporating both direct medical costs and, where reported, indirect societal costs. Data were analyzed using Microsoft Excel (Microsoft Corporation, USA) and Zotero (Corporation for Digital Scholarship, USA) software. Literature review results are presented according to the PRISMA flowchart and checklist.

RESULTS

We conducted a comprehensive search of several databases using predefined keywords. The initial search yielded 672 articles from PubMed, 895 from ScienceDirect, 21 from ProQuest, 57 from Nature, and 1,580 from Google Scholar. After applying the inclusion criteria, limiting the number of original research articles to those written in English, a total of 1,045 articles remained. After removing duplicate articles and those that did not meet the inclusion criteria, 10 articles were identified for further review. Eight articles were included in the final analysis after a thorough screening of titles and abstracts, focusing on alignment with the study's objectives, methodologies, and outcomes relevant to the secondary research question. The PRISMA flow diagram used in this study is shown in Figure 1.

Study characteristics

The characteristics of the eight included studies are presented in Table 1, including study origin, patient demographics, health services provided, total costs, and major findings.

Methodological quality

The methodological quality of the included studies was systematically evaluated using the CHEERS checklist. A comprehensive appraisal of each study is summarized in Table 2.

The studies by Nguyen et al,[12] Shaikh et al,[13] Fernández et al,[14] Guarino et al,[15] Becherucci et al,[16] Huang et al,[17] Wu et al,[18] and Sowa et al[19] were scrutinized to ascertain the healthcare costs associated with CAKUT. Additionally, each report's bias risk was assessed using the ROBINS-I (Figure 2).

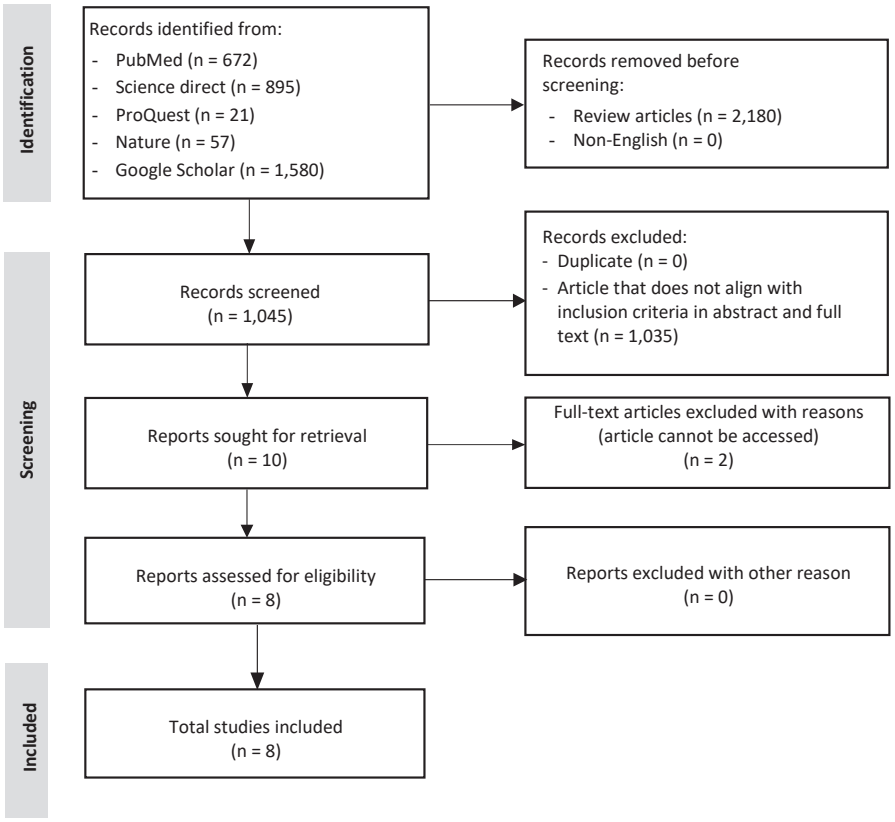


Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart of the study selection process

