INEQUITIES IN KIDNEY HEALTH AND KIDNEY CARE

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Abstract (200words)

Health inequity refers to unnecessary and unfair differences in the capacity to achieve optimal health and appropriate accessibility of care. Kidney diseases [including acute kidney injury (AKI) and chronic kidney disease (CKD)] have strong associations with inequity. This is largely due to the intrinsic risks of kidney diseases, the heavy burden of comorbidities and the high cost of therapies, e.g. for dialysis on wich survival for many may depend. However, inequities occur across the entire clinical course of kidney diseases. This review offers a comprehensive overview of the array of inequities in kidney health and kidney care, including inequities between countries, regions and social classes, inequities in healthcare, inequities specific to therapeutic modalities, and health-economic and ethical implications. This review also proposes solutions, which may inspire nephrology professionals to recognize and mitigate inequities. In addition to the main text that summarizes the relevant elements, and interested readers are referred to the comprehensive tables (including case stories) and references, which review some facets more deeply. It is the responsibility of all implicated to call attention to inherent risks of inequity in their immediate and broader environments, and to pursue the best possible solutions together with their communities.

Introduction (7915 words)

Health inequality refers to differences in health or health resources between persons, populations or nations such as those caused by age or genetic predisposition[1]. Inequities in healthcare are unfair, avoidable and remediable differences between groups, based on socioeconomic, demographic or geographic factors[2]. The distinction between inequities and inequalities is not always clear. Importantly, underlying inequalities frequently contribute to inequities, e.g. when genetic predisposition, age or sex intersect with race/ethnicity, socio-economic status, possibilities to adhere to healthy lifestyle or level of education

In this manuscript we review different aspects of inequity which impact kidney health and kidney care across the globe. For all the discussed elements a number of potential solutions are reviewed at the end. The aim here is to offer practical guidance to all those involved on how to avoid inequities, as these are among the most concerning social injustices in modern clinical nephrology. Throughout this manuscript, inequalities will sporadically be referred to if they impact inequities.

Health inequities affect the capacity to achieve optimal health, which also includes appropriate accessibility of care[4]. This capacity is far from equally distributed globally, especially across regions and social classes[5-8]. The awareness of health inequities has not translated into sufficient corrective and collective action, because health inequities are multifactorial and multisectoral. They arise from differences not only in medical care but also from differences in global policy, sociology, ecology, geography, ethics, economics, psychology, culture, religion and tradition (Table 1) . A further barrier is the fatalistic view that the problem is too large, too broad, or too complex[9]. Inequities evolve over the life course, such that disadvantaged fetal or childhood development may predispose to compromised health throughout life[10,11]. An avoidable lack of screening and preventive care may also lead to late presentation of disease and seriously jeopardize health outcomes[12]. Kidney diseases do not escape these rules, but rather epitomize them[13].

Appreciation of the importance of kidney diseases by the medical community, policy makers, and the public has lagged behind that of other common conditions for multiple reasons[14,15]. First, the rapid growth of dialysis and transplantation since 1960 has focused on the needs of patients requiring these expensive therapies diverting attention from prevention that is more scalable and applicable everywhere[15,16]. Second, the lack of consistent definitions of kidney diseases until the 2000s, and of reliable epidemiologic data in some regions, has hidden the full extent of the problem, limiting the development of appropriate interventions[17,18]. Third, the lack of awareness among primary care providers, together with deficiencies in health information systems, have also hampered prevention, detection and early treatment[19-21].

Based on the mounting evidence regarding population prevalence and poor outcomes[22-24], kidney diseases should be considered a public health priority, but thus far have not been prioritized on the global non-communicable disease (NCD) agenda[25]. This has resulted in the most fundamental inequity that affects all kidney patients without distinction: insufficient investment in screening, prevention, research, and innovation compared to other common NCDs, which themselves remain chronically underfunded [26]. Chronic kidney disease (CKD), despite affecting 10-15% of society globally[17,26], is not a health research focus for the European Union (EU)[27]. Neither does CKD figure among the 56 health topics considered relevant by World Health Organization (WHO) Europe[28]. In the 2022 EU Healthier Together Initiative, four disease-specific NCD strands are targeted, excluding CKD[25,29]. This lack of awareness among policy makers is compounded by the ignorance of the kidney's functions and its pathologies. Most individuals do not know what the kidneys do, let alone how to care for them[30]. At best, policy makers see kidney diseases as a co-morbidity of cardiovascular disease (CVD) or diabetes, which postpones diagnosis for many, and leaves others entirely behind[31].

This manuscript is coordinated by European Kidney Health Alliance (EKHA), a non-governmental organization advocating for kidney health at European Union (EU) level and beyond[3]. This article collates in a global context perspectives from diverse inequity experts, representing various continents, age groups and backgrounds, including kidney patients. It seeks to reposition the need for equity in kidney health and care as a global priority and offers a basis for further exploration for all involved stakeholders.

Inequities across countries/regions

Epidemiologic distribution

The Global Burden of Disease (GBD) study attributed more than 3 million deaths in 2019 to kidney dysfunction[32]. Most CKD deaths occurred in India and China[17]. In Latin-America, the Middle-East and North- Africa, CKD falls within the top 5 most common causes of death[33]. Globally millions of deaths probably result each year from the lack of accessibility of kidney replacement therapy (KRT),[34] and from acute kidney injury (AKI)[35], and those remain largely uncounted in lower-resource countries.[36,37]. Inequities across regions are also further enhanced by environmental factors, such as increasing number of heat waves and droughts, pollution, water contamination and increased distribution of tropical diseases[38-40], which do not affect all countries and people equally.

Applying the definition of CKD[41,42], a systematic analysis of worldwide population-based data estimated the age-adjusted global prevalence of all-stage CKD in 2010 at 10.4% in men and 11.8% in women more than 20-years-old[43]. Subsequent estimates yielded relatively consistent results, although with regional variations from 6 to 20%[44,45]. CKD prevalence increases with age and appears higher in lower-resource settings[43].

The GBD study showed a 15-fold global variation between countries of CKD burden [specified as age-standardized CKD-linked disability-adjusted life-years (DALYs)] , highlighting potential inequities in both accessibility of diagnostic possibilities and risk factor distribution[33]. It is even more difficult to estimate the contribution of AKI[46]. A pooled incidence of hospital-acquired AKI was reported as 34 and 22% among hospitalized children and adults[47] respectively but with promounced regional variations, raising questions of plausibility and generalizability[37,48].

Risk distribution

The risk of kidney diseases is associated with country income level [51] with people developing CKD and dying from CKD at a younger age in lower-resource settings compared to high income countries (HICs)[52,53]. The association between age-adjusted CKD prevalence and KRT incidence is positive in HICs, but explains only 40% of the variance[54]. This association is negative in Central and Eastern-Europe, and null elsewhere[54], which highlights differences in incident KRT that cannot be explained by CKD prevalence, even in HICs where accessibility of KRT is generally unlimited.

In Central and Eastern-European countries, gross domestic product (GDP) is highly heterogeneous, a legacy of the Cold War and the Iron Curtain. Many CKD risk factors are more prevalent than in Western-Europe, especially in countries with lower GDPs, likely contributing to a higher regional incidence of CKD[55]. Other disparities in this region related to kidney care include variable availability of specific KRT modalities and expensive medication, relative number of nephrologists, and tracking of the prevalence of CKD[56-61].

Within HICs, in part due to the legacy of colonialism and slavery, stark disparities across racial, geographic and socio-economic strata exist[13,68,69]. Moreover, patients with socio-economically deprived backgrounds develop kidney impairment 5 years earlier in their life course and suffer from more comorbidities[13].

Global distribution of KRT

Registries of KRT were introduced in the 1960s-1970s in Europe and the US and have expanded to most HICs but are less available elsewhere. Across countries reporting to the United States Renal Data System (USRDS), the incidence of KRT ranged from 16 per million people (pmp) in South-Africa (2018) to 570 pmp in Jalisco, Mexico (2019), and the prevalence of treated kidney failure varied over 30-fold across countries (2019), which reflects disparities in accessibility of KRT rather than in true incidence[34,70]. KRT incidence is rising in most lower-income settings[70], however predominantly in the private sector (e.g. South-Africa and India), leaving many without possibilities to be treated or exposed to significant catastrophic health expenditures (CHE – out-of-pocket healthcare payments which impoverish a household)[71-74].

To permit equitable accesibility of care, provision of sustainable KRT requires robust health systems and financing. A higher country Gini coefficient (indicating greater within-country inequity) directly correlates with greater prevalence of stage 5 CKD remaining untreated by KRT[75,76]. In areas with greater equity, there is more accessibility of KRT[75,76]. In lower-resource settings a small fraction of those requiring KRT receive it long-term[34]. For example, most African countries have healthcare systems with poor/no health insurance coverage, leaving the vast majority of people with kidney failure unable to obtain KRT[77,78]. Elsewhere, macro-economic factors and services for kidney care are also more strongly related to KRT incidence than demographics or general health[79]. In Eastern-Europe, variability in incidence and prevalence of KRT results in multiple-fold differences in dialysis and transplantation uptake between countries, as well as less home dialysis and conservative care compared with Western-Europe[60,61].

In brief, country location and wealth distribution substantially impact kidney health and accessibility of kidney care across the world. Inequities exist even within a relatively homogeneous region like Europe.

Factors associated with inequitable health care

Diagnosis and treatment

A complex interplay between structural risk factors for AKI and CKD and rapid progression of disease due to limited accessibility of primary care limits possibilities to mitigate these risks[64-67]. Diagnosis of CKD and AKI requires blood and urine tests, which are not routinely available everywhere[49]. In 2017, two-thirds of low income countries (LICs) were unable to measure serum creatinine in primary care, and none provided quantitative albumin or protein urinalysis[49]. Availability of medicines required for kidney care is often limited in lower-resource settings, but even within HICs inequities may arise based on coverage differences between patients and insurers[62,63]. Similarly the nephrology workforce is unequally distributed across the globe: the number of nephrologists per million population (pmp) ranges from 31 in Western Europe to 1 or less in Africa[50]. Thus, diagnosis, availability of treatment and tracking of the burden of kidney diseases is highly inequitable globally.

