

Global Epidemiology of End-Stage Kidney Disease and Disparities in Kidney Replacement Therapy

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Keywords

Global epidemiology · End-stage kidney disease · Kidney replacement therapy · Dialysis · Hemodialysis · Peritoneal dialysis · Kidney transplant · Disparities · Income · Mortality

Abstract

Background: The global epidemiology of end-stage kidney disease (ESKD) reflects each nation's unique genetic, environmental, lifestyle, and sociodemographic characteristics. The response to ESKD, particularly regarding kidney replacement therapy (KRT), depends on local disease burden, culture, and socioeconomics. Here, we explore geographic variation and global trends in ESKD incidence and prevalence and examine variations in KRT modality, practice patterns, and mortality. We conclude with a discussion on disparities in access to KRT and strategies to reduce ESKD global burden and to improve access to treatment in low- and middle-income countries (LMICs). **Summary:** From 2003 to 2016, incidence rates of treated ESKD were relatively stable in many higher income countries but rose substantially predominantly in East and Southeast Asia. The prevalence of treated ESKD has increased worldwide, likely due to improving ESKD

survival, population demographic shifts, higher prevalence of ESKD risk factors, and increasing KRT access in countries with growing economies. Unadjusted 5-year survival of ESKD patients on KRT was 41% in the USA, 48% in Europe, and 60% in Japan. Dialysis is the predominant KRT in most countries, with hemodialysis being the most common modality. Variations in dialysis practice patterns account for some of the differences in survival outcomes globally. Worldwide, there is a greater prevalence of KRT at higher income levels, and the number of people who die prematurely because of lack of KRT access is estimated at up to 3 times higher than the number who receive treatment. **Key Messages:** Many people worldwide in need of KRT as a life-sustaining treatment do not receive it, mostly in LMICs where health care resources are severely limited. This large treatment gap demands a focus on population-based prevention strategies and development of affordable and cost-effective KRT. Achieving global equity in KRT access will require concerted efforts in advocating effective public policy, health care de-

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Introduction

End-stage kidney disease (ESKD) is a rapidly increasing global health and health care burden. The inability to care for many patients at risk for and in need of treatment for ESKD disproportionately impacts low- and middle-income countries (LMICs). Defining global ESKD epidemiology is an essential first step in evaluating international response. In this review, we explore geographic variation and global trends in treated ESKD incidence and prevalence based on national reports and registry data. The United States Renal Data System (USRDS) compiles and publishes international survey data annually from 79 countries and regions [1]. Data include only those ESKD patients who are on dialysis or have received a kidney transplant (i.e., treated ESKD). This underestimates true incidence and prevalence, due to unrecognized ESKD and limited access to kidney replacement therapy (KRT) in many countries. Notably, national ESKD data are not available in many LMICs in Africa and 2 populous developing nations – China and India.

The international response to ESKD is complex, influenced by local disease burden, culture, and socioeconomic factors. An estimated 2.6 million people received KRT worldwide in 2010 [2]. However, 4.9–9.7 million people were estimated to require KRT in 2010, suggesting that ≥ 2.3 million people might have died because of lack of access to this life-sustaining therapy. Thus, only half or less of all people needing KRT worldwide had access to it. Further, the proportion of people with ESKD not receiving KRT was much higher in low (96%) and lower-middle (90%) income countries than in upper-middle (70%) and high (40%) income countries [3]. The largest treatment gaps occurred in low-income countries, particularly in Asia and Africa. In Asia, 17–34% of people needing KRT received treatment. In Africa, 9–16% of people needing KRT received treatment [2]. By 2030, worldwide use of KRT is projected to more than double to 5.4 million people, with the most growth in Asia [2].

Given the anticipated global growth in ESKD, it is imperative to understand how international outcomes differ according to KRT management strategies. Therefore, we examine international variations in KRT modality and practice patterns, mortality, disparities in access to KRT

at the country level, and when data are available disparities at the individual level within a country. We conclude with a discussion of strategies to reduce global ESKD burden and inequities in KRT access.