Table 1. Characteristics of included studies

First author, year	Country	Anomalies	Age	Health services	Total costs	Key findings
Nguyen,[12] 2018	USA	BRA	0–28 days	Intubation, invasive mechanical ventilation, chest tube placement, peritoneal dialysis, and amnioinfusion during infancy	BRA: USD 26,032	Hospital care costs during the first year of life exceeded USD 250,000 for 5.7% of infants with BRA, respectively vs. 0.1% of non-case infants (p<0.05).
Shaikh,[13] 2020	USA	VUR with UTI	<6 years	Prophylaxis treatment	VUR grade IV: USD 37,903/QALY	Prophylactic antimicrobial treatment effectively prevented complications and demonstrated cost-efficiency only grade IV VUR.
Fernández,[14] 2022	Colombia	CAKUT	4 months–11 years	Conventional surgery	USD 6,256.01	Active surveillance with telephone follow-up can significantly reduce unmet goals for surgical intervention.
Guarino,[15] 2022	Italy	CAKUT from CSFK	18–33 years	RUS	Cost reduced: 38.6% to 55.3% USD (USD 181,232 to USD 85,885)	The ERUSA approach reduced costs by 38.6–55.3% across follow-up methods, with the RUS approach achieving the highest savings of 65.7–85.7%. Importantly, ERUSA ensured no cases of kidney injury in adulthood were missed.
Becherucci,[16] 2023	Italy	CAKUT	Median: 0–5 years	Early genetic diagnostic testing	Cost reduced: USD 2,203 (USD 11,078 to USD 8,875)	Early genetic testing, particularly using WES, led to cost savings of 20% per patient.

Table continued on next page

Table 1. (Continued)

First author, year	Country	Anomalies	Age	Health services	Total costs	Key findings
Huang,[17] 2023	USA	CAKUT	8.1–20.7 years	RALS	- VUR: USD 8,716 - Congenital hydronephrosis: USD 8,259 Cost increased: USD 3,319 (more expensive than conventional laparoscopic)	RALS is more advantageous in pediatric surgical conditions where complex procedures are expected and when patient hospitalization costs are higher.
Wu,[18] 2023	Australia	CAKUT	5–38 years	Genomic testing	- Genomic : conventional test = USD 2,155 : USD 731 - Cost increased 284% - ICER: USD 13,075.05/ additional diagnosis	Genomic testing for CAKUT patients improved diagnostic rates but incurred additional expenses.
Sowa,[19] 2024	Australia	CAKUT	Mean: 58.2 years	Comparison of total costs between patients with GKD and non-GKD	GKD: USD 3,388 in 1st year, up to USD 8,362 in 7th years, more expensive than non-GKD	GKD patients had more hospital admissions than non-GKD, with excess annual admissions increasing from 5.2 in year 1 to 13.4 in year 7. Their hospital costs also rose, from USD 5,265 to USD 12,993 annually. In 2011–2012, annual hospital costs per person were USD 8,992 for non-GKD and USD 14,257 for GKD, rising to USD 14,979 and USD 27,971 by 2017–2018, highlighting a steeper cost increase for GKD patients.

BRA=bilateral renal agenesis; CAKUT=congenital anomalies of the kidney and urinary tract; CSFK=congenital solitary functioning kidney; ERUSA=early renal ultrasound algorithm; GKD=genetic kidney disease; ICER=incremental cost-effectiveness ratio; QALY=quality-adjusted life year; RALS=robotic-assisted laparoscopic surgery; RUS=renal ultrasound; USD=United States dollar; UTI=urinary tract infection; VUR=vesicoureteral reflux; WES=whole exome sequencing

Direct economic burden from healthcare cost

The direct financial burden associated with healthcare interventions for CAKUT varies significantly based on treatment location, healthcare system structure, and cost-reducing strategies. Table 3 presents a comparative analysis of the direct economic burden of the different interventions.

In a study by Fernández et al,[14] the total expenditure for the care of all patients with CAKUT was USD 5,800 (now USD 6,256), with an average cost per patient of USD 193.33. In contrast, a study in the USA by Nguyen et al[12] examined the healthcare costs among infants with congenital anomalies. The study reported that infants with bilateral renal agenesis (BRA) incurred an average of USD 26,032 during the first year of life, with a 1-year survival rate of 15.1% and an average hospital length of stay (LOS) of 11.9 days. In comparison, anencephaly, a condition with a 1-year survival rate of only 2.4%, had the lowest average cost of USD 5,537 and a shorter average LOS of 5.3 days. Meanwhile, skeletal dysplasia had the highest costs, with an average cost of USD 131,223, 1-year survival rate of 28.9%, and the longest LOS of 64.1 days.[12]

