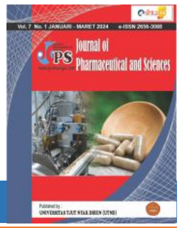
Journal of Pharmaceutical and Sciences
Electronic ISSN: 2656-3088 DOI: https://doi.org/10.36490/journal-jps.com
Homepage: https://journal-jps.com



REVIEW ARTICLE JPS. 2026, 9(2), 1419-1434

Economic Burden of Kidney Transplantation as Renal Replacement Therapy in End-Stage Chronic Kidney Disease Patients: A Systematic Review

Beban Ekonomi Transplantasi Ginjal sebagai Terapi Pengganti Ginjal pada Pasien Penyakit Ginjal Kronik Stadium Akhir: Tinjauan Sistematis

Qurrata Akyuni [a], Dwi Endarti [a], Auliya Abdurrohim Suwantika [b] Wening Wulandari [c]

[a,b] Faculty of Pharmacy, University of Gadjah Mada, Yogyakarta, Indonesia
[c] Department of Pharmacy, Faculty of Pharmacy, University of Padjajaran, West Java, Indonesia
[d] Department of Pharmacy, Faculty of Pharmacy, University of Jenderal Soedirman, Central Java, Indonesia

Corresponding Authors: qurratakyuni@mail.ugm.ac.id

Abstract
End-stage renal disease (ESRD) imposes a substantial economic burden on healthcare systems worldwide, extending well beyond its clinical implications. This burden is predominantly attributable to the requirements of renal replacement therapy (RRT), with kidney transplantation representing one of the most cost-intensive components of ESRD management. The complexity and continuity of long-term care needs further amplify the financial pressure on health systems globally. This systematic review was undertaken to identify and evaluate the economic burden associated with chronic kidney disease (CKD) across various RRT modalities, namely hemodialysis, peritoneal dialysis, and kidney transplantation, within diverse healthcare contexts. A systematic literature search was conducted in Scopus, PubMed, SpringerLink, and ProQuest, encompassing English-language observational studies and economic evaluations published between 2015 and 2025 that reported direct medical costs, non-medical costs, productivity losses, and related economic indicators. A total of 15 studies from multiple countries were analyzed, revealing a broadly consistent pattern of findings. Healthcare expenditures were found to escalate markedly with advancing CKD stage and the initiation of RRT. Multiple economic evaluation frameworks were employed, including disease burden analysis, cost-benefit analysis, comparative cost analysis, and cost-utility analysis. Hemodialysis incurred the highest annual costs, followed by peritoneal dialysis. While kidney transplantation requires a greater upfront investment, it has considerably lower long-term annual costs than continuous dialysis. The review ultimately affirms that kidney transplantation constitutes a more economically efficient therapeutic strategy for ESRD management, with meaningful potential to alleviate the broader global economic burden associated with this condition.

Keywords: ***Chronic Renal Disease; End-Stage Renal Disease; Renal Replacement Therapy; Kidney Transplantation; Healthcare Costs; Economic Evaluation.***

Abstrak
Penyakit ginjal tahap akhir (ESRD) tidak hanya berdampak pada kondisi klinis pasien, tetapi juga menimbulkan tekanan ekonomi yang besar bagi sistem layanan kesehatan di seluruh dunia. Beban ini sebagian besar didorong oleh kebutuhan terapi pengganti ginjal (RRT), dengan transplantasi ginjal sebagai salah satu komponen biaya terbesar dalam perawatan ESRD. Kebutuhan perawatan jangka panjang yang kompleks dan berkelanjutan semakin memperparah tekanan finansial pada sistem kesehatan secara global. Tinjauan sistematis ini bertujuan untuk mengidentifikasi dan mengevaluasi beban ekonomi penyakit ginjal kronis (CKD) berdasarkan berbagai modalitas RRT, yaitu hemodialisis, dialisis peritoneal, dan transplantasi ginjal, dalam berbagai konteks sistem kesehatan. Pencarian literatur dilakukan secara sistematis melalui basis data Scopus, PubMed, SpringerLink, dan ProQuest, mencakup studi observasional dan evaluasi ekonomi berbahasa Inggris yang diterbitkan antara 2015 dan 2025, dengan fokus pada biaya medis langsung, biaya non-medis, kehilangan produktivitas, dan indikator ekonomi terkait. Sebanyak 15 studi dari berbagai negara dianalisis dan menunjukkan pola temuan yang cukup konsisten. Pengeluaran layanan kesehatan meningkat secara signifikan seiring dengan perkembangan stadium CKD dan dimulainya RRT. Berbagai pendekatan evaluasi ekonomi digunakan, termasuk analisis beban penyakit, analisis biaya-manfaat, analisis biaya komparatif, dan analisis biaya-utilitas. Hemodialisis mencatat biaya tahunan tertinggi, diikuti oleh dialisis peritoneal. Meskipun transplantasi ginjal memerlukan investasi awal yang lebih besar, modalitas ini terbukti menghasilkan biaya tahunan jangka panjang yang jauh lebih rendah dibandingkan dengan dialisis. Tinjauan ini menyimpulkan bahwa transplantasi ginjal merupakan strategi yang lebih efisien secara ekonomi dan berpotensi mengurangi beban ekonomi global akibat ESRD.

Kata Kunci: Penyakit Ginjal Kronis; Penyakit Ginjal Stadium Akhir; Terapi Pengganti Ginjal; Transplantasi Ginjal; Biaya Layanan Kesehatan; Evaluasi Ekonomi.

Article History:
Received: 03/03/2026,
Revised: 18/05/2026,
Accepted: 18/05/2026,
Available Online: 27/05/2026.
QR access this Article

https://doi.org/10.36490/journal-jps.com.v9i2.1505

Introduction

Chronic kidney disease (CKD) represents a major global public health challenge with a steadily increasing burden worldwide. [1]. The global prevalence of chronic kidney disease (CKD) is estimated to range from 11% to 13%, with relatively higher rates found in East Asia and Europe. [2]This condition is known to be closely associated with increased mortality, morbidity, and a significant economic burden. [1]. According to a report from the Global Burden of Disease (GBD) study, an estimated 697 million people worldwide are living with CKD. [3]. The global prevalence of chronic kidney disease (CKD) is projected to increase to 25 million cases by 2030. This condition is estimated to occur more frequently in women aged ≥60 years, and is closely related to major risk factors such as type 2 diabetes mellitus and hypertension [4]. Consequently, CKD has emerged as one of the leading contributors to global mortality, ranking 11th among causes of death between 1990 and 2019 [5].