Geographic Variation and Global Trends in the Incidence of Treated ESKD

Based on the International Society of Nephrology's (ISN) 2019 Global Kidney Health Atlas (GKHA) cross-sectional survey of 160 participating countries, information on treated ESKD incidence was available in 79 countries, and the average number of new ESKD diagnoses worldwide was 144 individuals per million general population (pmp) [3]. In 2016, USRDS-reported incidence rates of treated ESKD varied greatly across countries (see online suppl. Table 1; see www.karger.com/doi/10.1159/000514550 for all online suppl. material) [1]. Taiwan, the USA, the Jalisco region of Mexico, and Thailand reported the highest incidences of treated ESKD (493, 378, 355, and 346 pmp/year, respectively). The lowest treated ESKD incidences, ranging from 22 to 85 pmp/year, were reported by South Africa, Ukraine, Belarus, Bangladesh, Russia, Jordan, Peru, Colombia, Iran, Albania, and Estonia.

Among high-income countries (HICs), ESKD incidence is the lowest in Nordic countries, other European countries, Australia, and New Zealand [4]. These have nearly universal health care systems, including KRT access, so the lower rates could be due to relatively low incidence or delayed chronic kidney disease (CKD) progression. Other potential explanations include dialysis commencement at lower glomerular filtration rates, greater adoption of conservative care management, and health care reform strategies focusing on cost containment [5]. ESKD incidence is much higher in the USA and high-income East and Southeast Asian countries, likely reflecting greater CKD burden and associated risk factors such as diabetes, hypertension, obesity, and glomerular diseases (e.g., IgA nephropathy in Asia), greater health care spending, and improving survival among those with CKD. Government policies have also improved KRT access. In Taiwan, the National Health Insurance program provides full coverage for dialysis therapy without copayment [6]. In Thailand, implementation of a “PD-first” universal coverage policy in which all eligible patients are offered peritoneal dialysis (PD) with the more costly hemodialysis (HD) restricted to patients with a clinical indication or private insurance coverage has led to expansion of ESKD care [7].

Among HICs, the incidence rate *trends* for treated ESKD are relatively stable, either declining modestly or increasing slightly by ~2 pmp/year from 2003 to 2016, including Nordic and other European countries, Australia, New Zealand, Japan, and the USA [1]. This may suggest that treatment of diabetes and hypertension has improved over this 14-year period, reducing CKD onset and slowing its progression [4]. In contrast, treated ESKD incidence rates have risen substantially from 2003 to 2016 in East and Southeast Asian countries, including Thailand, Malaysia, the Republic of Korea, Singapore, the Philippines, and Taiwan [1]. This may reflect an aging population; an increased burden of diabetes, hypertension, and obesity; and economic development that improved KRT access [8].

Incidence Rates of ESKD in the USA

Since 2011, the crude ESKD incidence rate in the USA has risen; however, the age-sex-race standardized incidence rate appears to have plateaued [1]. The standardized ESKD incidence rate rose sharply in the 1980s and 1990s, leveled off in early 2006, and has declined slightly since. This downward trend may suggest improved prevention or delay of ESKD onset. However, projected demographic, clinical, and lifestyle characteristics of the US population may reverse the current downward trend. A simulation model incorporating trends in population demographics, obesity, diabetes, and hypertension projected an 11–18% increase in crude incidence rate from 2015 to 2030 [9]. Combined with ESKD mortality declines, this could increase prevalence by 29–68%. The projected rise in ESKD incidence and prevalence in the USA is due to an aging population, rising diabetes and hypertension burden, decreasing ESKD mortality due to improved care, and an increasing proportion of African-Americans in the US population.

African-Americans and other racial/ethnic minority and socially disadvantaged groups account for a disproportionate share of the ESKD population in the USA, largely reflecting inequities in health care access and delivery and associated increased disease burden and poor clinical outcomes [10]. Mechanisms underlying these racial and ethnic disparities represent a complex interplay of genetic, biological, environmental, sociocultural, socioeconomic, and health care system level factors [11]. According to the World Health Organization Commission on Social Determinants of Health, the social gradient in health within and between countries is caused by unequal distribution of power, income, goods, and services,

mainly due to unjust social and economic policies [12]. Social determinants of health include health services (e.g., access to and quality of care and insurance status), social environment (e.g., discrimination, income, and education level), physical environment (e.g., place of residence, living conditions, and transportation), health literacy, and legislative policies [13, 14]. The maldistribution of these factors is associated with increased development and progression of CKD and CKD risk factors, lower access to health care, and worse morbidity and mortality in the CKD and ESKD population [15].