A study by Sowa et al[19] in Australia highlighted the increasing healthcare demands of patients with genetic kidney disease (GKD) compared to those without such conditions. Over time, patients with GKD exhibit a significant increase in both hospital admissions and associated costs. Specifically, the average annual excess number of hospital admissions escalated from 5.2 in the first year to 13.4 by the seventh year. Correspondingly, the average annual excess cost increased from USD 3,388 to USD 8,362 in the seventh year. These findings underscore the growing

Table 2. Methodological quality assessment of included studies using the CHEERS checklist

	Nguyen,[12] 2018	Shaikh,[13] 2020	Fernández,[14] 2022	Guarino,[15] 2022	Becherucci,[16] 2023	Huang,[17] 2023	Wu,[18] 2023	Sowa,[19] 2024
Title compliance	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Abstract and introduction	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Methods	Partial	Yes	Partial	Partial	Yes	Yes	Partial	Partial
Target population	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Timeframe	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Setting	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Economic evaluation	No	Yes	Partial	Partial	Yes	Yes	Partial	Partial
Data source	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes
Analytical methods	Partial	Yes	Partial	Partial	Yes	Yes	Partial	Partial
Results reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Discussion	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Conclusions	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Funding and conflict of interest	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Other CHEERS Items	Partial	Partial	No	No	Partial	Partial	Partial	Partial

CHEERS=consolidated health economic evaluation reporting standards

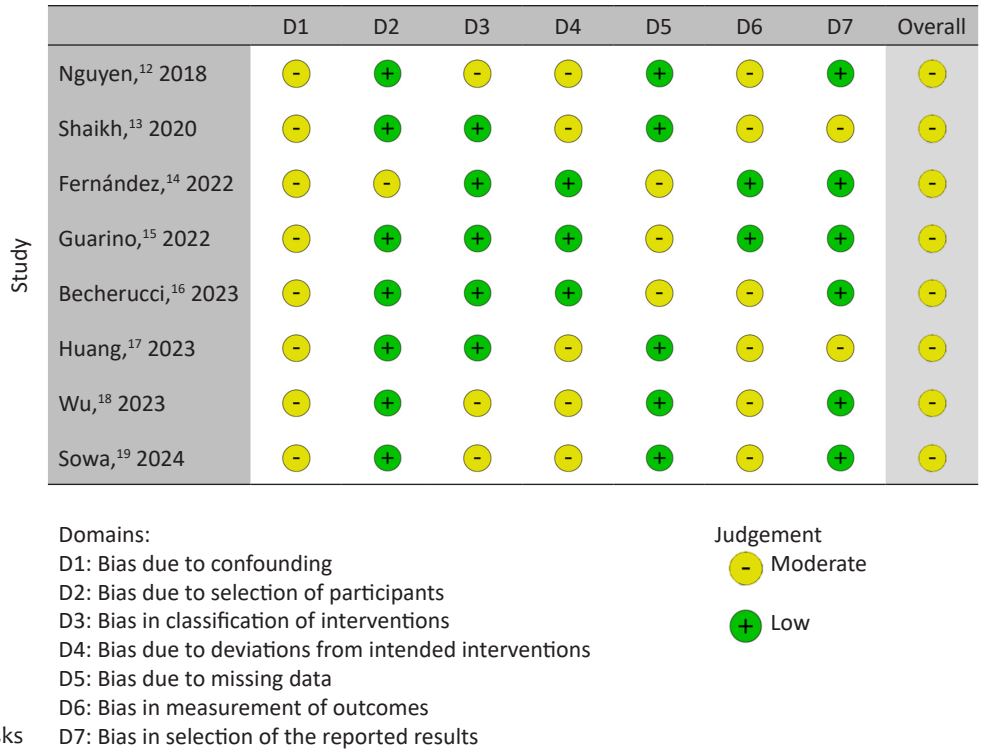


Figure 2. Bias analysis for bias risks

financial strain on long-term CAKUT management. Further analysis of hospital expenditures revealed a widening gap in costs between patients with GKD and non-GKD. In the 2011–2012 financial year, the average hospital cost per person was USD 6,214 for non-GKD and USD 9,853 for GKD. By 2017–2018, these costs

Table 3. Direct economic burden comparison between interventions

Study	Diagnosis	Intervention	Total cost	Key findings
Nguyen,[12] 2018	BRA	Intensive care and hospitalization	USD 26,032 (1 year)	Average hospital LOS: 11.9 days; 15.1% 1-year survival rate.
Fernández,[14] 2022	CAKUT	Conventional surgeries	Total: USD 5,800 (USD 193.33 per patient)	No hospital charges; surgeons worked voluntarily; no transportation, accommodation, or meal costs.
Guarino,[15] 2022	CSFK	ERUSA	USD 85,885 (ERUSA) vs. USD 181,232 (traditional approach)	Savings up to 55.3% with ERUSA compared to traditional protocols.
Sowa,[19] 2024	GKD	Hospital admissions	USD 3,388 (Year 1) to USD 8,362 (Year 7)	Significant increase in admissions and costs over time, particularly by Year 7.