CKD is clinically characterized by a persistent decline in kidney function, defined as a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 or the presence of markers of kidney damage for at least three months [6]. As the disease progresses, patients may develop end-stage kidney disease (ESKD), a condition that requires kidney replacement therapy (KRT), including hemodialysis, peritoneal dialysis, or kidney transplantation. [7]. Based on the Global Burden of Disease (GBD) 2023 analysis, it is estimated that in 2023, there will be 4.76 million (4.17–5.08 million) people worldwide living with kidney replacement therapy. [8], with hemodialysis, is the most common form of KRT [9]. The incidence of ESKD is increasing each year. [10] . It is projected that around 2.5 million individuals are currently availing Kidney Replacement Therapy (KRT) as a result of ESKD, with this figure predicted to increase to 5.4 million by the year 2030 [3].

In addition to its clinical consequences, chronic kidney disease (CKD) places a significant economic burden on individual healthcare systems. Renal replacement therapy (RRT) is considered one of the most expensive long-term interventions in modern medical practice. In many countries, dialysis services impose a significant economic burden on national health. Even though individuals undergoing renal replacement therapy (RRT) constitute only about 5.3% of the total diagnosed chronic kidney disease (CKD) population, this group represents 45.9% of the overall financial burden. [11], with the highest average annual cost associated with transplantation at US$26,903 in the initial year [12]. In many other countries, renal replacement therapy (RRT) entails substantial financial consequences. In Spain, it is reported that chronic kidney disease (CKD) is projected to represent at least 60% of national healthcare expenditure, with an increasing trajectory anticipated to persist until 2027 [13]. Meanwhile, in Brazil, the costs of dialysis services have exceeded 40% of the total public health budget. [14]. In some developing countries, the economic burden is borne directly by patients, with the cost of RRT exceeding 70% of their annual income. Although kidney transplantation is most expensive in the first year, studies have shown that in the long term, particularly over the next five years, this procedure provides better clinical outcomes and economic efficiency than continuous dialysis therapy. [15].

However, the economic implications of various renal replacement therapy (RRT) modalities vary significantly across countries. These differences are influenced by a variety of factors, including healthcare systems, resource availability, financing or reimbursement policies, and the readiness of transplant infrastructure. In addition, disparities in access to transplantation and dialysis services complicate cross-country comparisons and limit the generalizability of economic evidence. Although economic evaluations of KRT (HD, PD, and transplantation) are increasing, truly comprehensive and cross-contextual evidence remains limited. Therefore, this review aims to analyze the economic impact of kidney transplantation compared with other renal replacement therapies across countries.

Methods

Search Strategy

The search strategy was based on relevant scientific articles. In this review, the literature was searched to identify published studies that described or conducted research on "Kidney Failure, Chronic," "Kidney Transplantation," and "Economic Burden."

These studies were searched using Scopus, PubMed, SpringerLink, and ProQuest. The search included studies conducted between 2015 and 2025, with English-language studies identified through an extensive database search. Articles that met the inclusion criteria were those on the economic burden or cost implications of patients undergoing renal replacement therapy through kidney transplantation compared with other modalities. Meanwhile, the exclusion criteria included Systematic Reviews, Meta-Analyses, and studies for which the full text was not available.

Citations were reviewed based on their titles and abstracts, and relevant articles were selected for further exploration in the full text. Researchers also scrutinized the reference lists in the selected articles to find studies that the initial search may have missed. After that, the full-text articles were independently assessed, and a decision was made on whether to include them in the systematic review. Only articles that met the eligibility criteria were finally selected.

Quality Assessment tools

Although this review was not prospectively registered with PROSPERO because the study commenced before protocol development and registration, it was conducted using a predefined and systematically applied methodological framework. The methodology was conducted in accordance with the PRISMA 2020 guidelines to ensure methodological transparency and consistency. Quality assessment was conducted using two instruments, the ECOBIAS checklist and the CHEERS checklist. The ECOBIAS tool consists of 22 assessment items designed to identify potential sources of bias in economic evaluation studies. Each item is scored based on the level of bias risk: 0 indicates a low risk of bias, 0.5 indicates a potential risk of bias, and 1 indicates a high risk of bias. This instrument was designed to systematically identify methodological biases that could affect the validity of research findings. Accordingly, the reporting of studies included in this review was assessed using the CHEERS (Consolidated Health Economic Evaluation Reporting Standards) checklist. This evaluation instrument consists of 28 components, each evaluated using a binary scoring system that assigns a score of 1 for indicators met and 0 for those not met. CHEERS was used to assess the level of completeness, transparency, and consistency of reporting in health economic evaluation studies. Meanwhile, methodological quality was also assessed using the ECOBIAS checklist to identify potential sources of bias in the studies.

Data Extraction

The characteristics of the analyzed studies are presented in Table 1. A total of 15 articles were reviewed and categorized by country, study population, costing methods, and cost components for transplant and non-transplant interventions. The extracted information included: (1) study characteristics, such as year of publication, study design, population studied, comparators used, and the economic perspective adopted; and (2) data related to the economic burden or cost implications for patients undergoing renal replacement therapy. Data were analyzed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 stage, which includes several steps: Identification, screening, inclusion, and eligibility assessment of articles found. The articles will then be thoroughly analyzed before conclusions are drawn after data collection. The data selection process is shown in Figure 1.

Results

Screening Results and Characteristics

There were 988 potentially relevant records identified through the initial literature search conducted in the Scopus, PubMed, ProQuest, and SpringerLink databases. After removing 147 duplicate records, the remaining studies were screened based on their titles and abstracts. During this stage, 974 articles were excluded for various reasons. A final assessment of 15 studies that met the predefined inclusion criteria was conducted. Thus, 15 studies were ultimately included in this systematic review. The study selection process, in accordance with the PRISMA 2020 guidelines, is illustrated in Figure 1.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

The characteristics of the analyzed studies are presented in Table 1. A total of 15 articles were reviewed. Country, population, and costing methods categorized the studies, and cost components were identified for transplant and non-transplant procedures. The results of the study characteristics review are summarized in Table 1.