Inequities conflicting with living well

Good healthcare is a key component to living well[80]. To achieve this equitably, health providers must meet people at their different levels of disadvantage (Figure 1) and support them to face personal challenges and priorities. Patient priorities may, but do not always align with those of healthcare providers[81,82]. Kidney diseases exacerbate vulnerabilities, including health, social, and financial hardship[83,84]. Of note, most often, vulnerability is not an intrinsic condition but due to system failures. Health decision-making is influenced by wider contexts, including one’s own understanding, finances, social support, geography, culture, beliefs, and freedoms. Healthcare providers must appreciate these wider determinants, both to consider patients holistically, and to avoid blaming individuals for risks and outcomes caused by external factors.[10]

A complex relationship exists between the unique challenges posed by kidney diseases, broader individual and environmental contexts, and healthcare and societal factors which promote or undermine health. Accessibility of kidney care is complex, with many intersecting and compounding challenges, as discussed elsewhere [5,10,13,30,65,80,84-120] and summarized in Table 1. Many of these factors are global problems. The Sustainable Development Report 2022[121] highlights major challenges and insufficient data regarding inequity indicators especially across lower-resource settings[121], which exacerbate the inherent “invisibility” of kidney diseases. The implications for specific groups are expanded on below, with accompanying scenarios and quotes in box 1, partly based on published observations[115,122-129].

Socio- economics

Social and economic position (SEP) is consistently associated with health risks and accessibility of care, across countries, and across lifecourse[104]. People of all ages are at risk of kidney diseases, which constrains opportunities for well-being, education, employment, and attaining life-goals. The relationship between SEP and kidney health is bidirectional, with increased risk of falling into poverty as kidney diseases progress[130].

Particular challenges exist in lower-resource settngs[78,131]. In most of Africa for example, many people with CKD are of working age. They often present late, with kidney failure resulting in poor outcomes[132,133]. This is driven in part by low health literacy, and a preference for potentially nephrotoxic traditional remedies and faith-based healers[134,135], but also by a lack of infrastructure and adequate workforce to enable early detection, prevention, and community surveillance[50,101]. If lower-resource countries provide coverage for dialysis, it typically is limited to only two sessions per week[100]. Others exclude kidney failure from coverage schemes[99], necessitating prohibitive out-of-pocket costs if dialysis or transplantation are availabile[77 85,136]. Thus, many people in lower-resource settings are unable to sustain treatment for kidney failure, and struggle with the economic burden on their family, creating difficult moral trade-offs in the allocation of household resources[137,138].

Even in HICs with universal health coverage (UHC), deprived individuals experience less preventative care, more rapid progression of kidney diseases, a greater need to rely on emergency services, and stigmatisation[13]. Poor neighborhoods are associated with poor education and employment opportunities. Residents have less ability to obtain and navigate preventative healthcare, limited availability of recreation services or exercise facilities, and greater exposure to environmental toxins, overcrowding, and food insecurity[65,88,97]. These represent barriers to a healthy lifestyle, good nutrition, and ability to cope with stressors[5,95].

Those who are uninsured , homeless or undocumented migrants also suffer limited accessibility of preventive care. One in three undocumented migrants with kidney failure in the U.S. receive only emergency dialysis, with grave prognostic implications[117]. Irrespective of country, refugees experience similar difficulties to the disadvantaged in navigating healthcare and maintaining a healthy lifestyle[118]. During humanitarian crises, this includes reduced accessibility of life-saving treatments such as dialysis and immunosuppression[139].

Discrimination

Systemic racism continues to drive persistent inequities in kidney health, whereby race should be understood as a social construct rather than a biological indicator and disparities in health and outcomes as the consequences[140].

Globally, people of Black race and minoritized backgrounds are more likely to have kidney diseases, and progress to kidney failure[141,142]. In the U.S., Black patients with kidney failure are less likely to be evaluated and referred for transplantation [143-145], are listed later[144,146-148], wait longer for transplantation[149-152], and receive poorer overall care[153-156] than White patients.

Discrimination against minority groups, including race and sexual and gender minorities (SGM), occurs at the intersection with wider health determinants and causes differences in how healthcare is used and experienced[65,94]. Due to systemic inequities and policies (e.g. redlining), patients from minoritized backgrounds are overrepresented in poorer neighborhoods[65,157-159]. Inequitable structural investment in local community environments perpetuates these disadvantages into future generations[160,161]. In addition, the direct experience of discrimination can cause long-term stress and negative coping, leading to overeating, alcohol or other drug abuse, smoking, poorer mental health, and less trust in sources of support[65,162,163]. Importantly such discrimination not only impacts individuals, but markedly increases total health care costs, which further weakens health systems. In 2018, the economic burden of racial and ethnic health inequities and education-related health inequities in the US, (measured as excess medical care expenditures, lost productivity, and the value of excess premature death combined), wer estimated at over $420 billion and over $940 billion respectively[164]. Most of the excess costs was contributed by the Black population and those without a high school education.

Patients from minoritized groups may distrust professionals if discrimination is witnessed, with a detrimental impact on health-related decision-making[94]. A patient experiencing discrimination may leave and never return. Effort should be made to provide education and support that is culturally and socially sensitive, but clinician-patient relationships vary across minorities and cultural groups[149], with clinicians investing unconsciously more in people with whom they have greater affinity. Without awareness of these biases, nephrologists may be prone to spend less time with those from minorities discussing treatment options such as transplantation, or new therapeutic options such as sodium-glucose transporter (SGLT)-2 inhibitors[93] (if reimbursed).

Algorithms and guidelines

Algorithms are used to assess, monitor, predict, and support clinical decisions. Such tools risk introducing biases, if based only on selected (privileged) groups or only approximative parameters with a magnitude of error that depends on person characteristics[165,166] (label bias). These biases carry the risk of hidden discrimination[167]. For example, healthcare policies are often based on analytical algorithms of health event administrative coding. Such codes usually represent expenditure on care, rather than illness severity or need. This can lead to structural discrimination, because people of Non-White race experience reduced accessibility of care compared to their White counterparts with similar illness severity[166 168,169]. Such analyses invisibly perpetuate unfair recommendations hidden behind algorithms that assume that Non-White people need less care.

Kidney care is especially dependent on measurement. However, availability of possibilities and capacity to monitor kidney health is uneven between and within social groups, regions, and countries[98]. This compromises interpretability, and the visibility of underrepresented groups. The inadequacy of explicit inclusion of a Black race coefficient within kidney function (eGFR) estimating equations in previous formulae (i.e. MDRD and CKD-EPI equations) was especially important because GFR estimates are cascaded as presumed "results" into numerous kidney and non-kidney tools and guidelines beyond the reach of the kidney specialist[170]. This over-medicalization and biological misinterpretation of race may inadvertently have led to unfair barriers to referral, guideline-based care and provision of support[93,140]. Although not supported universally[171], leading nephrology societies now recommend using eGFR equations without the Black race coefficient[172-174] . Coefficients for age and sex remain, and similarly may require cautious interpretation[111-113,175].

Health illiteracy

Health literacy is "the degree to which individuals have the capacity to obtain, process and understand basic health information" to inform their health decisions[176]. Health illiteracy is to a considerable extent attributable to failures in the education system, as well as failures in information systems. This may be exacerbated by insufficient health, social and cultural literacy of care providers, as kidney diseases require not only medical understanding, but also understanding how to support patients with living with an increasingly complex chronic disease. Low health literacy is linked to increased mortality, hospitalization, medication errors and poor management of chronic diseases[177,178]. Efforts to improve health literacy in patients with CKD have focused on the individual, with little attention for the health system environment or the appropriateness of information[179]. For patients and families, their ability to understand CKD and treatments is variable and impacted by many factors including the skills and patience of the clinician providing education, patient health, presence of a caregiver, time of day of appointment, and current and anticipated future treatment modality. These factors cannot be changed by those needing care[180], and may result in decreased healthcare accessibility and utilization of services.

Geography and accessibility

People from rural/remote communities often commence their journey with CKD in a disadvantaged position, especially regarding socioeconomic status, educational attainment, and opportunities to benefit from primary prevention[181]. Regarding KRT, many barriers, including late referral to nephrologists, necessary relocation to obtain treatment, transportation barriers, and financial hardship[125] contribute to an increased risk of mortality, morbidity and hospitalization among those residing in more remote locations[181]. For in-center hemodialysis, longer travel time to treatment is associated with higher mortality, and decreased quality of life[182]. Centralisation of most transplantation units to major cities, adds an extra layer of difficulty for patients from remote areas as possibilities to complete transplant work-up and specialist care may not be available locally..

Inequities among therapeutic options

Inequities in kidney care pervade across individual conditions (cause of kidney diseases, lifestyle, the timing of preventive and therapeutic interventions and disparate accessibility of different KRT modalities), wider communities, healthcare systems (e.g. private *versus* public healthcare sectors) and countries (Figure 1). Combined, these have major impacts on patient outcomes.

Acute kidney injury

Although AKI is potentially preventable and reversible, accessibility of appropriate diagnosis and care is inequitable. In HICs, AKI is common among multimorbid individuals who often need prolonged dialysis in intensive care with little chance of recovery.[35]. In many lower-resource countries, awareness/confidence to manage AKI is low among healthcare workers[183]. Although AKI is common in children and young adults, often as a single condition[35], even basic intravenous fluids for rehydration may be lacking[184], let alone accessibility and affordability of dialysis[37,184,185]

Chronic kidney disease

In the early stages of CKD, only people with specific kidney conditions such as polycystic kidney disease or glomerulonephritis typically receive care in specialist nephrology clinics. For many people with early stage CKD due to more common causes (e.g. related to hypertension or diabetes), care is coordinated through primary care or non-nephrology specialty units and is subject to inequities in surveillance, diagnosis and quality of care[13].

Multiple barriers in CKD care, including lack of accessibility of essential diagnostics and drugs to slow progression of kidney diseases, and of knowledge among healthcare professionals, contribute to inequities (Table 1). Accessibility of appropriate medication depends on availability, reimbursement and/or ability to self-pay. A survey of resource-limited countries reported that approximately 75% of patients had to pay themselves for diagnosis and treatment of glomerulonephritis, while the lack of kidney biopsy and subsequent interpretation often led to inappropriate immunosuppression[186]. Quality of care is therefore an additional concern even if some resources may be available/accessible, highlighting the need for capacity building among the nephrology workforce[16].