Geographic Variation and Global Trends in the Prevalence of Treated ESKD

In 2016, 2,455,004 patients were treated for ESKD across all countries reporting data to the USRDS [1]. Based on the ISN's 2019 GKHA survey, information on treated ESKD prevalence was available in 91 countries, and the average number of people receiving treatment for ESKD globally was 759 pmp [3]. The USA has the most, with 709,501 treated patients (29%), followed by Japan (328,000; 13%) and Brazil (180,000; 7%). Treated ESKD prevalence varied nearly 30-fold across represented countries (online suppl. Table 1) [1, 16]. Taiwan reported the highest treated ESKD prevalence (3,392 pmp), followed by Japan (2,599 pmp) and the USA (2,196 pmp). The lowest prevalences, 117–540 pmp, were reported by Bangladesh, South Africa, Ukraine, Belarus, Iraq, Russia, Indonesia, Guatemala, Albania, Peru, Latvia, Serbia, and Bulgaria.

Although ESKD incidence has stabilized or decreased in many countries, ESKD prevalence has increased by a median 43% from 2003 to 2016 [1]. Countries with the highest percentage rise in ESKD prevalence were Taiwan, the USA, the Republic of Korea, Thailand, the Jalisco region of Mexico, Chile, Malaysia, Turkey, Brazil, the Philippines, and Russia [1]. Rising ESKD prevalence worldwide may be due to improved survival; aging of the world population; increases in diabetes, hypertension, and obesity, associated with urbanization and changes in diet and physical activity; and increasing KRT access in countries with growing economies [2, 4].

ESKD in China, India, and Africa

In China, the most populous country in the world (1.4 billion people), there are ongoing efforts to establish a national kidney registry [17]. The China Kidney Disease

Network (CK-NET) was initiated in 2014, with its mission to integrate various sources of data in China to better inform health care policy, strengthen academic research, and promote effective management in patients with kidney disease. Using 2 large nationwide claims databases (China Health Insurance Research and Commercial Health Insurance), the estimated age-adjusted incidence rate of dialysis was 122 pmp/year. Also, in 2015, the estimated prevalence of HD and PD was 402 and 40 pmp, respectively (553,000 HD and 55,000 PD patients).

India, the 2nd most populous country in the world, also lacks a national registry for ESKD [18]. Most estimates are extrapolated from subregions of India or hospital-based registries. A population-based study from a large urban cohort estimated an age-adjusted ESKD incidence of 232 pmp [19]. In 2010, 52,273 adult CKD patients were analyzed, and 61% of those with ESKD were not on any form of KRT, 32% were on HD, 5% on PD, and 2% were evaluated for transplant [20].

In Africa, the vast majority of cases of ESKD likely remain undiagnosed and untreated, leading to almost certain mortality [21]. Limited aggregate data exist to accurately characterize ESKD rates, which are likely quite high, and steps to establish a continent-wide registry are ongoing [22]. The prevalence of treated ESKD in sub-Saharan Africa is lower than that of other developing countries (<100 pmp) [23, 24], despite comparable incidence rates, and is likely due to limited access to KRT (only ~10% of adults with incident ESKD remained on dialysis ≥3 months) [21]. KRT access generally requires self-funding, even in wealthier countries like South Africa, which only provides government funding for KRT if a patient is eligible for transplant [25].

Global Variation in KRT Modality and Practice Patterns

Although kidney transplantation is the preferred treatment for eligible ESKD patients, dialysis is the predominant therapy in the majority of countries (online suppl. Table 2) [1]. Considerable variation exists in access to and use of kidney transplantation. In 2013, transplantation for ESKD patients ranged from 57–72% in Nordic countries, Estonia, and the Netherlands to <10% in some Asian and eastern European countries [4]. Countries with the highest transplantation rates – mostly Nordic and several other European countries – also have some of the lowest ESKD incidence rates. In such countries, transplantation may be offered to a higher proportion of ESKD patients

because of the relatively low number of incident cases. In some countries, by focusing on transplantation or home dialysis, <1/3 of ESKD patients used in-center HD [4]. These include Hong Kong, Estonia, the Netherlands, New Zealand, and some Nordic countries. This differs from many East and Southeast Asian countries where ≥85% of patients receive in-center HD. Japan is notable because it has a large and mature ESKD program with excellent clinical outcomes, but very low transplantation and home dialysis use. In-center HD is favored over home dialysis partly for historical reasons (dialysis facilities are available and easily accessible, with many placed intentionally near public transportation stops), and kidney donation rates are low, in part due to spiritual beliefs.