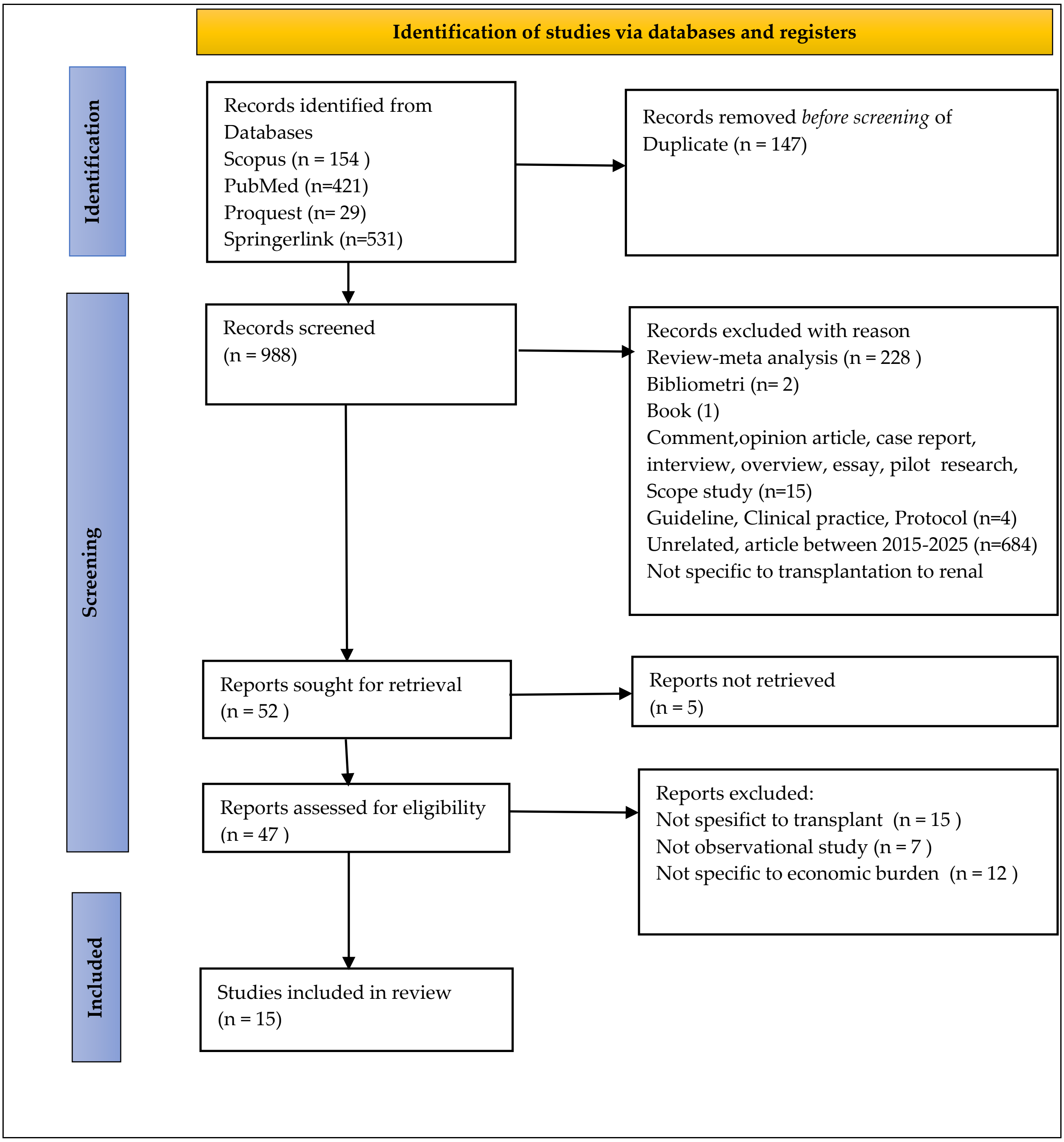


Figure 1. PRISMA Flow diagram of a systematic review of the literature to select studies evaluating the Economic Burden of Kidney Transplantation as Renal Replacement Therapy in End-Stage Chronic Kidney Disease Patients.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Table 1. Characteristic Included studies

Author	Country	Setting	Participants	Time Horizon	Study Population	Study Design	Intervention	Comparator
Abdi *et al.*, (2022) [15]	Iran	Hospital	266	1 year	Patients with end-stage kidney disease	Cross sectional	KT	N/A
Aoun *et al.*, (2022) [16]	Lebanon	Hospital clinic	160	1 year	Patients with chronic kidney disease	Cross sectional	N/A	N/A
Eriksson *et al.* (2016) [17]	Sweden	National health registry	2,432	1 year	Patients with chronic kidney disease	Cohort	Kidney disease (CKD) stage 4 or 5, not on dialysis, peritoneal dialysis, hemodialysis, or in transplanted patients	General population
Zhang *et al.* (2023) [18]	Sweden	Swedish renal registry	693	3 years	Patients with end-stage kidney disease	Cohort	KT	Dialysis
Camargo *et al.* (2018) [19]	Brazil	Hospital	30	40-50 months	Patients with end-stage kidney disease	Cohort	KT	Hemodialysis (daily or conventional hemodialysis)
Helanterä *et al.*,(2019) [20]	Finland	National Renal Registry	338	1 year	End-stage CKD patients undergoing RRT	Cohort	Kt	Dialysis
Villanueva *et al.*,(2025) [21]	Philippines	National kidney and transplant institute	204	1 year	Patients with chronic kidney disease	Cross sectional	N/A	N/A
López-Sánchez *et al.*,(2020) [22]	Spain	National registry	767	1 year	End-stage CKD patients undergoing RRT	Cohort	Renal replacement therapy (KT, HD, PD)	N/A
Gouveia *et al.*,(2017) [23]	Brazil	Health system	Not stated	Not stated	End-stage CKD patients undergoing RRT	Cohort	Renal replacement therapy (KT, HD, PD)	N/A
De Vries *et al.*,(2021) [24]	Netherland	Health system	230	1 year	End-stage CKD patients undergoing RRT	Cross sectional	Renal replacement therapy (KT, HD, PD)	N/A

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Wu *et al.*,(2020) [25]	China	Hospital	298	January-August 2018	End-Stage CKD Patients Undergoing RRT	Cross Sectional	Renal replacement therapy (KT, HD, PD)	N/A
Kolivand *et al.*,(2025) [26]	Iran	Healthcare facility	469,581	Not stated	End-stage CKD patients	Cross sectional	End-stage kidney disease	N/A
Nguyen *et al.*,(2023) [27]	USA	Hospital	12,020	Not Stated	Kidney Donors	Cross Sectional	Expanded criteria living kidney donation	Non-expanded criteria living kidney donation
Taliwal *et al.*,(2024) [28]	USA	Hospital	23,980	Not Stated	Chronic kidney disease	Cohort	Chronic kidney disease (Stage 1-5)	N/A
Zhang *et al.*,(2020) [29]	China	Patient's claims database	5,160	1 year	End-stage CKD patients undergoing RRT	Cohort	Renal replacement therapy (KT, HD, PD)	N/A