Advanced kidney disease: dialysis and conservative care

Accessibilty and quality of dialysis, availability of home dialysis and focus on patient well-being varies between and within countries and between individual nephrologists as outlined above (Table 1). Most variations in dialysis accessibility and availability relate to economic factors – cost, health coverage, distribution of dialysis centers, number of nephrology professionals including nurses, quality of patient education, support for vascular and peritoneal access creation, and management of comorbidities[58].

Hemodialysis is available (although not necessarily accessible to all) in most countries and tends to be the default form of KRT[16]. In-center hemodialysis is time- and resource-intensive and is highly centralized. PD is more scalable and flexible, less hospital dependent, can be done anywhere with rudimentary infrastructure, is preferred by many patients[187], and is especially suitable for children[188]. Counterintuitively, however, PD costs more than hemodialysis in many lower resource settings[189-191]. Efforts to make PD supplies less expensive and to increase awareness of the advantages and impact of PD are key to increasing its global availability[192]. In terms of quality, cost is again a major source of inequity where reduced hemodialysis sessions or PD exchanges are often used as compromises to cut costs, but unavoidably reduce dialysis quality[137].

Older or frail individuals, and those with learning difficulties are usually committed to in-center hemodialysis unless assistance is provided at home. Even in high-income Western European countries, healthcare-funded assistants for dialysis were available in only 5 of 13 surveyed countries [193].

Similar arguments hold for inequity of avalability of conservative care, with less than half of countries providing support from multi-professional teams, or enabling shared decision making needed to embark on conservative care[61]. Even in countries which purportedly support conservative care, such as France, this option is often not discussed as an alternative to dialysis[194].

Advanced kidney disease: transplantation

Many patients in need of KRT prefer kidney transplantation over dialysis, due to better survival and quality of life[195,196]. Globally, the WHO estimates that only 10% of the demand for kidney transplantation is met[197]. The donor organ shortage is worsening as more people worldwide require KRT.

Transplantation is available in 74% of countries (publicly funded in 53%) with waiting lists in only 62%[198]. Pre-emptive transplantation is only recorded in 10% of countries[198]. Higher-resource settings have higher rates of deceased and living donation than other countries[199,200], along with transplant registries enabling greater transparency. The availability of kidney transplantation through UHC in higher-resource settings enables people from lower socioeconomic classes to obtain transplantation. Nevertheless, even in higher-resource settings inequities remain pervasive [143-145] and there are huge disparities among countries in transplantation uptake[201]. In LICs accessibility is largely restricted to those who can pay.

Racial disparities are well documented particularly in minority groups, migrants and Indigenous and First Nations People, who despite a higher burden of kidney failure, are less likely to receive a transplant[202]. Females are more likely to be living donors than men[203], an observation likely impacted by multiple factors, including the slower progression of kidney diseases among women[204]

In 2007, apprimately 10% of transplantations worldwide resulted from organ trafficking after graft purchase from poor and individuals rendered vulnerable by their life circumstances[205,206].. The Declaration of Istanbul provides guidance for organ donation and transplantation worldwide, to promote equitable sharing of the limited transplant resources by those in need, and prevent harm through exploitation[207]. Nevertheless, equitable allocation of graft organs remains complex and changing viewpoints might necessitate revision of rules when appropriate[206].

Pediatric care

Accessibility of specialized pediatric nephrology is very limited in LICs, but regional variations occur everywhere[208]. Data on the epidemiology and outcomes of pediatric kidney diseases are limited to registries in HICs and small studies from lower-resource settings, probably underestimating true disparities in care.

The 0 by 25 initiative highlighted the disparities in early diagnosis and accessibility of dialysis for children with AKI in lower-resource settings[37].

Community-acquired, preventable AKI due to infections like dengue, dehydration or nephrotoxic drugs is more common in low-resource settings and exacerbated by poverty and malnutrition[35,37,185]. Mortality in children with AKI is >50 times higher in lower-resource settings than in HICs, especially when dialysis unaccessible[209]. Non-recovery of kidney function is 3 times more frequent[209].

Pediatric CKD is often diagnosed late, especially in countries with poor antenatal and primary healthcare, and in rural/remote areas[210]. Accessibility of pediatric dialysis and subsequent outcomes correlate with national wealth, even in Europe[211]. Mortality risk is also greater with late diagnosis requiring ‘urgent start’ dialysis[211] and is very high if dialysis cannot be provided or continued[78].

The barriers to pediatric kidney transplantation in lower-resource settings include unavailability of pediatric transplantation expertise, catastrophic out-of-pocket expenditure and the absence of deceased donor organ sharing networks[212,213].

Inequities resulting from health economic factors

Differences driven by country wealth

Kidney care comes at a high societal and personal cost[26]. Global reimbursement for maintenance dialysis (excluding out-of-pocket payments) amounts to around 57 billion US dollars, 80% of which is spent in HICs, 17% in MICs, and only 3% in LICs[190]. Dialysis, if universally provided, is funded by varying state financing schemes[214]. In HICs, >2% of national healthcare budgets is directed to KRT, for only 0.15% of the population[15]. Global costs for AKI are unknown, but in the US, in 2013, AKI reportedly caused $9 billion excess annual hospital costs[35].

In higher income settings, expenses for associated non-kidney care further increase the financial burden[15,215]. Productivity loss (unemployment, sick leave, premature retirement, death) impacts patients, their next of kin and society overall[216]. Individuals in vulnerable positions (temporary, contractual, physical workers, unemployed) are at higher risk of productivity loss and impoverishment when struck by CKD[84].

In low-resource settings where the direct and indirect costs of kidney care and KRT often must be paid out-of-pocket, the risk of impoverishment is even higher. A systematic review comparing out-of-pocket payments for several diseases revealed kidney diseases as the leading cause of catastrophic health expenditure (CHE), across lower-resource settings, thus exacerbating inequities between countries, individuals and groups.

Both higher and lower-income countries are therefore at risk of inequities but the problems are not necessarily the same (table 2). Accessibility of kidney care without experiencing financial hardship is highly inequitable across the globe, with the most severe consequences (death and/or CHE) especially affecting the poorest[78,138,185,217-219].

Kidney replacement therapies

Dialysis is available in almost all countries[16], but the clinical, financial and ethical dilemmas associated with its (un)accessibility cannot be ignored. Cost-effectiveness assessments are used to rank healthcare interventions aiming at maximal population health gains, often expressed in Quality Adjusted Life Years (QALYs), for a given cost[220]. A systematic review of cost-effectiveness analyses concluded that the ability to identify the mix of dialysis modalities that provides best outcomes for patients and health budgets is uncertain, particularly given the frequent inconsistencies between published studies and non-consideration of societal perspectives[221]. In addition, cost-effectiveness as sole criterion for decision making has been criticized, since it overlooks crucial factors such as budgetary impact, financial risk protection for individuals, and equity in distribution of interventions[222,223].

In many higher income countries, the budgetary impact of dialysis has been accepted, as the choice to save lives has prevailed over costs[217]. This has led to exponential growth in patient numbers and a dialysis industry generating considerable profit in a sector with few competitors. Rising patient numbers, especially in emerging countries, will further inflate costs[224]. Health system and societal costs for PD, home hemodialysis and transplantation are lower than for in-center hemodialysis in many countries[58,190,201,225-227], but their uptake and/or availability is inadequate and divergent[190,228,229]. Additionally, health-economic factors favoring one therapeutic alternative over another in HICs differ in lower-resource settings, where labor is cheaper and imports more expensive[225].

Especially in low-income settings, policy makers face the challenge of simultaneously pursuing UHC, setting priorities across the whole health system and progressively fulfilling the human right to health[217,230]. It would be naive to insist that KRT be funded immediately everywhere for all, as the opportunity costs (money spent on KRT cannot be spent elsewhere) are high. For example, if Kenya, Nigeria and Senegal would try to meet their estimated national dialysis needs, this would require from 8 to close to 40% of government health expenditure[231]. Consequently, in lower-resource settings, KRT is currently largely available only to those who can pay[137].

CKD not on kidney replacement therapies

The costs of kidney care do not only impact those on KRT. The poor may not even be able to afford simple care to prevent the evolution of early CKD to kidney failure. This intensifies inequities because as disease progresses, higher levels of care and personal expenditure are required[137].

The optimal solution to forestall CKD costs is to reduce disease risk and/or progression, both intimately intertwined with inequities in many places[15,232,233]. However, in most countries investment in initiatives to promote prevention is minimal, in spite of the high value for money compared to the financing of treatment or cure[12,15,190,234,235]. The value for money gained through prevention of illness is not restricted to the health sector. A recent publication from the WHO highlighted the important long-term return on investment of prevention of NCDs. For example, investment of 1 dollar in lower-resource settings to reduce population salt intake in 2018 would yield 13 dollars in return by 2030, given the lower subsequent health expenditures and greater productivity gained with healthier people[236]. Thus, there are also longer-term opportunity costs, which apply especially to many lower-resource settings, where current health budgets are disproportionately channeled to secondary and tertiary care, necessitated by the poor investment into prevention[190,225,237].

Marketing of drugs

A threat to reimbursement systems and costs is the marketing of therapies for specific kidney diseases which are often only available at extremely high prices, either because of patents, or the small market size if a condition mainly affects children (e.g. cysteamine)[238,239]. There is little transparency in the price setting of such drugs (e.g. eculizumab)[240], for which in addition evidence may be low[241]. They are also frequently used off-label for indications for which they are not approved and not evidenced, or used in children and adolescents where they have not been tested (e.g. tolvaptan)[242]. Inflated costs and excessive profits not corresponding to investment[240] initiate and exacerbate inequities among countries and regions[243], and depend on whether countries have orphan drug legislation and reimbursement schemes. Inequities in accessibility of such medications have a negative impact on patient outcomes[244], in low-income but also in high-income settings, as incomplete of absent coverage may necessitate out-of-pocket payments, that are not possible for all.

In summary, the current health-economic model supporting kidney care is flawed. The focus on expensive and/or late stage therapies favors inequity, both across countries and among individuals. Differences in cost of essential therapies between countries, without clear transparency about the prices and the reasons, further exacerbate global inequities[245].