Worldwide, HD is the most common dialysis modality [26]. In 2016, in most countries, ≥80% of chronic dialysis patients received in-center HD [1]. Home HD therapy was provided to 9 and 17% of dialysis patients in Australia and New Zealand, respectively [1]. PD was used by 71% of dialysis patients in Hong Kong, by 61% in the Jalisco region of Mexico, and by 57% in Guatemala [1]. While international differences in dialysis outcomes derive to some extent from variations in patient population, survival differences may also be affected by modifiable variation in dialysis practices, including vascular access, HD session duration, and dialysis adequacy [4], based on global data reported by the USRDS and observational data from the international prospective cohort study of HD patients in Dialysis Outcomes and Practice Patterns Study (DOPPS) [27].

Vascular Access

The native arteriovenous fistula (AVF) is widely considered the preferred option of vascular access for most HD patients, providing the best outcomes overall compared with arteriovenous grafts (AVG) or central venous catheters (CVC) [28]. In 2013, Japan and Russia had the highest prevalent use of AVF (>90%) among 20 participating countries in the DOPPS [29]. AVF use in prevalent HD patients was 49–92% across these DOPPS countries, while catheter use ranged from 1 to 45% [29]. In the USA, the Centers for Medicare & Medicaid Services' (CMS) Fistula First Breakthrough Initiative spurred increased AVF use (24 to 68%) and decreased AVG (49 to 18%) and CVC use (27 to 15%) from 1997 to 2013 [29]. Large variations in vascular access type also exist in other regions of the world. In South Africa, the prevalence of AVF, AVG, and CVC was 51, 7, and 39%, respectively, in 2017 [30]. In Argentina, the prevalence of AVF, AVG, and CVC was

70, 15, and 15%, respectively, in 2018 [31]. In Vietnam, the prevalence of AVF, AVG, and CVC was >95, 4, and 1%, respectively, in 2018 [32]. Further, DOPPS data demonstrate substantial international differences in the creation location and successful use of AVFs [33]. Specifically, successful use of newly created AVFs (≥ 30 days of continuous use) was 87% in Japan, 67% in Europe/Australia and New Zealand, and 64% in the USA. Median time until first successful AVF use was 10 days in Japan, 46 days in Europe/Australia and New Zealand, and 82 days in the USA. The factors that may explain these AVF outcomes include differences in patient characteristics, surgical training, dialysis unit staffing, and HD prescription such as dialysis blood flow [34].

Hemodialysis Session Duration

Although a recent pragmatic trial evaluating the effect of session duration on clinical outcomes was inconclusive [35], multiple observational studies have demonstrated an association between longer treatment time and improved survival among HD patients [36–38]. In many HICs, in-center HD treatment time is ≥ 4 h thrice weekly, with Australia/New Zealand, Germany, and Sweden having some of the longest treatment times among DOPPS countries [37]. More recent data indicated that 92% of patients dialyzed in Australia had session lengths from 240 to 300 min [39]. In contrast, dialysis session length has shortened in the USA (mean 214 min) [37] with higher dialysis blood flow and larger dialyzer size versus other DOPPS countries, partly because of greater reliance on small solute (urea) clearances as a measure of dialysis adequacy than other metrics such as volume management and patient-reported outcomes [40]. This variation in session length reflects an interplay between clinical practice guidelines, reimbursement measures, HD unit policies, and provider and patient preferences [4]. Dialysis treatment time is similarly short in the Gulf Cooperation Council (GCC) countries (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates) based on DOPPS data from 2012 to 2018, with a mean of 222 min and 43% prevalence for low treatment time (< 240 min) [41].