Table 2. Summary of studies included in the systematic review

Author	Costing Method	Perspective	Economic Evaluation	Cost Components	Data Collection Year	Transplant Costs	Non-Transplant Costs	Result/ Recommendation
Abdi *et al.*, (2022) [15]	Bottom-up approach	Patients	CBA	Direct medical costs (visits, surgery, diagnostic tests, ultrasound, and pharmaceutical items)	2021	$947.0*	N/A	Kidney transplantation demonstrated economic benefits of 5.39, indicating that it was prioritized in national policy and resource allocation.
Aoun *et al.*, (2022) [16]	Bottom-up approach	Societal and payer/provider	COI	Direct medical medications, Diagnostic tests (laboratory and imaging, inpatient and outpatient care) Direct non-medical (transportation costs)	2019-2020	N/A	The median total annual cost across all CKD categories Societal Perspective = USD 5,412* Third-Party Perspective	Hemodialysis (HD) and peritoneal dialysis (PD) were associated with a higher cost burden compared with kidney transplantation and non-dialysis CKD.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

				Indirect medical (productivity loss)			= USD 4,262*	
Eriksson *et al.* (2016) [17]	Top-down approach	Payer/provider	Comparative cost analysis	Direct medical cost (patient care, outpatient care visits, primary care, pharmaceutical care)	2009-2010	USD 17,157*	HD =USD 10,626* PD =USD 64,874* CKD 4-5 non-dialysis =USD 10,626*	Severe non-dialysis CKD demonstrated the lowest annual cost, followed by kidney transplantation, whereas hemodialysis and peritoneal dialysis imposed the highest economic burden.
Zhang *et al.* (2023) [18]	Top-down approach	Payer/provider	Comparative cost analysis	Direct medical costs (inpatient, outpatient, and primary care costs)	1998-2012	1st Year = USD 97,950*	1st Year = USD 81,680* Cost savings amounted to USD 62,140*	Kidney transplantation resulted in substantially lower healthcare costs than remaining on dialysis.
Camargo *et al.* (2018) [19]	Bottom-up approach	Healthcare	Comparative cost analysis	Direct medical cost (material, medicine, equipment, medical fees, administrative costs, daily rates of hospitalization, physiotherapy, nutrition, nursing, administrative fees, equipment, wages, and laboratory tests)	2007-2013	$1,991/Month*	$3,668/Month*	Hemodialysis costs were nearly twice as high as those of kidney transplantation.
Helanterä *et al.*,(2019) [20]	Bottom-up approach	Payer/provider	Comparative Cost Analysis	Direct medical cost (inpatient care, outpatient visits, dialysis, transplantation procedure, medications, and laboratory tests)	2009-2015	Non-medical & indirect costs 1st year = USD 71,270* Subsequent years after transplant = USD 14,410*	Non-medical & indirect costs, median annual cost of dialysis = USD 63,730*	Kidney transplantation resulted in healthcare costs of less than one-third of those incurred by patients who remained on dialysis after the first year.
Villanueva *et al.*,(2025) [21]	Bottom-up and top-down approach	Payer/provider	COI	Direct medical cost (costs for procedures, inpatient care, outpatient care, medicines, and diagnostic examinations)	2019-2023	Non Diabetic KT =USD 34,541* Chronic management KT	Acute HD = USD 10,678* Chronic HD =USD 10,156* Acute HD	Healthcare costs increased markedly with the progression of CKD stages and at the initiation of renal replacement

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

						= USD 8,360/year*	=USD 8,966* Chronic PD =USD 7,272*	therapy (RRT). In contrast, kidney transplantation provided long-term economic advantages and should be prioritized in CKD financing policies.
López-Sánchez *et al.*,(2020) [22]	Top-down approach	Payer/provider	COI	Direct medical cost (hospitalization, personnel, drugs, procedures)	2013-2015	USD 33,110*	PD = USD 6,320* HD = USD 13,230*	Hemodialysis patients experienced the highest hospitalization rates during the first year of renal replacement therapy (RRT), increasing the burden on the regional hospital system.
Gouveia *et al.*,(2017) [23]	Top-down approach	Payer/Provider	Comparative Cost Analysis	Direct Medical Cost (hospitalizations, medications, medical visits, and procedures)	January-June 2014	1st year Living donors =USD 6,200–7,100* Cadaver donors =USD 6,500-7,400*	N/A	Kidney transplantation incurred higher costs than hemodialysis and peritoneal dialysis during the first year and part of the second year. Still, it became the least costly modality by the end of the second year and thereafter.
De Vries *et al.*,(2021) [24]	Bottom-up approach	Societal	COI	Direct non-medical costs (transportation, parking, and other out-of-pocket costs) Indirect costs (productivity)	November 2016-January 2017	USD 7,850*	USD 22, 150*	Dialysis patients incurred higher non-healthcare costs and productivity losses than kidney transplant patients, indicating that transplantation was associated with a lower non-medical economic burden from both patient and societal perspectives.
Wu *et al.*,(2020) [25]	Bottom-up approach	Societal	Cost Analysis and CUA	Direct medical costs (expenses for dialysis, kidney transplantation, hospitalization, outpatient	January- August 2018	Annual cost ("unit" expense per patient)	Annual cost ("unit" expense per patient) HD	Kidney transplantation incurred the highest annual costs but demonstrated the greatest

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

				visits, medications, and laboratory examinations) Direct non-medical costs (transportation, accommodation, and meal expenses related to treatment) Indirect costs (productivity loss)		USD 17,700 ± 9,560* The cost of improving one unit of quality of life (QOL) USD 523*	=USD 9,70 ± 337 PD =USD 9,260 ± 594 The cost of improving one unit of quality of life (QOL) HD =USD 1,763* PD =USD 1,198*	cost–utility efficiency per unit improvement in quality of life.
Kolivand *et al.*,(2025) [26]	Top-down approach	Payer/Provider	COI	Direct medical costs (visit consultation, drugs, laboratory, imaging, nursing, surgery, hospital bed & ICU, and dialysis)	2012-2022	N/A	N/A	End-stage renal disease (ESRD) in Iranian hajj pilgrims has resulted in a large direct medical cost burden, mainly driven by the costs of hospitalization and dialysis services, with variations in the economic burden by age, gender, province, and time period.
Nguyen *et al.*,(2023) [27]	Top-down approach	Payer/Provider	Comparative Cost Analysis	Direct medical cost (hospital charges included length of stay and hospital-incurred costs)	2008-2019	N/A	N/A	Expanded-criteria living kidney donors achieve early clinical outcomes comparable to those of standard donors, without significant increases in hospital inpatient costs.
Taliwal *et al.*,(2024) [28]	Top-down approach	Payer/Provider	Comparative Cost Analysis	Direct medical cost (inpatient hospitalization cost, length of stay)	2016-2022	N/A	N/A	Hospitalization of pediatric patients with chronic kidney disease results in a large burden of hospital costs, which increases with the severity (stage) of CKD, so that advanced-stage CKD