The ethical context

Inequitable accessibility: an ethical dilemma

Clinicians are familiar with the 4 principles of biomedical ethics. The principles of autonomy, beneficence (doing good) and non-maleficence (not doing harm) are readily applicable at the bedside. The principle of justice, however, has implications beyond the bedside and addresses issues of fairness and inequities between individuals. In resource-constrained settings, physicians often realize that autonomy, beneficence and non-maleficence conflict with justice, as an individual patient’s needs may be overridden by lack of available therapies, poverty or the needs of others competing for the same treatment[78]. Inequities in nephrology constitute moral dilemmas because patient outcomes are adversely affected by structural injustice and vulnerability, that increase risk of kidney diseases and impact accessibility of care[68]. Although inequity is often thought to begin with a lack of accessibility of healthcare, patients with kidney diseases encounter inequities that extend beyond the healthcare sector, beginning with the conditions in which they are conceived, born, work and live[233]. The social and structural determinants of health include factors like age, gender, poverty and geographical location in the world and within a country. These factors are inequitably distributed, resulting in vastly different outcomes for patients with the same disease living under different circumstances - highly resourced versus low resource settings, or people who are wealthy versus the poor. These social determinants of health play a large role in pre-determining who lives longer and who dies earlier[246]. Accessibility of kidney care is also inequitably distributed at all levels – from screening, early diagnosis and preventative care up to KRT or comprehensive conservative care for kidney failure.

If inequity in healthcare is inherently 'unjust', an ethical dilemma arises for the provider (the principle of justice is violated)[78]. Inequities in kidney care occur in all resource settings and at any stage of disease, but the impact is compounded with worsening kidney function, as life-saving but expensive treatments become necessary. Out-of-pocket costs exacerbate these inequities in low-resource settings, where minorities, women, the poor, elderly and health illiterate, as well as those living remotely, are disproportionately affected. Examples of structural inequities in nephrology are presented as case studies in **Table 3**, highlighting the ethical dilemmas encountered[137,206,217,247-256]. Such moral dilemmas are omnipresent: at the bedside, during shared decision-making, in society, for national governments and at a global level (**Figure 2**).

Responsible stakeholders

In his philosophical approach to health justice, Venkatapuram states that health is not the absence of disease, but a positive ability to be and to do things[257]. People have a moral entitlement to be as healthy as they can, and patients need to be capable of leading productive and quality lives. Expressing health as a human right is an important complement to advancing health equity because it stresses that the responsibility for care delivery lies with the state, which has an obligation to provide care to whatever extent possible in an equitable manner[230]. The global nephrology community also has an ethical imperative to address/call attention to all the factors underlying inequity, including the social determinants of health, as well as every level of accessibility of kidney care. It is the ethical responsibility of all professionals to reduce inequities in kidney care and improve patient outcomes and to advocate this objective[258]. Governments must be held accountable to acknowledge this and to commit to the progressive realization of the right to kidney care for all.

Solutions

As outlined above, inequities in opportunities to optimize kidney health and to provide accessibility of all forms of kidney care are multiple across the globe. The origin of health inequities can often be narrowed down to both social and systemic injustices[259], related to complex, multisectoral factors. Solutions require leadership, responsibility, and political will. Improvement in accessibility of health care may mitigate the immediate impact of social and systemic injustices to an individual, but lasting progress can only be made through seeking system solutions that prevent the underlying causes at a population level. Accordingly, if medical communities are to make collective progress towards dismantling inequities, the underlying causes must first be acknowledged and understood before they can be solved. This in turn requires collaboration on global, local and individual levels. Suggested actions to tackle the global inequities in kidney health and kidney care per stakeholder group are summarized in table 4 and outlined relative to policy/individual level in what follows.

Global level

Recognize kidney diseases as an important public health problem

Multiple factors have contributed to kidney diseases being relatively overlooked as a public health concern, which include lack of data in many places due to global inequities in accessibility of essential and reliable diagnostics for kidney diseases and rudimentary health information systems which do not track kidney diseases. The focus of global health agendas was initially driven by funding and targets set for infectious diseases and maternal and child health, and subsequently for cardiovascular, cancer, respiratory diseases, diabetes and mental health, but not kidney diseases[29,260]. If the burden of kidney diseases is to be meaningfully impacted, advocacy and strong leadership are required to acknowledge and reduce existing inequities in disease risk and accessibility of care, to strengthen the provision of integrated quality care for NCDs including kidney diseases, to generate robust health-economic evidence on interventions and their impact to guide financing, to improve data capture to identify areas that lag behind, and to track achievement of all sustainable development goals (SDGs), as each SDG impacts kidney health world-wide[233].

Just as health inequities cut across countries, so also do potential solutions. Over the short and medium term, harmonization among countries and classes can be advanced by material, financial or in-kind external support, and by promoting exchange of learning, innovations and best practices[261]. Such initiatives might be optimally managed by umbrella institutions, including governments, supranational political structures (e.g. the European Union), coordinating agencies (e.g. WHO), or non-governmental organizations (e.g. Médecins sans Frontières, European Kidney Health Alliance), but may also result from private initiatives (e.g. Gates Foundation) and professional societies (e.g. International Society of Nephrology, European Renal Association). Over the longer term, countries must be encouraged and supported to finance and deliver sustainable and comprehensive local quality kidney care.

Support affordable innovation to improve kidney care for all

Transparency in investment and in development and production of novel technologies and drugs, especially for orphan kidney diseases, is urgently needed[240]. Structured stakeholder networks, like the virtual European Reference Network on rare diseases of the European Commission, may help to support high quality, sustainable and equitable therapies[262]. Tiered pricing mechanisms adapting the cost of technologies and material to the welfare of a country in mutual agreement between rich and poor countries may improve affordability[263].

Innovation should not only focus on sophisticated technologies, but must also include the development of new approaches to improve uptake of prevention strategies, and accessibility and delivery of primary care for those currently left behind. Implementation and operational research are needed to identify and scale up effective and affordable strategies, including dialysis[264]. Governments, learned societies, clinicians, researchers and patient organizations should work hand in hand to foster innovation at all levels as a means to reduce global inequities.

Country level

Prevention and early detection

The best approach to reduce the burden and cost of NCDs, especially kidney diseases, is prevention[15]. This universal tenet applies to all countries. Unfortunately, only small proportions of healthcare budgets world-wide target prevention[15,58,190]. Timely and appropriate screening for kidney diseases occurs rarely and is often not systematized or harmonized[265].

Prevention is most efficient when risk or disease are identified early. This requires identification of barriers, creating awareness and building trust, especially among vulnerable populations, where the deficiencies in early identification and delivery of evidence-based care are most prominent. Governments should invest in prevention and screening, especially among high risk groups[53,266] and vulnerable populations[267,268]. Not doing so forces health systems towards more expensive "rescue" solutions like dialysis, which exacerbate inequities[91].

Socio-economic status relates differently to healthy lifestyle across the globe, with higher socio-economic status being related to lower risk of NCDs in high-income settings, but higher NCD risk in lower-income settings as middle classes emerge[65,269] . Modification of these inherent sources of inequity requires a multi-sectoral approach to health and well-being such as that embodied by the SDGs, as well as population education about healthy lifestyle[233,270].

Data required to support decision making

The core social determinants that make up the building blocks of health represent societal injustices in how governments and authorities prioritise the vulnerable, spend resources on those in need, and ensure adequate provision for those affected by ill health. To motivate those who have power to act, knowledge and understanding must be guided by good quality data, moral advice, and a society that holds policymakers to account. Social and healthcare data from real-life practice, research efforts and actions by charities/NGOs should be integrated to improve the availability of meaningful intersectional health. Decision-making and priority setting processes are hampered when incidence, prevalence and health-economic data is lacking[217]. Countries must invest in systematic data collection to permit understanding of disease burden, distribution, costs of care, financial hardships incurred, and to identify and address inequities. Rigorous health technology assessments, based on reliable local evidence of disease burden and costs to the health system and to individuals, are required to support priority setting.

Facilitate fair reimbursement of treatment costs

Universal Health Care (UHC) is a crucial target of the SDG3[271]. True UHC is needed to prevent exclusion of the disadvantaged and reduce inequities[272] (Figure 3). Even if UHC is not currently affordable, governments should commit to its expansion through transparent processes, to progressively realize the right to health for all[230], with stepwise inclusion of expensive therapies, when this becomes possible. Clear societal thresholds should be set regarding the willingness to pay for gain of Quality Adjusted Life Years (QALYs), accounting for the medical need and affordability, also called Value Informed and Affordable Pricing[273]. Such processes should not only include cost and disease burden, but must also take financial hardship and equity into account[274]. For example, two health sector interventions which score highly in terms of equity in the poorest nations are acute dialysis and kidney transplantation for children, but lack of cost-effectiveness data precludes their recommendation for coverage[275]. Cost-effectiveness analyses can however only be based on intervention studies including diasadvantaged groups.

Improve affordable care

Technologic options like hemodialysis should be made affordable and more reliable, accounting for the harsher conditions frequently encountered in low resource situations (e.g. more resistant to heat, humidity, energy-efficient)[276]. Costs for dialysis supplies can be reduced by waiving importation taxes or by local production of PD material[190,228]. In higher-resource settings, home dialysis uptake could be stimulated through financial incentives, policy measures (PD first), fair price setting by industry, patient education, and benchmarking[277]. Health systems should be strengthened to include safe and legal transplantation programs.

Local level

Raise awareness of kidney diseases

All those concerned with kidney health and care (including non-professionals) have a responsibility to be aware of and to create awareness of the problems related to kidney diseases[26]. This includes addressing the causes and consequences of the structural determinants of health which entrench inequities. Healthcare professionals should be trained throughout their studies and continued education to identify and address these problems through advocay and/or concrete measures[278]. Patient associations and NGOs play an important role in this process to improve equity and should engage in training initiatives to optimize their own advocacy skills [3,279]. Patients must raise their voices in holding healthcare planners and leaders to account, activate partnerships for harmonization among regions/countries and expose organizational shortcomings, e.g. calling for availability of specific medication, dialysis or transplantation.