Dialysis Adequacy

The 2015 update of the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Hemodialysis Adequacy recommends a target single

pool Kt/V (spKt/V) of 1.4 per HD session for patients treated thrice weekly, with a minimum delivered spKt/V of 1.2 [42]. Since 1996, an increase in dialysis dose has been observed with lower proportions of HD patients with spKt/V < 1.2 in DOPPS countries [43]. Recent DOPPS data from 2015 to 2018 showed that 34% of HD patients from GCC countries had low spKt/V < 1.2 versus 5–17% in Canada, Europe, Japan, and the USA [41]. In the USA, Kt/V dose (not dialysis duration) is tied to the CMS' payment policy to dialysis facilities, with 97% of HD patients achieving spKt/V ≥ 1.2 [1]. In Japan, treatments are longer, with lower blood flow rates, thought to better ensure hemodynamic stability and greater middle molecule clearance, despite a greater likelihood of spKt/V < 1.2 [4]. Among 5,784 HD patients from Japan DOPPS from 1999 to 2011, spKt/V < 1.2 was observed in 26% of patients and was associated with greater mortality (adjusted hazard ratio per 0.1 lower spKt/V = 1.10; 95% CI: 1.05–1.14) [44]. However, survival in the Japanese HD population overall is considerably better than most other countries, with a crude mortality of 9.8% in 2013 [45]. Thus, despite this relatively low mortality rate, opportunities remain to improve the dialysis dose in Japan. In LMICs such as India, twice-weekly HD is a common practice, with about one-fourth of patients undergoing dialysis once a week or “as needed” due to financial constraints [46]. In a single-center study of 463 HD patients in Southern India, only 50% of the treatments delivered a spKt/V ≥ 1.0 [47]. In another single-center study of 50 patients on twice-weekly HD, only 28% of sessions delivered standardized Kt/V ≥ 2.0 per week (mean 1.4) [48].

Global Variation in Mortality Rates in ESKD

According to the 2013 Global Burden of Disease Study, age-standardized death rate caused by CKD increased from 11.6 to 15.8 per 100,000 between 1990 and 2013 [49]. In 2013, CKD ranked 19th for global years of life lost, a measure of premature death. Although most ESKD registries report incidence and prevalence data, survival data are preponderantly from HICs (online suppl. Table 1). For patients with ESKD onset from 2004 to 2008, treated with dialysis or transplantation, unadjusted 5-year survival was 41% in the USA, 48% in Europe, and 60% in Japan, despite patients being 2–3 years older on average in Europe and Japan versus the USA and Japan having few transplant patients [4]. Excluding transplant, unadjusted 5-year survival for dialysis was 39% in the USA, 41% in Europe, and 60% in Japan [4]. The European Re-

nal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry Annual Report 2016 showed that for patients starting dialysis from 2007 to 2011 across European countries, 5-year unadjusted survival was stable at 42% [50]. DOPPS analyses demonstrate that demographic factors and comorbid diseases accounted for some, but not all, of the differences in dialysis mortality between the USA, Europe, and Japan [51]. Other factors, such as variations in dialysis practice, may contribute to differing survival outcomes.

Mortality in the USA

In 2016, adjusted mortality rates for ESKD, dialysis, and transplant patients were 134, 164 (166 for HD and 154 for PD patients), and 29 per 1,000 patient-years, respectively [1]. Overall mortality rates among ESKD (dialysis and transplant) patients have declined from 2001 to 2016, with rates leveling during recent years (the adjusted death rate decreased by 29% over this period). Specifically, reductions in adjusted mortality rates from 2001 to 2016 were 28% for HD and 43% for PD patients. The reasons for increased ESKD survival are unknown, but may relate to technical advances in dialysis, new pharmaceutical agents, and improved practice guidelines adherence [52]. Increased access to transplant and improved allograft survival may also be contributory. Nonetheless, absolute mortality rates remain high in ESKD, particularly for maintenance dialysis.

Global and Socioeconomic Disparities in the Burden of ESKD and Access to KRT

CKD is a global health challenge, especially in LMICs [53]. A majority of people in developing countries have limited incomes and cannot afford health insurance, which risks personal financial crises from out-of-pocket medical costs for both CKD care and KRT [54]. There is a greater prevalence of KRT among groups of people with a higher income level [55], which is consistent with the notion that KRT access is highly dependent on health care expenditures and economic strength of individual countries (online suppl. Table 2) [56]. Most KRT patients (93%) live in high-income and upper-middle-income countries, with only 7% living in lower-income countries [2]. The ISN's 2019 GKHA survey showed a treated ESKD prevalence of 966 pmp in high-income, 550.2 pmp in upper-middle, 321 pmp in lower-middle, and 4.4 pmp in