BRA=bilateral renal agenesis; CAKUT=congenital anomalies of the kidney and urinary tract; CSFK=congenital solitary functioning kidney; GKD=genetic kidney disease; LOS=length of stay; ERUSA=early renal ultrasound algorithm; USD=United States dollar

Table 4. Indirect economic burden comparison between interventions

Study	Intervention	Outcome	ICER/QALY	Key notes
Shaikh,[13] 2020	Prophylactic antimicrobial treatment for VUR	Effective in preventing complications	Not calculated	Cost per QALY is significantly below the accepted threshold.
Becherucci,[16] 2023	WES	67% diagnostic yield and 41% cost reduction	Not calculated	Diagnostic costs reduced by an average of USD 2,203 per patient.
Huang,[17] 2023	RALS	Improved postoperative outcomes and shorter surgery time	USD 58,724.01/QALY to USD 60,873.20/QALY	Remains below the USD 100,000/QALY threshold.
Wu,[18] 2023	Genomic testing for CAKUT	13% diagnostic rate	USD 12,932/QALY	Additional cost of USD 1,624 per new diagnosis.

CAKUT=congenital anomalies of the kidney and urinary tract; ICER=incremental cost-effectiveness ratio; RALS=robotic-assisted laparoscopic surgery; QALY=quality-adjusted life year; USD=United States dollar; VUR=vesicoureteral reflux; WES=whole exome sequencing

had risen to USD 10,352 and USD 19,330, respectively, demonstrating a significantly steeper increase in healthcare expenses for patients over time.[19]

Guarino et al[15] showed that the use of renal ultrasound (RUS) in managing patients with congenital solitary functioning kidneys provided both clinical insights into kidney risk and cost efficiency by following the early RUS algorithm (ERUSA). The total cost of the follow-up protocols was reduced from USD 181,232 to USD 85,885 using the traditional ERUSA approach. The cost of RUS decreased from USD 84,723 to USD 35,301, with the highest saving of 85.7%. The total cost savings from applying ERUSA ranged from 38.6% to 55.3% across all analyzed protocols, including the costs for urinalysis, lab tests, and follow-up visits.[15]

Indirect economic burden from healthcare costs

In addition to direct expenses, certain interventions can influence the overall healthcare costs by improving diagnostic efficiency and reducing unnecessary expenditures. Table 4 compares the indirect economic burden across the different interventions, highlighting the cost reductions achieved through advanced diagnostic approaches.

Several interventions have been shown to reduce healthcare costs for patients. Becherucci et al[16] conducted a detailed quantitative study to evaluate the cost-effectiveness of a diagnostic workflow using whole exome sequencing (WES) for GKD. The workflow achieved a diagnostic yield of 67%, confirming clinical diagnoses in 48% of the cases and modifying them in 19% of the cases. This study compared two diagnostic models: early WES application *versus* delayed WES. The early WES model demonstrated a 20% cost reduction per patient, lowering the average diagnosis cost from USD 11,078 to USD 8,875 and resulting in USD 2,203 saved per patient. In a subgroup of 66 patients, early WES achieved a 41% cost reduction.[16] Additionally, a study by Fernández et al[14] identified 60 patients with congenital urological conditions in Colombia between

November 2018 and December 2019, due to financial and travel challenges, only 44 attended consultations, with 29 of them underwent conventional surgeries, most frequently for hypospadias (14 cases). Their total care cost was USD 5,800, averaging USD 193.33 per patient.[14]

One study conducted by Huang et al[17] compared the cost-effectiveness of robotic-assisted laparoscopic surgery (RALS) *versus* standard laparoscopic surgery (LS) for pediatric urological disease. RALS showed consistent improvements in operative time, with inpatient costs amounting to USD 10,816.72, USD 9,145.44, USD 8,414.29, and USD 7,973.58, respectively. The extra costs of RALS over LS were USD 3,523.44, USD 3,200.20, USD 3,049.79, and USD 3,043.66, respectively, while the incremental quality-adjusted life years (QALYs) were 0.060, 0.054, 0.051, and 0.050, respectively. The incremental cost-effectiveness ratios (ICERs) for each condition treated with RALS were determined to be USD 58,724.01, USD 59,262.95, USD 59,799.79, and USD 60,873.20 per QALY, all of which remained below the USD 100,000 per QALY threshold.[17]