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

								contributes the most to the economic burden of the health system.
Zhang *et al.*,(2020) [29]	Top-down approach	Payer/Provider	Comparative Cost Analysis	Direct Medical Cost (laboratory and diagnostic costs, medication costs, non-medication treatment costs, bed fees, and other services)	2010-2012	1st Year = USD 25,800* 2st Year = USD 18,200*	HD = USD 18,500* PD = USD 15,800*	Peritoneal dialysis was the modality with the lowest annual cost; hemodialysis was about 17% more expensive than peritoneal dialysis, while kidney transplantation had the highest cost in the first year but decreased in the second year to be lower than hemodialysis, making transplantation a more cost-efficient option in the medium term.

Notes: CBA = Cost-Benefit Analysis; COI = Cost-of-Illness; CUA = Cost-Utility Analysis; KT = Kidney Transplantation; HD = Hemodialysis; PD = Peritoneal Dialysis; LD = Living Donor; OOP = Out-of-Pocket; LOS = Length of Stay; * =The cost values are adjusted to the currency value (USD) in the year of publication of each study.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Risk of Bias Assessment

The ECOBIAS assessment conducted across the 15 included studies indicated an overall moderate risk of bias, reflected by a mean score of 32.84% and a median of 32.3%. The observed scores ranged from 19.4% to 55.3%, demonstrating heterogeneity in methodological quality and potential sources of bias among the included studies. Importantly, only a single study exhibited a relatively high bias score of 55.3%, whereas most studies had lower scores, indicating generally acceptable methodological rigor and consistency. No studies achieved complete reporting across all 28 CHEERS checklist items. Nonetheless, CHEERS assessments indicated generally good reporting quality among the 15 included studies, with compliance scores ranging from 57.14% to 89.29%, with a mean of 73.81% and a median of 75.00%. Overall, most studies adequately adhered to recommended reporting standards, demonstrating acceptable transparency and completeness, although there was some variation across domains. Detailed findings are presented in the supplementary material, particularly in Supplementary Tables 2 and 3.

Characteristics of Included Studies

A total of 15 studies met the inclusion criteria and were included in this systematic review. Studies included in the analysis were published between 2016 and 2025, with the majority (n=10; 66.7%) published after 2019. This demonstrates the increasing attention paid to economic evaluation research in kidney disease management in recent years. Based on the results of a geographical perspective, from ten countries, including Sweden (n=2), Brazil (n=2), Iran (n=2), China (n=2), the United States (n=2), and one study each from Lebanon, the Philippines, Spain, Finland, and the Netherlands. This broad geographic distribution includes high-income countries such as Sweden, Finland, the Netherlands, the United States, and Spain, as well as upper- and lower-middle-income countries such as Brazil, China, Iran, Lebanon, and the Philippines. This diversity allows for a comparative analysis of the economic burden of kidney disease on health care systems with varying levels of resource availability. From a methodological perspective, cross-sectional studies dominate, with 9 studies, followed by cohort studies with 6. No randomized controlled trial was identified among the included studies, which is consistent with the observational nature of cost-of-illness and economic evaluation research. Sample sizes varied considerably across studies, ranging from 30 participants. [19] to 469,581 patients [26], reflecting differences in study scope, from single-center clinical evaluations to large-scale national registry analyses. The time horizons of the included studies ranged from a single year to 40–50 months. [19], and one study [18] utilized a three-year follow-up derived from a registry spanning 1998–2012.

The study population in the majority of included studies (n=10, 66.7%) consisted of patients with end-stage Renal disease (ESRD), defined as patients with a glomerular filtration rate of less than 15 mL/min/1.73 m² (CKD Stage 5) or patients who had already initiated renal replacement therapy. The remaining studies (n=5, 33.3%) focused on patients with chronic kidney disease (CKD) at varying stages of progression, including pre-dialysis CKD stages 1–5 [28]CKD stages 4–5 not yet on dialysis [17], and patients across all CKD categories [16][21][27]. The most frequently employed economic evaluation method was comparative cost analysis (n=8). Cost of illness (COI) analysis was the second most common approach (n=5), which quantifies the total economic burden of a disease from a defined perspective without comparing alternative interventions, followed by cost-benefit analysis (CBA) (n=1), and combined cost analysis with cost-utility analysis (CUA) (n=1). Notably, no cost-effectiveness analysis (CEA) or full economic evaluations incorporating health outcomes such as quality-adjusted life years (QALYs) were identified, except [25] who applied CUA using the SF-36 quality-of-life instrument.

The analytical perspective approaches used in various studies show considerable variation. Three studies adopted a societal perspective in their analyses [16][24] [25]. The societal perspective encompasses cost components outside the formal healthcare system, such as patient and family expenses, informal care, and lost productivity. Meanwhile, the payer or provider perspective was the most dominant approach (n=9), as it focuses on costs directly related to the healthcare financing system. Only one study specifically used the patient perspective [15]. The analysis found that direct medical costs were the most frequently identified aspect across articles that met the inclusion criteria (n=15). These cost components included inpatient care, outpatient services, medication procurement, particularly immunosuppressive therapy for transplant patients, laboratory and diagnostic tests, dialysis procedures and consumables, and surgical procedures. Indirect costs, on the other hand, were only found in four studies. The most frequently identified cost components included decreased productivity due to absenteeism and decreased work performance,

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

indicating limited documentation of these aspects in the articles analyzed [16][24][25][20]. Transportation, accommodation during treatment, and personal expenses not covered by insurance were also reported in four of the studies found. Meanwhile, indirect costs, including time and effort provided by family members or caregivers, were only identified in one study [24]. Nevertheless, these cost categories have the potential to contribute significantly to the total economic burden. The limited reporting of these non-healthcare cost components suggests a methodological gap that requires attention. This is important because these components may account for a significant proportion of the social burden of kidney disease, particularly among patients undergoing dialysis therapy.