low-income countries [3]. Although patients receiving KRT represent a small fraction of the global population (~0.038%) [2], they absorb 2–4% of the health care budget of some countries, creating problems of prioritization and opportunity costs [57]. Dialysis in LMICs is primarily provided in the private sector, and high out-of-pocket expenses often lead to household financial depletion, followed by treatment discontinuation and death once resources are exhausted [58]. In a single-center study of 320 ESKD patients initiated on maintenance HD in Nigeria, >80% of the patients funded dialysis treatments from out-of-pocket payment [59]. Within 12 weeks of initiation, 98% had dropped out of the program through deaths and abandonment, and only 2% were able to fund treatments beyond 12 weeks.

Disparity in access to KRT is not limited to LMICs. Some of the most explicit examples of inequity are evident in undocumented immigrant ESKD care. In the USA, undocumented immigrants with ESKD (currently estimated between 5,500 and 8,857) [60] are ineligible for Medicare, and coverage decisions are made at state or local levels [61]. The 2 main treatment options, emergency-only hemodialysis (EOHD) and chronic outpatient dialysis, highlight the dilemma between principles of justice and societal standards. Some patients on EOHD are dialyzed once to twice weekly while others just once a month [62]. Not surprisingly, EOHD is associated with psychosocial distress, life-threatening physical symptoms, and poor outcomes with a mean dialysis vintage of 16 months at the time of death [63, 64]. A retrospective cohort study involving 211 undocumented patients in 3 states demonstrated a 14-fold increase in 5-year relative hazard of mortality for EOHD versus standard chronic outpatient dialysis [65]. Enrollment in private health insurance coverage and subsequent standard thrice weekly dialysis results in improved 1-year mortality and cost savings in undocumented patient care [66]. In 12 states, undocumented immigrants are able to receive chronic outpatient dialysis through Emergency Medicaid coverage [67]. In other states, outpatient dialysis services may be acquired through private insurance (sometimes provided by non-profit and charitable organizations) or through county-funded and safety-net hospital-funded outpatient dialysis centers. Thus, ESKD care for this vulnerable population is highly variable between states, leaving many undocumented patients relying on EOHD with resultant poor health outcomes that can only be ameliorated by clinically sound, humane, and economically sensible health policy [68].

Table 1. Strategies to reduce global burden of ESKD and inequities in access to KRT

1. Promote a global focus on creating and supporting a culture of health, with an emphasis on primary prevention of CKD
2. Increase awareness of CKD as a public health issue among the population, health care providers, and policymakers
3. Implement effective and affordable early detection, prevention, and treatment programs for CKD Management of noncommunicable diseases to include hypertension, diabetes, obesity, and cardiovascular disease Blockade of the renin-angiotensin system Prevention of AKI and CKD from environmental exposures (nephrotoxic effects from herbal medicines and contaminated water and soil) Management of communicable diseases to include HIV and waterborne diseases
4. Develop an appropriate national government policy of KRT delivery to promote equity in resource allocation
5. Promote cost-effective home dialysis modality such as PD and develop affordable dialysis techniques (using domestic manufacturing of dialysis consumables to reduce costs, point-of-care dialysate production)
6. Lower barriers for patients to receive kidney transplant since it is the most cost-effective KRT modality and results in the best clinical outcomes (using generic immunosuppressive drugs)
7. Finance prevention and treatment of ESKD with a mix of government, private, and nongovernmental, not-for-profit funding
8. Assess and promote approaches in relation to the local and national levels of economic development and resources through a lens of justice and equity
9. Increase manpower resources (nephrologists, nephrology nurses, dialysis technicians, and general practitioners)
10. Educate and train local community experts in partnership with governments, nongovernmental organizations, and the pharmaceutical industry
11. Implement global evidence-based guidelines and professional standards in the provision of KRT with guidance on ethical issues

ESKD, end-stage kidney disease; KRT, kidney replacement therapy; CKD, chronic kidney disease; PD, peritoneal dialysis; AKI, acute kidney injury; HIV, human immunodeficiency virus.