Improve accessibility of equitable quality care

Holistic kidney care requires strong health systems and public health strategies to reduce burden of kidney diseases, and to promote early detection and treatment, integration of kidney care into existing programmes for NCDs and some infectious diseases, and reduction of organ specialty-linked silos. The common diagnostic tools for kidney diseases (serum creatinine and albuminuria) are simple and affordable in many (but not all) countries, and should be made available as much as possible, but also ensuring this is followed by appropriate interpretation and therapeutic intervention. Primary care and non-nephrology physicians and other healthcare workers could play an essential role, but may be insufficiently familiar with kidney diseases and should be educated appropriately[19,280]. Since kidney patients have multiple comorbidities and require multiple healthcare providers, integration of care is quintessential. Capacity building and audit-based education may support implementation of appropriate preventative measures[281]. Accessibility of essential medications should be assured to permit early intervention and stop/delay progression of acute and chronic kidney diseases. Telemedicine and eHealth should be harnessed for remote outreach[282]. Quality assurance activities, including tracking of inequities, should be integrated into clinical routines.

Avoid cherry-picking

In poorly designed pay-for-performance systems, self-interest with utility as the prevailing principle could lead clinicians, hospitals and dialysis units to target high throughput by favoring inclusion of patients with greater resources and more favourable (less complex) clinical characteristics[283]. If applied to the extreme, this morally dubious practice creates an additional disadvantage for the less privileged, as they will start with less favorable conditions and will be driven towards less favorable therapeutic environments[284]. Conflicts of interest may lead to fewer transplantation referrals from private dialysis units[285]. Reporting and monitoring of patient mixes and outcomes is mandatory, especailly in dialysis units where this data is easily obtained.

Individual level

Tackle health illiteracy

To improve health literacy, a coordinated health systems approach informed by consumers and representatives of the concerned groups is needed, with adapted and innovative educational methods to meet various needs. Specific support may be needed for children and families affected by kidney diseases, to optimize adherence and minimize disruptions associated with the high demands of kidney care.

One system level change adopted in other chronic diseases such as diabetes is the introduction of navigators[120,125], who assist patients and caregivers in understanding diseases and treatments and optimize self-care. Such programs have been successful in remote parts of Australia with Indigenous People. In the US, animation has been applied successfully for diabetes education where language barriers exist[286]. Medical professionals need to recognize their own limitations in terms of socal and cultural literacy. Since medical professionals are usually not well-trained in education, advice should be sought from experts in other fields (e.g. pedagogy, animation, telecommunication, health illiteracy)[287-289].

Patient empowerment

A move from paternalistic care (doctors making decisions without patient input) to shared decision making (decisions guided by deliberation between individual patients, their caregivers and practitioners)[290,291] as an approach to enhance equity in therapy choice contributes to more patient satisfaction, adherence and health[292]. All steps should be reported transparently, which helps to avoid imposing therapies for financial or other reasons that may not benefit the patient. Patient organizations may play a central role in facilitating this shift of paradigm. When interacting with patients, decreases in cognitive function should be taken into account, especially in advanced CKD[293], as this common complication affects alertness and hinders fast and accurate decision making. Extra care must be taken in children with kidney diseases and their families to enhance understanding of kidney care and cooperation.

Conclusions

Kidney diseases are associated with significant inequities that increase risk and are imposed by the many social and structural factors, the relative invisibility of the condition as a public health threat, and the time- and resource-intensive therapies required for advanced disease, especially dialysis.

All professionals involved in kidney care should be alert for local inequities and their impact on patient lives, as well as those occurring on a broader, regional, national and international level. Recognition is the first step towards developing actionable solutions.

Inequities include those specific to countries and regions, among social groups, and those related to accessibility of preventive and therapeutic modalities. In addition to adverse clinical outcomes, inequities also raise health economic and ethical concerns, and are heavily compounded by non-medical social and structural determinants such as poverty, social injustice, violence, racism, lack of education, and cultural and religious barriers.

Solutions range from the individual to the global level. Awareness of potential solutions is important to encourage advocacy and action by all stakeholders. Although not all solutions may be universally applicable or implemented, there is a collective need to develop and implement innovative strategies to tackle barriers to equitable kidney health and kidney care. All nephrology professionals should have the conviction to advocate within their communities, armed with local and international data, and to engage with policy makers, administrators and insurers, to raise awareness about inequities in kidney health and to improve kidney care across the globe.

Keypoints:

- Insufficient investment across the spectrum of kidney health and kidney care (from awareness raising, to prevention, diagnosis and treatment) is a fundamental source of inequity. This affects all people at risk of, or living with kidney diseases.
- Social and structural inequities are major risk factors for, and contribute to poorer outcomes in kidney diseases both within and between countries.
- There is insufficient accessibility of essential diagnostics and medications to treat kidney diseases and to track their burden. This disadvantages patients in low- and middle-income countries from the very beginning of their disease course.
- Ability to access the entire spectrum of kidney care (from basic medication to dialysis and transplantation) without experiencing financial hardship is very inequitable across the globe. Transplantation is the most equitable form of kidney replacement therapy, but is highly unaccessible in lower income settings. This results in vastly different outcomes and live courses for patients with the same diseases living under different circumstances.
- Novel therapies for rare (orphan) diseases are often only available at extremely high prices, which frequently affects or excludes children and adolescents.
- All nephrology professionals should become skilled at advocating on behalf of their patients to communities, policy makers, administrators and insurers, to develop constructive strategies and collectively reach optimal solutions to improve equity in accessibility of quality kidney care locally and across the globe.

CAPTIONS TO FIGURES

Figure 1: Factors contributing to inequities by increasing risk and by affecting accessibility of preventative measures, care and therapies. The description considers global, national/regional, community-related, health system-related and individual elements.

Figure 2: Ethical dilemmas in inequitable accessibility of kidney care: from global to local.

Figure 3: The Universal Health Coverage cube: expanding universal healthcare coverage for kidney diseases in low resource settings. The health needs of the population are depicted by the larger transparent box, the funds available for health financing are depicted in the blue box. In many high-income countries the size of the blue and the transparent boxes are very similar (almost all health needs are covered), whereas in low resource settings the blue box is considerably smaller than the transparent box, meaning that many health needs that do not fall within the blue box are not covered by the health system and must be provided/paid for by individuals. As countries set health priorities and expand their health coverage they must consider the impact across all 3 dimensions: who should be covered, which services should be provided and how much of the costs can be covered by the health system. KRT falls outside of the blue box in most low-resource settings. Suggestions here include how accessibility of kidney care can be progressively expanded under universal heath coverage. Priority setting must consider prevalence of a condition, cost of therapeutic options and available resources. AKI: acute kidney injury; CKD: chronic kidney disease; KRT: kidney replacement therapy; CHE: catastrophic health expenditure. *: data on disease burden missing in many places.

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“Making fair choices on the path to universal health coverage: final report of the WHO consultative group on equity and universal health coverage. https://apps.who.int/iris/bitstream/handle/10665/112671/9789241507158_eng.pdf?sequence=1&isAllowed=y Figure 1.1, page 5, Copyright (2014)."

Box 1: Motivating scenarios for inequitable care specific groups of people

Social and economic position

“When you enter through the emergency department, you arrive in bad shape...you need to have a high potassium or they send you home even though you feel you are dying. Sometimes, you crawl out when they decide to not do dialysis. You eat a banana because it is high in potassium even though you may die and you go back and wait and hope that they will do dialysis so that you don’t feel like you are drowning and so that the anxiety goes away.”
(An undocumented immigrant in the USA receiving only emergency dialysis services)[123]

"We have a population of about 30 million people and have less than 20 trained nephrologists. Unfortunately, due to lack of knowledge about kidney disease and its management, over 70% of patients report late to the teaching hospital with kidney failure and since care is not reimbursed by the National Health Insurance scheme, about a third of patients with kidney disease die on admission for which we have to sign death certificates and this does not include those who are stable enough to be discharged home with no hope of sustaining themselves on dialysis. It’s really sad. Without money you die when you have kidney failure."
(A health professional’s perspective on kidney care in Ghana)[126]

Discrimination

“In my doctors they used to have this thing that when you signed in it was on a screen and you had to select in front of everyone in the waiting room whether you were male or female. Even that half a second just breaks my brain every time and I’m like, I kind of don’t want to go to this appointment now”.
(An LGBTQ+ patient on attending their appointment)[127]

“My doctor[s]... be shocked when I asked them, well why is there so many Black people on dialysis and they don't have no real answer for me. I really don't like that. And so then on top of that he only spends ninety seconds with me... I'm like wow, I feel like cattle.”
(A patient receiving dialysis discussing mistrust in their nephrologists connected with race)[122]

Inequity within algorithms and guidelines

A 54 year old woman of mixed race is opportunistically found to have a low eGFR when attending hospital with a minor injury. She is advised that this is probably due to muscle mass and goes home. Several months later she reattends hospital in need of emergency dialysis.

“The insights about sexist and racist biases... are important because information organizations, from libraries to schools and universities to governmental agencies, are increasingly reliant on being displaced by a variety of web-based "tools" as if there are no political, social, or economic consequences of doing so.”
(Safiya Umoja Noble, on reinforcing structural discrimination by use of algorithms)[294]

Health literacy

“I'd say about the hardest part was when he was on the prednisolone when he's on a high dosage, it's very lunatic. And then we went to the doctor to what's going on. Oh, it's the prednisolone. It causes anger and stress. So, more information and education of the carers as to what possible side effects could be and talk to you about this is what's going to happen.”
(A caregiver’s perspectives on kidney transplant aftercare and education)[115]

“I would have really liked to have sat and talked with somebody who had gone the journey before me, and to give me a heads up on about what I'm going to experience from the importance of taking the medication, understanding what the kidney function is in my body, understanding about my fluids, my nutrition, all of those coming together of the importance, because as a primary school teacher, you're having to say it at least 20 times before it clicks.”
(A care partner)[125]

“All the patient navigators that I've met, have been on dialysis and going through transplant and their second transplant. They know exactly what it's like to sit in that chair, and have treatment for hours on end, the restrictions that you're on, the medications that your body must handle after transplant. And although someone can sit and tell you about this importance, I think it comes at another level with someone else who's experienced that and been successful, and that you can draw on and build a relationship with, and it's kind of upskilling.”
(A patient’s perspective of lay navigators)[128]

Geography and accessibility of care

J lives in a town with no dialysis services, the closest is 175kms away. He is ineligible for a transplant or home dialysis. His only choice is to move or receive conservative care.