The characteristics of the analyzed studies indicate a variety of cost estimation approaches: six studies employed a bottom-up approach, seven used a top-down approach, and one combined the two through mixed methods. This relatively balanced distribution reflects the methodological diversity in health economics research focused on kidney disease, which ultimately impacts the comparability of cost estimation results. Collecting detailed individual-level cost data is possible through approaches that include the value of indirect care time, out-of-pocket expenses, and lost productivity. However, this approach requires significant resources, can introduce bias into study results, and often yields limited sample sizes. This situation is reflected in one of the analyzed studies [19]. Involving only 30 participants. Conversely, the top-down approach offers the advantage of a larger sample size, making it more representative of the population, and minimizing bias through systematic use of collected information. However, this approach has limitations because it relies solely on cost components recorded in national billing or claims systems. As a result, expenditures outside the scope of the formal health system may be overlooked, potentially leading to an underestimation of the economic burden.

Overall, the included studies demonstrated moderate methodological quality according to the ECOBIAS checklist, with considerable variability in the risk of bias across individual studies. In contrast, assessment using the CHEERS checklist demonstrated generally good reporting quality, indicating that most studies adequately adhered to established standards for reporting economic evaluations. These findings suggest that although reporting practices were largely consistent and satisfactory, as reflected in the CHEERS criteria, methodological rigor differences identified through ECOBIAS persist across the studies. Such variability may impact internal validity and comparability of the evidence base and should be considered when interpreting the overall findings.

Discussion

Renal Replacement Therapy Cost

Eight of the fifteen studies analyzed reported transplant costs. Due to differences in cost-calculation methods, currencies, time periods, and cost components, results are presented narratively rather than statistically. In general, transplant costs exhibited a consistent two-stage pattern: high costs in the first year, followed by a significant, stable decline in subsequent years. Zhang *et al*.[18] reported first-year costs of USD 97,950, decreasing to USD 18,200 in the second year, with cumulative savings over dialysis of USD 62,140 in the third year. A similar pattern was found by Helanterä *et al.*[20], with first-year costs of USD 71,270 that decrease to USD 14,410 in subsequent years, significantly lower than annual dialysis costs. In Brazil, Gouveia *et al.* [23] reported first-year transplant costs of USD 6,200–7,400, depending on donor type, while Camargo *et al.* [19] reported a monthly cost of transplantation of USD 1,991 compared to USD 3,668 for hemodialysis.

In China, Wu *et al.* [25] reported an annual transplantation cost of USD 17,700 ± 9,560, influenced by surgery, immunosuppressive medications, and patient accommodation at the referral center. Despite the higher initial costs, transplantation provided better economic value, with a lower cost per health outcome compared to dialysis and peritoneal dialysis. In Iran, Abdi *et al.* [15] also found that transplantation provided greater economic benefits than costs, with a benefit-cost ratio of 5.39. Overall, hemodialysis was the most costly therapy in many studies. Eriksson *et al.* [17] reported an annual cost of hemodialysis of USD 10,626, which was higher than those for both peritoneal dialysis and post-transplant care. A similar pattern is seen in Spain [22] and China[25], where hemodialysis is consistently more expensive than other alternatives. A study from the Netherlands [24] adds that dialysis patients also incur indirect costs such as lost income and additional care costs, which can be more than double those of transplant patients. Furthermore, disease severity also influences costs. Villanueva *et al.* [21] showed that costs increased with CKD progression in the

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Philippines, while Taliwal *et al*. [28] found a similar pattern in pediatric patients in the United States. In Iran, Kolivand *et al.* [26] confirmed that hospitalization and dialysis are the main contributors to ESRD costs, and costs are also influenced by factors such as the patient's age, gender, and location of residence.

Direct Medical Costs and Social Burden of Kidney Disease

Direct medical costs were the most consistently reported component across all 15 studies and were a major factor in the total cost burden of kidney disease. In this category, cost differences between modalities were primarily driven by the characteristics of each service. Hemodialysis has higher costs due to its repetitive nature, typically three times per week in a healthcare facility, and the need for disposable equipment, trained healthcare personnel, vascular access maintenance, and specialized air infrastructure. This combination of fixed and recurring costs explains why hemodialysis is consistently more expensive than both peritoneal dialysis and post-transplant care across healthcare systems. [17][19][25].

In kidney transplantation, costs after the first year are primarily influenced by the long-term use of immunosuppressive medications. Gouveia *et al.* [23] showed that the choice of drug regimen significantly impacted costs, with tacrolimus costing USD 11,987 per year compared to USD 6,179 for cyclosporine. In low- and middle-income countries, the availability of generic drugs is a key factor in reducing long-term costs while preventing graft failure. One important finding from this observation is the limited reporting of non-medical costs. Indirect costs were reported in only four studies. [16][20][24][25], direct non-medical costs in four studies [16][20][24][25], and informal care costs in only one study [24]. De Vries *et al.* [24] provided the most comprehensive picture using a social perspective, showing that dialysis patients incurred more than twice the non-medical costs compared to transplant patients. Furthermore, informal care time was 2.5 times higher in the dialysis group, with productivity loss being the largest component due to chronic fatigue and long therapy times. Methodologically, these findings suggest that analyses that focus solely on direct medical costs tend to underestimate the economic benefits of transplantation relative to dialysis. Therefore, using a social perspective that includes productivity loss, informal care costs, and non-medical expenditures is crucial for producing more accurate cost estimates and reflecting the true economic burden borne by patients, families, and society.

Determinants of Cost Variation

This systematic review showed large cost differences across countries and health systems, even though the therapies being compared were clinically similar. Annual hemodialysis costs ranged from $11,784 in China. [25] to $95,484 in Sweden [17], while first-year transplant costs ranged from $8,149–$9,684 in Brazil [23] and $58,070 in Finland [20]. The health financing systems and economic conditions in each country likely influence these differences.

1. **National Health Care Financing Structure**

The structure of health financing strongly influences cost variations between countries. Countries with universal health coverage systems, such as Sweden [17], Finland [20], and the Netherlands [24]generally report that costs are largely covered by the public system or compulsory insurance, resulting in relatively low direct patient burdens. In contrast, in countries with out-of-pocket financing, such as Iran [15][26], Lebanon [16], the Philippines [21], and parts of China [25]Patients bear a larger proportion of the costs. Studies in Lebanon [16] and the Philippines [21] have shown that low public insurance coverage increases the financial burden on patients, particularly for renal replacement therapy. Therefore, cost comparisons between countries need to consider the financing mechanisms and the distribution of the cost burden within each health system.