Wu et al[18] assessed the cost-effectiveness of genomic testing in patients with CAKUT using ICER. The test cost USD 2,133, and achieved a 13% diagnostic rate, with an additional expense of USD 1,624 per new diagnosis. The ICER was USD 12,932 per QALY gained through genomic testing.[18] Similarly, Shaikh et al[13] demonstrated that prophylactic antimicrobial treatment for children with grade IV vesicoureteral reflux (VUR) effectively prevented complications and was cost-efficient, with a QALY cost well below the standard threshold.

DISCUSSION

A comprehensive review of eight studies on CAKUT anomalies revealed significant differences in healthcare spending and economic impact across various treatments and countries. Most financing in these studies was calculated based on the QALY or disability-adjusted life year (DALY). Both QALY and DALY are health economics metrics used to assess the effectiveness of medical treatments.[14,20] Both evaluate improvements in lifespan and health quality during the years following the intervention. This measure aids decision makers in evaluating the cost-effectiveness of treatments by balancing health benefits against costs.[18] Childhood disabilities are a major contributor to DALYs, particularly in low- and middle-income countries (LMICs), where approximately 150 million children live with disabilities and face limited access to medical care. However, there is limited research on the effects of delayed surgical interventions for congenital anomalies despite their substantial contribution to long-term disabilities. In 2019, CAKUT had a prevalence of 167.11 per 100,000 people, a mortality rate of 0.30, and 32.22 DALYs, with the highest burden in children aged 0–4 years. While the prevalence declined from 1990 to 2019, the DALYs remained the highest in India, Nigeria, and Pakistan. Both mortality and DALYs decreased with each 0.1 increase in the sociodemographic index.[21]

The relatively modest average patient cost reported by Fernández et al[14] (approximately USD 193.33) contrasts sharply with the substantially higher costs noted in the USA for more severe anomalies such as skeletal dysplasia (USD 131,223) and BRA (USD 26,032), with differing survival rates and lengths of hospital stay. This disparity underscores how healthcare resource utilization is intricately tied to clinical complexity and patient outcomes, affirming that severe congenital anomalies pose greater financial challenges to healthcare systems. Additionally, the authors found that all surgeons resided in the same city as the treatment facility, eliminating the need for transportation, accommodation, and meal costs, which are typically substantial components of medical mission expenses. Furthermore, hospital logistical advantages significantly reduced overhead expenses. Additionally, hospital care was provided at no charge, eliminating costs related to hospital stays, nursing care, and facility usage. Importantly, surgeons did not receive monetary compensation, thereby further reducing direct labor costs.[14]

Australian research found that patients with GKD faced higher hospitalization rates and healthcare costs.[19] It emphasized the progressive nature of financial demands in GKD, as increased hospital admissions and associated costs compound over time. The doubling of the average hospital costs over several years reflects a chronic burden and supports the need for cost-containment strategies through early intervention and efficient resource allocation. Early interventions such as WES and RALS could save approximately USD 2,203 per patient.[16] Although inpatient costs for RALS were higher, its improved postoperative results support it as a cost-effective approach for treating pediatric conditions.[17] These

findings underscore the clinical and economic value of integrating genomic testing early in the diagnostic pathway.

Cost-effectiveness of diagnostic and treatment innovations emerged as a key theme. Expanded access to genetic testing has enabled faster differentiation between monogenic CKD and other types of CKD, although the expense remains substantial, posing a challenge for healthcare payers to justify genetic testing based on clinical benefits and cost-effectiveness. Trends in the likelihood of admission and expenses showed similar patterns for surgical and medical reasons over time. Cardiovascular diseases and infections are major factors driving higher admission rates and costs for patients with CAKUT, with possible contributions from cancer, immune disorders, mental health issues, dementia, and neurological diseases. A deeper understanding of these trends could offer ways to reduce hospitalizations if they represent avoidable cases.[19]