“Just the understanding, like if you're having a transplant, you've got to deal with the city hospital and they say, "Okay, I'll book you in 8:00 in the morning, tomorrow morning, can you make it?" Well, I live in XXX. All right, well can you travel? Well, it's six hours away and I've got a family to organize and I'm on dialysis so it's like they don't get it. And then they'll say, "Come back next week and see me." Like, you're kidding. Can't you have

the one stop thing?”
(A patient experience of lack of accessible care due to remoteness)[125]

Abbreviations: LGBTQ+, lesbian, gay, bisexual, transgender, queer, and other

Acknowledgements

The European Kidney Health Alliance (EKHA) is a not-for-profit organization defending the case of the kidney patients and the nephrological community at the level of the European Commission. The EKHA network has five full members (the European Renal Association, the International Society of Nephrology, the European Kidney Patients Federation, the European Dialysis and Transplant Nurses Association-European Renal Care Association and the Dutch Kidney Foundation) next to 27 National or Regional Societies as affiliated members.

European Kidney Health Alliance is the recipient of support by the European Union in the context of the Annual Work Program 2022 on prevention of non-communicable diseases of EU4Health, topic ID EU4H-2022-PJ02, project # 101101220 PREVENTCKD

Disclosures: RV is advisor to AstraZeneca, Glaxo Smith Kline, Fresenius Kabi, Novartis, Kibow, Baxter, Nipro, Fresenius Medical Care and Nextkidney.
VL receives royalties as a co-editor of “The Kidney” textbook. LA is advisor to AstraZeneca and Baxter. BS received grant support from GSK, Fresenius Medical Care and Boehringer Ingelheim as part of the CKD-REIN study. EB is advisor to Baxter, IiberDi and AWAK and received speaker fees from Baxter and Vifor. All other authors declared no conflict.

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INEQUITIES IN KIDNEY HEALTH AND KIDNEY CARE

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Abstract (200words)

Health inequity refers to unnecessary and unfair differences in the capacity to achieve optimal health and appropriate accessibility of care. Kidney diseases [including acute kidney injury (AKI) and chronic kidney disease (CKD)] have strong associations with inequity. This is largely due to the intrinsic risks of kidney diseases, the heavy burden of comorbidities and the high cost of therapies, e.g. for dialysis on wich survival for many may depend. However, inequities occur across the entire clinical course of kidney diseases. This review offers a comprehensive overview of the array of inequities in kidney health and kidney care, including inequities between countries, regions and social classes, inequities in healthcare, inequities specific to therapeutic modalities, and health-economic and ethical implications. This review also proposes solutions, which may inspire nephrology professionals to recognize and mitigate inequities. In addition to the main text that summarizes the relevant elements, interested readers are referred to the comprehensive tables (including case stories) and references, which review some facets more deeply. It is the responsibility of all implicated to call attention to inherent risks of inequity in their immediate and broader environments, and to pursue the best possible solutions together with their communities.

Introduction (7915 words)

Health inequality refers to differences in health or health resources between persons, populations or nations such as those caused by age or genetic predisposition[1]. Inequities in healthcare are unfair, avoidable and remediable differences between groups, based on socioeconomic, demographic or geographic factors[2]. The distinction between inequities and inequalities is not always clear. Importantly, underlying inequalities frequently contribute to inequities, e.g. when genetic predisposition, age or sex intersect with race/ethnicity, socio-economic status, possibilities to adhere to healthy lifestyle or level of education.

In this manuscript we review different aspects of inequity which impact kidney health and kidney care across the globe. For all the discussed elements a number of potential solutions are reviewed at the end. The aim here is to offer practical guidance to all those involved on how to avoid inequities, as these are among the most concerning social injustices in modern clinical nephrology. Throughout this manuscript, inequalities will sporadically be referred to if they impact inequities.

Health inequities affect the capacity to achieve optimal health, which also includes appropriate accessibility of care[3]. This capacity is far from equally distributed globally, especially across regions and social classes[4-7]. The awareness of health inequities has not translated into sufficient corrective and collective action, because health inequities are multifactorial and multisectoral. They arise from differences not only in medical care but also from differences in global policy, sociology, ecology, geography, ethics, economics, psychology, culture, religion and tradition (Table 1). A further barrier is the fatalistic view that the problem is too large, too broad, or too complex[8]. Inequities evolve over the life course, such that disadvantaged fetal or childhood development may predispose to compromised health throughout life[9,10]. An avoidable lack of screening and preventive care may also lead to late presentation of disease and seriously jeopardize health outcomes[11]. Kidney diseases do not escape these rules, but rather epitomize them[12].

Appreciation of the importance of kidney diseases by the medical community, policy makers, and the public has lagged behind that of other common conditions for multiple reasons[13,14]. First, the rapid growth of dialysis and transplantation since 1960 has focused on the needs of patients requiring these expensive therapies diverting attention from prevention that is more scalable and applicable everywhere[14,15]. Second, the lack of consistent definitions of kidney diseases until the 2000s, and of reliable epidemiologic data in some regions, has hidden the full extent of the problem, limiting the development of appropriate interventions[16,17]. Third, the lack of awareness among primary care providers, together with deficiencies in health information systems, have also hampered prevention, detection and early treatment[18-20].

Based on the mounting evidence regarding population prevalence and poor outcomes[21-23], kidney diseases should be considered a public health priority, but thus far have not been prioritized on the global non-communicable disease (NCD) agenda[24]. This has resulted in the most fundamental inequity that affects all kidney patients without distinction: insufficient investment in screening, prevention, research, and innovation compared to other common NCDs, which themselves remain chronically underfunded [25]. Chronic kidney disease (CKD), despite affecting 10-15% of society globally[16,25], is not a health research focus for the European Union (EU)[26]. Neither does CKD figure among the 56 health topics considered relevant by World Health Organization (WHO) Europe[27]. In the 2022 EU Healthier Together Initiative, four disease-specific NCD strands are targeted, excluding CKD[24,28]. This lack of awareness among policy makers is compounded by the ignorance of the kidney's functions and its pathologies. Most individuals do not know what the kidneys do, let alone how to care for them[29]. At best, policy makers see kidney diseases as a co-morbidity of cardiovascular disease (CVD) or diabetes, which postpones diagnosis for many, and leaves others entirely behind[30].

This manuscript is coordinated by European Kidney Health Alliance (EKHA), a non-governmental organization advocating for kidney health at European Union (EU) level and beyond[31]. This article collates in a global context perspectives from diverse inequity experts, representing various continents, age groups and backgrounds, including kidney patients. It seeks to reposition the need for equity in kidney health and care as a global priority and offers a basis for further exploration for all involved stakeholders.

Inequities across countries/regions

Epidemiologic distribution

The Global Burden of Disease (GBD) study attributed more than 3 million deaths in 2019 to kidney dysfunction[32]. Most CKD deaths occurred in India and China[16]. In Latin-America, the Middle-East and North-Africa, CKD falls within the top 5 most common causes of death[33]. Globally millions of deaths probably result each year from the lack of accessibility of kidney replacement therapy (KRT),[34] and from acute kidney injury (AKI)[35], but those remain largely uncounted in lower-resource countries.[36,37]. Inequities across regions are further enhanced by environmental factors, such as increasing number of heat waves and droughts, pollution, water contamination and increased distribution of tropical diseases[38-40], which do not affect all countries and people equally.

Applying the definition of CKD[41,42], a systematic analysis of worldwide population-based data estimated the age-adjusted global prevalence of all-stage CKD in 2010 at 10.4% in men and 11.8% in women more than 20-years-old[43]. Subsequent estimates yielded relatively consistent results, although with regional variations from 6 to 20%[44,45]. CKD prevalence increases with age and appears higher in lower-resource settings[43].

The GBD study showed a 15-fold global variation between countries of CKD burden [specified as age-standardized CKD-linked disability-adjusted life-years (DALYs)] , highlighting potential inequities in both accessibility of diagnostic possibilities and risk factor distribution[33]. It is even more difficult to estimate the contribution of AKI[46]. A pooled incidence of hospital-acquired AKI was reported as 34 and 22% among hospitalized children and adults[47] respectively but with promounced regional variations, raising questions of plausibility and generalizability[37,48].

Risk distribution

The risk of kidney diseases is associated with country income level [49] with people developing CKD and dying from CKD at a younger age in lower-resource settings compared to high income countries (HICs)[50,51]. The association between age-adjusted CKD prevalence and KRT incidence is positive in HICs, but explains only 40% of the variance[52]. This association is negative in Central and Eastern-Europe, and null elsewhere[52], which highlights differences in incident KRT that cannot be explained by CKD prevalence, even in HICs where accessibility of KRT is generally unlimited.

In Central and Eastern-European countries, gross domestic product (GDP) is highly heterogeneous, a legacy of the Cold War and the Iron Curtain. Many CKD risk factors are more prevalent than in Western-Europe, especially in countries with lower GDPs, likely contributing to a higher regional incidence of CKD[53]. Other disparities in this region related to kidney care include variable availability of specific KRT modalities and expensive medication, relative number of nephrologists, and tracking of the prevalence of CKD[54-59].

Within HICs, in part due to the legacy of colonialism and slavery, stark disparities across racial, geographic and socio-economic strata exist[12,60,61]. Moreover, patients with socio-economically deprived backgrounds develop kidney impairment 5 years earlier in their life course and suffer from more comorbidities[12].

Global distribution of KRT

Registries of KRT were introduced in the 1960s-1970s in Europe and the US and have expanded to most HICs but are less available elsewhere. Across countries reporting to the United States Renal Data System (USRDS), the incidence of KRT ranged from 16 per million people (pmp) in South-Africa (2018) to 570 pmp in Jalisco, Mexico (2019), and the prevalence of treated kidney failure varied over 30-fold across countries (2019), which reflects disparities in accessibility of KRT rather than in true incidence[34,62]. KRT incidence is rising in most lower-income settings[62], however predominantly in the private sector (e.g. South-Africa and India), leaving many without possibilities to be treated or exposed to significant catastrophic health expenditures (CHE – out-of-pocket healthcare payments which impoverish a household)[63-66].