2. **Immunosuppressant Drug Pricing Policy**

The use of immunosuppressant medications significantly influences the long-term costs of kidney transplantation. A Brazilian study [23] showed that tacrolimus-based regimens had higher annual costs than cyclosporine ($11,987 vs $6,179), indicating that the choice of pharmacological therapy contributes significantly to total post-transplant costs. Drug pricing policies, negotiation mechanisms, and the availability of generics contribute to the affordability of therapy, particularly in low- and middle-income countries. The high cost of immunosuppressants can also increase the risk of non-adherence and graft failure, ultimately increasing the cost burden due to the need for return to dialysis. Therefore, policies that support access to affordable immunosuppressant medications are crucial for the sustainability of kidney transplant programs.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

3. Availability of Transplant Infrastructure

The availability and capacity of transplant infrastructure influence the cost of procedures and the distribution of renal replacement therapy. Countries with established transplant systems, such as Finland [20] and Sweden [17][18], tend to have higher transplant volumes and more efficient costs due to the support of national registries, specialized facilities, and adequate expertise. Conversely, limited infrastructure in some countries leads to patients being more dependent on more expensive, long-term hemodialysis. A study in China [25] showed that limited geographic access increases indirect costs, such as transportation and accommodation. Furthermore, a study in Brazil [23] found that reimbursement schemes favoring dialysis services can contribute to low transplant referral rates. These findings suggest that transplant infrastructure is closely linked to the financing system and patterns of healthcare utilization.

4. Underestimated Indirect Cost

The most consistent methodological gap in this review is the underreporting of indirect costs in economic analyses of kidney disease. Of the 15 studies, only four [16][20][24][25] included productivity losses, two [16][24] included direct non-medical costs, and one [24] reported the costs of informal care. This suggests a potential bias that could lead to an underestimation of the economic burden. A Dutch study [24] showed that non-medical costs for dialysis patients were more than double those for transplantation patients, primarily due to productivity losses and longer treatment time requirements. In countries with out-of-pocket financing, such as Lebanon [16] and the Philippines [21]Indirect costs, such as transportation and lost income, can contribute to the risk of catastrophic poverty, although they are often undocumented. The predominance of the payer or provider perspective over the social perspective (9 vs.3 studies) is a major factor in this underestimation. Overall, neglecting indirect costs can lead to incomplete economic evaluations, suggesting that the benefits of transplantation over dialysis may be greater if all cost components are considered.

Based on the above factors, the structure of health financing, immunosuppressant drug prices, transplant infrastructure capacity, and limitations in indirect cost analysis differ between developed and developing countries. In developed countries with universal coverage and robust reimbursement systems, the public system bears the majority of the cost burden, so cost variations are primarily influenced by system efficiency and drug pricing policies. Conversely, in low- and middle-income countries, high out-of-pocket costs, limited transplant infrastructure, and the lack of indirect cost accounting significantly increase the financial burden on patients, even risking extreme poverty. While developed countries tend to produce more comprehensive cost estimates due to their broader social perspective, developing countries often underestimate the true economic burden due to data limitations and narrow analytical approaches. Overall, these differences emphasize that comparisons between countries must take into account the health system context to avoid biased interpretations in policymaking.

Limitations

This review has several limitations that should be considered when interpreting the results. There was significant heterogeneity in cost calculation methods, analytical perspectives, cost components, currencies, and study periods, limiting the analysis to a narrative review rather than a meta-analysis. The lack of international costing standards limits cross-country comparisons. Most studies were also observational without randomized trials, making causal relationships uncertain, and patient characteristics and service variations may influence results. Furthermore, the predominance of payer or provider perspectives led to underreporting of indirect and non-medical costs, potentially resulting in an underestimation of the true economic burden. The available data were also predominantly from high-income and upper-middle-income countries, limiting generalizability to low-income countries. Differences in study periods and currency conversion processes continue to create uncertainty in cost comparisons. In contrast, most studies included only short-term follow-up and therefore did not capture long-term costs such as graft failure or return to dialysis. Overall, the main limitations lie in methodological heterogeneity, limited cost perspectives, limited geographic coverage, and the lack of long-term data. Therefore, future research should use cross-country designs with a social perspective and longer follow-up periods.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

Conclusions and Future Directions

This systematic review shows that the economic burden of chronic kidney disease (CKD) and its treatment modalities varies significantly across healthcare systems worldwide. Hemodialysis consistently emerges as the modality with the highest annual costs. At the same time, kidney transplantation has proven to be the most economically efficient long-term option for the management of end-stage renal disease. Globally, across healthcare systems, kidney transplantation can reduce healthcare expenditures to less than one-third of dialysis costs in the years following the procedure, despite requiring a larger initial investment. This provides significant economic benefits for both healthcare payers and patients. Furthermore, the increasing costs associated with CKD stage progression underscore the economic importance of early detection, timely referral to nephrology services, and implementation of secondary prevention strategies to delay progression to end-stage renal disease and the need for renal replacement therapy. Future research needs to standardize cost measurement methodologies across healthcare systems to enable more accurate international comparisons. Furthermore, the development of long-term economic models that comprehensively capture the financial impact of CKD progression and transplant interventions across the patient's life cycle is essential.

Conflict of Interest

All authors hereby declare that this research was conducted without any conflict of interest.

Supplementary Materials

Further details are available in the Supplementary Material.

Reference

[1] G. H. Metrics, "Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990 – 2017 : a systematic analysis for the Global Burden of Disease Study 2017," pp. 1990–2017, 2019, doi: 10.1016/S0140-6736(18)32279-7.

[2] N. R. Hill *et al.*, "Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis," pp. 1–18, 2016, doi: 10.5061/dryad. 3s7rd.Funding.

[3] Y. Li *et al.*, "Global, regional, and national burden of renal anemia, 1990 to 2019 and prediction to 2050," *Nephrol. Dial. Transplant, vol.* 40, no. June, pp. 2289–2299, 2025, doi: 10.1093/ndt/gfaf102.

[4] F. Shahbazi and A. Doosti-, "Global trends and projection of based chronic kidney disease incidence from 1990 to 2030 : a Bayesian age- - period- - cohort modelling study," pp. 1–13, 2025, doi: 10.1136/bmjopen-2024-088104.

[5] J. F. Navarro *et al.*, "Original article Projection of the clinical and economic burden of chronic kidney disease between 2022 and 2027 in Spain : Results of the Inside CKD project," *Nefrol. (English Ed.*, vol. 44, no. 6, pp. 807–817, 2027, doi: 10.1016/j.nefroe.2024.11.009.

[6] I. H. De Boer *et al.*, "Diabetes Management in Chronic Kidney Disease : A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease : Improving Global Outcomes (KDIGO)," vol. 45, no. December, pp. 3075–3090, 2022.

[7] V. Boima, A. B. Agyekum, K. Ganatra, F. Agyekum, E. Kwakyi, and J. Inusah, "Advances in kidney disease : pathogenesis and therapeutic targets," no. February, pp. 1–19, 2025, doi: 10.3389/fmed. 2025.1526090.