To reduce the diagnostic cost burden, Becherucci et al[16] developed a cost-saving diagnostic workflow that improved the accuracy and rate of GKD diagnosis in both children and adults. This method enhanced clinical management and lowered healthcare costs by optimizing workflow across the three tiers: nephrologists, diagnostic centers, and healthcare providers. The workflow led to a diagnostic rate of 67.0% in patients with different types of kidney disease of all ages. Healthcare costs can be reduced owing to the improved diagnostic yield, which avoids diagnostic procedures and therapeutic interventions.[11]

Guarino et al[15] demonstrate how ERUSA significantly reduced diagnostic and follow-up costs, reflecting the value of evidence-based clinical algorithms in optimizing care pathways. The incorporation of genomic testing and early WES further exemplifies this concept, with studies by Becherucci et al[16] and Wu et al[18] documenting meaningful cost reductions alongside improvements in diagnostic yield and health outcomes measured by QALYs. These findings underscore the growing recognition that advanced genomic diagnostics, although initially expensive, can ultimately yield net savings by preventing delayed diagnoses and unnecessary procedures.

For children with grade IV VUR, prophylactic antibiotics proved to be cost-effective at USD 37,903 per QALY and had better outcomes than the other treatment options. This finding supports prophylactic antibiotic treatment as a valuable, economically sound intervention for pediatric VUR management.[13] Zhao et al[22] found that children with bladder and bowel dysfunction (BBD) or grade IV VUR gained the most from extended antimicrobial prophylaxis, with a number of patients requiring treatment of four. These high-risk groups showed better outcomes and fewer recurrent urinary tract infections (UTIs), consistent with meta-analyses emphasizing the value of targeted antimicrobial strategies. Treatment effectiveness tended to be greater in high-risk subgroups, which also exhibited higher UTI rates. Both studies suggested that children with grade III VUR without BBD may not experience significant benefits from this treatment approach.[22]

Standardized selection criteria for genetic testing such as WES are crucial for the efficient management of financial and personnel resources. This allows streamlining of patient referrals from peripheral centers, providing open access to advanced genetic testing technologies in tertiary facilities. Although the use of specialized staff and WES technology is more expensive than conventional DNA testing, a centralized and direct workup reduces referrals and consultations. This also standardizes access to genetic evaluations of kidney diseases.[13]

The cost of WES limits its widespread use in clinical settings. Nevertheless, diagnostic strategies that incorporate WES can help reduce healthcare costs when applied through a structured diagnostic workflow, even with an early WES model. Financial advantages include the ability to diagnose previously unresolved cases and reclassify diseases, which can prevent unnecessary testing and treatments.[13]

The effectiveness of early diagnostic interventions depends on accessibility. In many LMICs, challenges such as limited antenatal care visits and restricted availability of first- and second-trimester ultrasound screenings contribute to delayed diagnoses of congenital anomalies, including CAKUT.[23] Limited access to early screening not only hinders timely intervention but may also increase the overall economic burden due to late-stage complications.

These findings have substantial implications for both the clinical and policymaking communities. Cost-effective interventions, such as ERUSA and targeted antimicrobial prophylaxis, highlight the value of reallocating resources for early diagnosis and precision care. Policymakers could leverage this

evidence to support broader insurance coverage or public health funding for genetic testing and early imaging protocols, potentially reducing the long-term disease burden and cost. Practitioners can apply these strategies to identify high-yield cases for intervention and promote individualized care while maintaining budgetary sustainability.

This study had several limitations. The included studies differed in methodology, population demographics, and cost-assessment frameworks, which may have affected comparability. Additionally, most economic analyses were derived from high-income countries, potentially limiting their generalizability to LMIC settings. Some studies had relatively small sample sizes, and regional disparities in the access to diagnostics or treatment options may have introduced bias. Larger multinational studies are warranted to validate these findings in diverse healthcare systems. Future studies should include large-scale economic evaluations in LMICs, and standardize cost assessment methods for better comparability. Longitudinal research using real-world data is required to capture long-term costs and outcomes. Additionally, continued research on cost-management strategies for CAKUT is essential for enhancing patient outcomes and healthcare efficiency.

In conclusion, this study showed that personalized nephrology is both practical and cost-effective in real-world clinical settings, supporting the integration of genomic medicine into routine kidney disease treatment. CAKUT imposes a significant economic burden with wide regional variations in treatment costs. Identifying and implementing cost-effective interventions is essential for optimizing care while reducing the financial impact on families and healthcare providers. This review highlights the need for ongoing research on cost management strategies for CAKUT to enhance patient outcomes and healthcare efficiency.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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