Significant global inequities also exist for kidney transplantation, which is the most cost-effective treatment for ESKD (particularly beyond the first year after transplant) due to reduced costs and improved survival and quality of life outcomes [69]. Gross domestic product per capita correlates with kidney transplant prevalence and kidney transplant as a proportion of overall KRT population, reflecting greater transplant rates in HIC [55]. Unmet needs for kidney transplantation disproportionately affect LMICs due to a lack of health care infrastructure, costs of transplant surgery and immunosuppressive drugs, infectious disease (e.g., tuberculosis), geographic remoteness, commercial incentives that favor dialysis, lack of a legal framework governing brain death, and religious and cultural beliefs [70]. In a single-center study of subsidized kidney transplantation in a public-sector hospital in India, 82% patients experienced financial crisis [71]. Greater than 20% of the transplant recipients sold property as a source of funding for treatment-related expenditure, and a majority did not have identified means to pay for immunosuppressive medications [71].

Strategies to reduce ESKD burden and KRT access inequities at a provider level include early CKD detection, prevention and treatment programs with attention to education and lifestyle intervention, communicable diseases, noncommunicable diseases (hypertension, diabetes, obesity, and cardiovascular disease), and avoidance of nephrotoxic agents (including over-the-counter and nontraditional remedies) [72]. At a community/system level, reductions in environmental toxins (air pollutants, heavy metals, agrichemicals, and contaminated water and soil) [73], improved access to healthy foods, education, and healthy living conditions by ensuring equitable access to housing and employment, health care provider capacity building, health system organization, and government policy grounded in environmental, social, and economic justice are necessary [55, 74, 75]. Table 1 lists strategies to improve KRT access within an ethical framework [76], through consideration of affordability, availability, and acceptability in KRT delivery [2, 77]. Using these strategies, a country may develop a tailored national management program that could account for resource

limitations and local needs [54]. International programs such as Kidney Disease Improving Global Outcomes (KDIGO) provide direction on how to adapt HIC-driven guidelines for LMICs [78]. LMICs can leverage support from international organizations (e.g., ISN), industry, and academic medical centers to address workforce capacity through educational ambassador programs, sister kidney centers, fellowships, web-based teaching programs, and telemedicine [79]. Finally, health information systems, such as registries, are essential in permitting accurate problem assessment and guiding resource allocation and policy development [80].

Conclusions

In this review, we explore the global epidemiology of ESKD and inequities in access to KRT. The incidence rates of treated ESKD have remained relatively stable from 2003 to 2016 in many higher-income countries (Nordic and other European countries, Australia, New Zealand, Japan, and the USA) but have risen substantially, predominantly, in East and Southeast Asian countries. The prevalence of treated ESKD has increased worldwide, likely due to improving ESKD survival, population demographic shifts, higher prevalence of risk factors for ESKD, and increasing KRT access in countries with growing economies. Unadjusted 5-year survival of ESKD patients receiving KRT was 41% in the USA, 48% in Europe, and 60% in Japan. Dialysis is the predominant KRT in the majority of countries, with HD being the most common modality. Variations in dialysis practice patterns account for some of the differences in survival outcomes globally. Worldwide, there is a greater KRT prevalence in higher-income populations, and the number of people who die prematurely because of lack of KRT access is estimated at up to 3 times higher than the number who receive treatment. Greater than 90% of ESKD patients receiving KRT in the world live in high-income and upper-middle-income countries. This large treatment gap demands a focus on population-based prevention strategies and devel-

opment of affordable and cost-effective KRT. Achieving global equity in access to KRT will require concerted efforts in advocating effective public policy, health care delivery, workforce capacity, education, research, and support from the government, private sector, nongovernmental, and professional organizations.

Acknowledgements

Part of this manuscript was based on the Epidemiology and Outcome of ESKD topic for the updated American Society of Nephrology's online Dialysis Core Curriculum, presented by Dr. Nee and Dr. Yuan.

Conflict of Interest Statement

The authors declare no conflicts of interests.

Funding Sources

This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors. Dr. Yan is supported in part by the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases grant R01DK112008. Dr. Norris is supported by NIH grants UL1TR000124 and P30AG021684.

Author Contributions

Concept and design: R.N. and C.M.Y.; manuscript drafting: J.T., M.J., G.Y., K.C.N., C.M.Y., and R.N.; manuscript critical revisions: J.T., K.C.N., L.Y.A., C.M.Y., and R.N. All authors approved the final version for submission.

Disclaimer

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