[8] K. Failure and R. T. Collaborators, "Articles Global, regional, and national prevalence of kidney failure with replacement therapy and associated aetiologies, 1990 – 2023 : a systematic analysis for the Global Burden of Disease Study 2023," pp. 1378–1395, 2025, doi: 10.1016/S2214-109X(25)00198-6.

[9] A. K. Bello, M. Wainstein, and D. W. Johnson, "Epidemiology of haemodialysis outcomes," vol. 18, no. June 2022, doi: 10.1038/s41581-022-00542-7.

[10] Y. He *et al.*, "Three decades of CKD due to diabetes mellitus type 2 in China, with projections of disease burden from 2022 to 2036 : a systematic analysis for the Global Burden of Disease Study 2021 analysis for the Global Burden of Disease Study 2021," *Clin. Kidney J.*, vol. 18, no. 10, pp. 1–19, 2025, doi:

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

10.1093/ckj/sfaf265.
[11] S. Chadban, A. Power, M. Wu, S. Mennini, J. Arango, and J. Garcia, "Articles Projecting the economic burden of chronic kidney disease at the patient level (Inside CKD): a microsimulation modelling study," vol. 72, pp. 1–11, 2024, doi: 10.1016/j.eclinm.2024.102615.
[12] A. K. Bello *et al.*, "Articles An update on the global disparities in kidney disease burden and care across world countries and regions," pp. 382–395, 2024, doi: 10.1016/S2214-109X(23)00570-3.
[13] C. V. P. I, I. Cristina, G. Leite, G. Fernandes, and F. Ii, "Spatial analysis of care for patients undergoing dialysis therapy in the state of Minas Gerais, Brazil, between 2015 and 2019. Análise espacial da assistência a pacientes em terapia dialítica no Estado de Minas Gerais, Brasil, entre 2015 e 2019", pp. 1–8, 2019.
[14] V. A. Luyckx and M. Sahay, "Equity and Quality of Global Chronic Kidney Disease Care : What Are We Waiting for ?" 2025, doi: 10.1159/000543485.
[15] F. Abdi, C. Alinia, A. T. Afshari, and H. Yusefzadeh, "Cost – benefit analysis of kidney transplant in patients with chronic kidney disease : a case study in Iran," *Cost Eff. Resour. Alloc.*, pp. 1–9, 2022, doi: 10.1186/s12962-022-00372-1.
[16] M. Aoun, E. Helou, G. Sleilaty, R. M. Zeenny, and D. Chelala, "Cost of illness of chronic kidney disease in Lebanon : from the societal and third - party payer perspectives," *BMC Health Serv. Res.*, pp. 1–11, 2022, doi: 10.1186/s12913-022-07936-0.
[17] J. K. Eriksson, M. Neovius, S. H. Jacobson, C. Elinder, and B. Hylander, "Healthcare costs in chronic kidney disease and renal replacement therapy : a population-based cohort study in Sweden," pp. 1–9, 2016, doi: 10.1136/bmjopen-2016-012062.
[18] Y. Zhang, U. G. Gerdtham, H. Rydell, T. Lundgren, and J. Jarl, "Healthcare costs after kidney transplantation compared to dialysis based on propensity score methods and real-world longitudinal register data from Sweden," *Sci. Rep.*, pp. 1–9, 2023, doi: 10.1038/s41598-023-37814-6.
[19] M. Fernanda *et al.*, "Cost analysis of substitutive renal therapies in children ☆," *J. Pediatr. (Rio. J).*, vol. 94, no. 1, pp. 93–99, 2018, doi: 10.1016/j.jped.2017.05.004.
[20] H. Isoniemi, "Association of Clinical Factors with the Costs of Kidney Transplantation in the Current Era," pp. 393–400, 2019, doi: 10.12659/AOT.915352.
[21] A. R. Villanueva *et al.*, "Cost-of-illness analysis of chronic kidney disease (CKD) management in the Philippines," *J. Med. Econ.*, vol. 28, no. 1, pp. 494–507, 2025, doi: 10.1080/13696998.2025.2481766.
[22] P. Lopez-Sanchez *et al.*, "Original article Impact of first year renal replacement therapy on the hospital admissions of a regional public health system ☆," *Nefrol. (English Ed.*, vol. 39, no. 6, pp. 653–663, 2019, doi: 10.1016/j.nefroe.2019.01.012.
[23] A. T. Bignelli *et al.*, "Original Article | Article Original Analysis of economic impact among modalities of renal," pp. 162–171, doi: 10.5935/0101-2800.20170019.
[24] E. F. De Vries, J. Los, G. A. De Wit, and L. H. Van Roijen, "Patient, family and productivity costs of end-stage renal disease in the Netherlands ; exposing non-healthcare related costs," *BMC Nephrol.*, pp. 1–9, 2021, doi: 10.1186/s12882-021-02548-y.
[25] H. Wu, Q. Li, Y. Cai, J. Zhang, W. Cui, and Z. Zhou, "Economic burden and cost - utility analysis of three renal replacement therapies in ESRD patients from Yunnan Province, China," *Int. Urol. Nephrol.*, vol. 52, no. 3, pp. 573–579, 2020, doi: 10.1007/s11255-020-02394-1.
[26] P. Kolivand, S. Azari, H. Saffari, T. Doroudi, A. Marashi, and M. Behzadifar, "Epidemiology and economic burden of end-stage kidney disease by age, gender, and province among Iranian Hajj pilgrims in 2012-22 : a retrospective study of 469, 581 participants," 2025.
[27] N. T. Q. Nguyen, A. E. Courtney, H. Q. Nguyen, M. Quinn, A. P. Maxwell, and C. O. Neill, "Early clinical and economic outcomes of expanded criteria living kidney donors in the United States International Classification of Diseases United Network for Organ Sharing," *J. Nephrol.*, vol. 36, no. 4, pp. 957–968, 2023, doi: 10.1007/s40620-022-01541-4.
[28] N. Taliwal, A. Pandya, A. Dixon, A. Tibrewal, R. J. Kumar, and K. Doshi, "Economic burden of inpatient hospitalizations for pediatric chronic kidney disease in the US," *Pediatr. Nephrol.*, vol. 40, no. 4, pp. 1059–1068, 2025, doi: 10.1007/s00467-024-06568-2.
[29] H. Zhang, C. Zhang, S. Zhu, H. Ye, and D. Zhang, "Direct medical costs of end-stage kidney disease and renal replacement therapy : a cohort study in Guangzhou City, southern," pp. 1–14, 2020.