To permit equitable accesibility of care, provision of sustainable KRT requires robust health systems and financing. A higher country Gini coefficient (indicating greater within-country inequity) directly correlates with greater prevalence of stage 5 CKD remaining untreated by KRT[67,68]. In areas with greater equity, there is more accessibility of KRT[67,68]. In lower-resource settings a small fraction of those requiring KRT receive it long-term[34]. For example, most African countries have healthcare systems with poor/no health insurance coverage, leaving the vast majority of people with kidney failure unable to obtain KRT[69,70]. Elsewhere, macro-economic factors and services for kidney care are also more strongly related to KRT incidence than demographics or general health[71]. In Eastern-Europe, variability in incidence and prevalence of KRT results in multiple-fold differences in dialysis and transplantation uptake between countries, as well as less home dialysis and conservative care compared with Western-Europe[58,59].

In brief, country location and wealth distribution substantially impact kidney health and accessibility of kidney care across the world. Inequities exist even within a relatively homogeneous region like Europe.

Factors associated with inequitable health care

Diagnosis and treatment

A complex interplay between structural risk factors for AKI and CKD and rapid progression of disease due to limited accessibility of primary care limits possibilities to mitigate these risks[72-75]. Diagnosis of CKD and AKI requires blood and urine tests, which are not routinely available everywhere[76]. In 2017, two-thirds of low income countries (LICs) were unable to measure serum creatinine in primary care, and none provided quantitative albumin or protein urinalysis[76]. Availability of medicines required for kidney care is often limited in lower-resource settings, but even within HICs inequities may arise based on coverage differences between patients and insurers[77,78]. Similarly the nephrology workforce is unequally distributed across the globe: the number of nephrologists per million population (pmp) ranges from 31 in Western Europe to 1 or less in Africa[79]. Thus, diagnosis, availability of treatment and tracking of the burden of kidney diseases is highly inequitable globally.

Inequities conflicting with living well

Good healthcare is a key component to living well[80]. To achieve this equitably, healthcare providers must meet people at their different levels of disadvantage (Figure 1) and support them to face personal challenges and priorities. Patient priorities may, but do not always align with those of healthcare providers[81,82]. Kidney diseases exacerbate vulnerabilities, including health, social, and financial hardship[83,84]. Of note, most often, vulnerability is not an intrinsic condition but due to system failures. Health decision-making is influenced by wider contexts, including one's own understanding, finances, social support, geography, culture, beliefs, and freedoms. Healthcare providers must appreciate these wider determinants, both to consider patients holistically, and to avoid blaming individuals for risks and outcomes caused by external factors.[9] A complex relationship exists between the unique challenges posed by kidney diseases, broader individual and environmental contexts, and healthcare and societal factors which promote or undermine health. Accessibility of kidney care is complex, with many intersecting and compounding challenges, as discussed elsewhere[4,9,12,29,73,80,84-120] and summarized in Table 1. Many of these factors are global problems. The Sustainable Development Report 2022[121] highlights major challenges and insufficient data regarding inequity indicators especially across lower-resource settings[121], which exacerbate the inherent "invisibility" of kidney diseases. The implications for specific groups are expanded on below, with accompanying scenarios and quotes in box 1, partly based on published observations[115,122-129].

Socio- economics

Social and economic position (SEP) is consistently associated with health risks and accessibility of care, across countries, and across lifecourse[104]. People of all ages are at risk of kidney diseases, which constrains opportunities for well-being, education, employment, and attaining life-goals. The relationship between SEP and kidney health is bidirectional, with increased risk of falling into poverty as kidney diseases progress[130].

Particular challenges exist in lower-resource settings[70,131]. In most of Africa for example, many people with CKD are of working age. They often present late, with kidney failure resulting in poor outcomes[132,133]. This is driven in part by low health literacy, and a preference for potentially nephrotoxic traditional remedies and faith-based healers[134,135], but also by a lack of infrastructure and adequate workforce to enable early detection, prevention, and community surveillance[79,101]. If lower-resource countries provide coverage for dialysis, it typically is limited to only two sessions per week[100]. Others exclude kidney failure from coverage schemes[99], necessitating prohibitive out-of-pocket costs if dialysis or transplantation are availabile[69 85,136]. Thus, many people in lower-resource settings are unable to sustain treatment for kidney failure, and struggle with the economic burden on their family, creating difficult moral trade-offs in the allocation of household resources[137,138].

Even in HICs with universal health coverage (UHC), deprived individuals experience less preventative care, more rapid progression of kidney diseases, a greater need to rely on emergency services, and stigmatisation[12]. Poor neighborhoods are associated with poor education and employment opportunities. Residents have less ability to obtain and navigate preventative healthcare, limited availability of recreation services or exercise facilities, and greater exposure to environmental toxins, overcrowding, and food insecurity[73,88,97]. These represent barriers to a healthy lifestyle, good nutrition, and ability to cope with stressors[4,95].

Those who are uninsured , homeless or undocumented migrants also suffer limited accessibility of preventive care. One in three undocumented migrants with kidney failure in the U.S. receive only emergency dialysis, with grave prognostic implications[117]. Irrespective of country, refugees experience similar difficulties to the disadvantaged in navigating healthcare and maintaining a healthy lifestyle[118]. During humanitarian crises, this includes reduced accessibility of life-saving treatments such as dialysis and immunosuppression[139].

Discrimination

Systemic racism continues to drive persistent inequities in kidney health, whereby race should be understood as a social construct rather than a biological indicator and disparities in health and outcomes as the consequences[140].

Globally, people of Black race and minoritized backgrounds are more likely to have kidney diseases, and progress to kidney failure[141,142]. In the U.S., Black patients with kidney failure are less likely to be evaluated and referred for transplantation [143-145], are listed later[144,146-148], wait longer for transplantation[149-152], and receive poorer overall care[153-156] than White patients.

Discrimination against minority groups, including race and sexual and gender minorities (SGM), occurs at the intersection with wider health determinants and causes differences in how healthcare is used and experienced[73,94]. Due to systemic inequities and policies (e.g. redlining), patients from minoritized backgrounds are overrepresented in poorer neighborhoods[73,157-159]. Inequitable structural investment in local community environments perpetuates these disadvantages into future generations[160,161]. In addition, the direct experience of discrimination can cause long-term stress and negative coping, leading to overeating, alcohol or other drug abuse, smoking, poorer mental health, and less trust in sources of support[73,162,163]. Importantly such discrimination not only impacts individuals, but markedly increases total health care costs, which further weakens health systems. In 2018, the economic burden of racial and ethnic health inequities and education-related health inequities in the US, (measured as excess medical care expenditures, lost productivity, and the value of excess premature death combined), were estimated at over $420 billion and over $940 billion respectively[164]. Most of the excess costs was contributed by the Black population and those without a high school education. Patients from minoritized groups may distrust professionals if discrimination is witnessed, with a detrimental impact on health-related decision-making[94]. A patient experiencing discrimination may leave and never return. Effort should be made to provide education and support that is culturally and socially sensitive, but clinician-patient relationships vary across minorities and cultural groups[149], with clinicians investing unconsciously more in people with whom they have greater affinity. Without awareness of these biases, nephrologists may be prone to spend less time with those from minorities discussing treatment options such as transplantation, or new therapeutic options such as sodium-glucose transporter (SGLT)-2 inhibitors[93] (if reimbursed).

Algorithms and guidelines

Algorithms are used to assess, monitor, predict, and support clinical decisions. Such tools risk introducing biases, if based only on selected (privileged) groups or only approximative parameters with a magnitude of error that depends on person characteristics[165,166] (label bias). These biases carry the risk of hidden discrimination[167]. For example, healthcare policies are often based on analytical algorithms of health event administrative coding. Such codes usually represent expenditure on care, rather than illness severity or need. This can lead to structural discrimination, because people of Non-White race experience reduced accessibility of care compared to their White counterparts with similar illness severity[166 168,169]. Such analyses invisibly perpetuate unfair recommendations hidden behind algorithms that assume that Non-White people need less care.

Kidney care is especially dependent on measurement. However, availability of possibilities and capacity to monitor kidney health is uneven between and within social groups, regions, and countries[98]. This compromises interpretability, and the visibility of underrepresented groups. The inadequacy of explicit inclusion of a Black race coefficient within kidney function (eGFR) estimating equations in previous formulae (i.e. MDRD and CKD-EPI equations) was especially important because GFR estimates are cascaded as presumed "results" into numerous kidney and non-kidney tools and guidelines beyond the reach of the kidney specialist[170]. This over-medicalization and biological misinterpretation of race may inadvertently have led to unfair barriers to referral, guideline-based care and provision of support[93,140]. Although not supported universally[171], leading nephrology societies now recommend using eGFR equations without the Black race coefficient[172-174] . Coefficients for age and sex remain, and similarly may require cautious interpretation[111-113,175].

Health illiteracy

Health literacy is "the degree to which individuals have the capacity to obtain, process and understand basic health information" to inform their health decisions[176]. Health illiteracy is to a considerable extent attributable to failures in the education system, and in information systems. This may be exacerbated by insufficient health, social and cultural literacy of care providers, as kidney diseases require not only medical understanding, but also understanding how to support patients living with an increasingly complex chronic disease.

Low health literacy is linked to increased mortality, hospitalization, medication errors and poor management of chronic diseases[177,178]. Efforts to improve health literacy in patients with CKD have focused on the individual, with little attention for the health system environment or the appropriateness of information[179]. For patients and families, their ability to understand CKD and treatments is variable and impacted by many factors including the skills and patience of the clinician providing education, patient health, presence of a caregiver, time of day of appointment, and current and anticipated future treatment modality. These factors cannot be changed by those needing care[180], and may result in decreased healthcare accessibility and utilization of services.

Geography and accessibility

People from rural/remote communities often commence their journey with CKD in a disadvantaged position, especially regarding socioeconomic status, educational attainment, and opportunities to benefit from primary prevention[181]. Regarding KRT, many barriers, including late referral to nephrologists, necessary relocation to obtain treatment, transportation barriers, and financial hardship[125] contribute to an increased risk of mortality, morbidity and hospitalization among those residing in more remote locations[181]. For in-center hemodialysis, longer travel time to treatment is associated with higher mortality, and decreased quality of life[182]. Centralisation of most transplantation units to major cities, adds an extra layer of difficulty for patients from remote areas as possibilities to complete transplant work-up and specialist care may not be available locally.

Inequities among therapeutic options

Inequities in kidney care pervade across individual conditions (cause of kidney diseases, lifestyle, the timing of preventive and therapeutic interventions and disparate accessibility of different KRT modalities), wider communities, healthcare systems (e.g. private *versus* public healthcare sectors) and countries (Figure 1). Combined, these have major impacts on patient outcomes.

Acute kidney injury

Although AKI is potentially preventable and reversible, accessibility of appropriate diagnosis and care is inequitable. In HICs, AKI is common among multimorbid individuals who often need prolonged dialysis in intensive care with little chance of recovery.[35]. In many lower-resource countries, awareness/confidence to manage AKI is low among healthcare workers[183]. Although AKI is common in children and young adults, often as a single condition[35], even basic intravenous fluids for rehydration may be lacking[184], let alone accessibility and affordability of dialysis[37,184,185]

Chronic kidney disease

In the early stages of CKD, only people with specific kidney conditions such as polycystic kidney disease or glomerulonephritis typically receive care in specialist nephrology clinics. For many people with early stage CKD due to more common causes (e.g. related to hypertension or diabetes), care is coordinated through primary care or non-nephrology specialty units and is subject to inequities in surveillance, diagnosis and quality of care[12].

Multiple barriers in CKD care, including lack of accessibility of essential diagnostics and drugs to slow progression of kidney diseases, and of knowledge among healthcare professionals, contribute to inequities (Table 1). Accessibility of appropriate medication depends on availability, reimbursement and/or ability to self-pay. A survey of resource-limited countries reported that approximately 75% of patients had to pay themselves for diagnosis and treatment of glomerulonephritis, while the lack of kidney biopsy and subsequent interpretation often led to inappropriate immunosuppression[186]. Quality of care is therefore an additional concern even if some resources may be available/accessible, highlighting the need for capacity building among the nephrology workforce[15].

Advanced kidney disease: dialysis and conservative care

Accessibilty and quality of dialysis, availability of home dialysis and focus on patient well-being varies between and within countries and between individual nephrologists as outlined above (Table 1). Most variations in dialysis accessibility and availability relate to economic factors – cost, health coverage, distribution of dialysis centers, number of nephrology professionals including nurses, quality of patient education, support for vascular and peritoneal access creation, and management of comorbidities[56].

Hemodialysis is available (although not necessarily accessible to all) in most countries and tends to be the default form of KRT[15]. In-center hemodialysis is time- and resource-intensive and is highly centralized. PD is more scalable and flexible, less hospital dependent, can be done anywhere with rudimentary infrastructure, is preferred by many patients[187], and is especially suitable for children[188]. Counterintuitively, however, PD costs more than hemodialysis in many lower resource settings[189-191]. Efforts to make PD supplies less expensive and to increase awareness of the advantages and impact of PD are key to increasing its global availability[192]. In terms of quality, cost is again a major source of inequity where reduced hemodialysis sessions or PD exchanges are often used as compromises to cut costs, but unavoidably reduce dialysis quality[137].

Older or frail individuals, and those with learning difficulties are usually committed to in-center hemodialysis unless assistance is provided at home.

Even in high-income Western European countries, healthcare-funded assistants for dialysis were available in only 5 of 13 surveyed countries [193].

Similar arguments hold for inequity of avalability of conservative care, with less than half of countries providing support from multi-professional teams, or enabling shared decision making, if patients need to embark on conservative care[59]. Even in countries which purportedly support conservative care, such as France, this option is often not discussed as an alternative to dialysis[194].

Advanced kidney disease: transplantation

Many patients in need of KRT prefer kidney transplantation over dialysis, due to better survival and quality of life[195,196]. Globally, the WHO estimates that only 10% of the demand for kidney transplantation is met[197]. The donor organ shortage is worsening as more people worldwide require KRT.

Transplantation is available in 74% of countries (publicly funded in 53%) with waiting lists in only 62%[198]. Pre-emptive transplantation is only recorded in 10% of countries[198]. Higher-resource settings have higher rates of deceased and living donation than other countries[199,200], along with transplant registries enabling greater transparency. The availability of kidney transplantation through UHC in higher-resource settings enables people from lower socio-economic classes to obtain transplantation. Nevertheless, even in higher-resource settings inequities remain pervasive [143-145] and there are huge disparities among countries in transplantation uptake[201]. In LICs accessibility is largely restricted to those who can pay.

Racial disparities are well documented particularly in minority groups, migrants and Indigenous and First Nations People, who despite a higher burden of kidney failure, are less likely to receive a transplant[202]. Females are more likely to be living donors than men[203], an observation likely impacted by multiple factors, including the slower progression of kidney diseases among women[204]

In 2007, apprimately 10% of transplantations worldwide resulted from organ trafficking after graft purchase from poor and individuals rendered vulnerable by their life circumstances[205,206]. The Declaration of Istanbul provides guidance for organ donation and transplantation worldwide, to promote equitable sharing of the limited transplant resources by those in need, and prevent harm through exploitation[207]. Nevertheless, equitable allocation of graft organs remains complex and changing viewpoints might necessitate revision of rules when appropriate[206].

Pediatric care

Accessibility of specialized pediatric nephrology is very limited in LICs, but regional variations occur everywhere[208]. Data on the epidemiology and outcomes of pediatric kidney diseases are limited to registries in HICs and small studies from lower-resource settings, probably underestimating true disparities in care.

The 0 by 25 initiative highlighted the disparities in early diagnosis and accessibility of dialysis for children with AKI in lower-resource settings[37]. Community-acquired, preventable AKI due to infections like dengue, dehydration or nephrotoxic drugs is more common in low-resource settings and exacerbated by poverty and malnutrition[35,37,185]. Mortality in children with AKI is >50 times higher in lower-resource settings than in HICs, especially when dialysis is unaccessible[209]. Non-recovery of kidney function is 3 times more frequent[209].

Pediatric CKD is often diagnosed late, especially in countries with poor antenatal and primary healthcare, and in rural/remote areas[210]. Accessibility of pediatric dialysis and subsequent outcomes correlate with national wealth, even in Europe[211]. Mortality risk is also greater with late diagnosis requiring 'urgent start' dialysis[211] and is very high if dialysis cannot be provided or continued[70].

The barriers to pediatric kidney transplantation in lower-resource settings include unavailability of pediatric transplantation expertise, catastrophic out-of-pocket expenditure and the absence of deceased donor organ sharing networks[212,213].

Inequities resulting from health economic factors

Differences driven by country wealth

Kidney care comes at a high societal and personal cost[25]. Global reimbursement for maintenance dialysis (excluding out-of-pocket payments) amounts to around 57 billion US dollars, 80% of which is spent in HICs, 17% in MICs, and only 3% in LICs[190]. Dialysis, if universally provided, is funded by varying state financing schemes[214]. In HICs, >2% of national healthcare budgets is directed to KRT, for only 0.15% of the population[14]. Global costs for AKI are unknown, but in the US, in 2013, AKI reportedly caused $9 billion excess annual hospital costs[35].

In higher income settings, expenses for associated non-kidney care further increase the financial burden[14,215]. Productivity loss (unemployment, sick leave, premature retirement, death) impacts patients, their next of kin and society overall[216]. Individuals in vulnerable positions (temporary, contractual, physical workers, unemployed) are at higher risk of productivity loss and impoverishment when struck by CKD[84].

In low-resource settings where the direct and indirect costs of kidney care and KRT often must be paid out-of-pocket, the risk of impoverishment is even higher. A systematic review comparing out-of-pocket payments for several diseases revealed kidney diseases as the leading cause of catastrophic health expenditure (CHE), across lower-resource settings, thus exacerbating inequities between countries, individuals and groups.

Both higher and lower-income countries are therefore at risk of inequities but the problems are not necessarily the same (table 2). Accessibility of kidney care without experiencing financial hardship is highly inequitable across the globe, with the most severe consequences (death and/or CHE) especially affecting the poorest[70,138,185,217-219].

Kidney replacement therapies

Dialysis is available in almost all countries[15], but the clinical, financial and ethical dilemmas associated with its (un)accessibility cannot be ignored. Cost-effectiveness assessments are used to rank healthcare interventions aiming at maximal population health gains, often expressed in Quality Adjusted Life Years (QALYs), for a given cost[220]. A systematic review of cost-effectiveness analyses concluded that the ability to identify the mix of dialysis modalities that provides best outcomes for patients and health budgets is uncertain, particularly given the frequent inconsistencies between published studies and non-consideration of societal perspectives[221]. In addition, cost-effectiveness as sole criterion for decision making has been criticized, since it overlooks crucial factors such as budgetary impact, financial risk protection for individuals, and equity in distribution of interventions[222,223].

In many higher income countries, the budgetary impact of dialysis has been accepted, as the choice to save lives has prevailed over costs[217]. This has led to exponential growth in patient numbers and a dialysis industry generating considerable profit in a sector with few competitors. Rising patient numbers, especially in emerging countries, will further inflate costs[224]. Health system and societal costs for PD, home hemodialysis and transplantation are lower than for in-center hemodialysis in many countries[56,190,201,225-227], but their uptake and/or availability is inadequate and divergent[190,228,229]. Additionally, health-economic factors favoring one therapeutic alternative over another in HICs differ in lower-resource settings, where labor is cheaper and imports more expensive[225].

Especially in low-income settings, policy makers face the challenge of simultaneously pursuing UHC, setting priorities across the whole health system and progressively fulfilling the human right to health[217,230]. It would be naive to insist that KRT be funded immediately everywhere for all, as the opportunity costs (money spent on KRT cannot be spent elsewhere) are high. For example, if Kenya, Nigeria and Senegal would try to meet their estimated national dialysis needs, this would require from 8 to close to 40% of government health expenditure[231]. Consequently, in lower-resource settings, KRT is currently largely available only to those who can pay[137].

CKD not on kidney replacement therapies

The costs of kidney care do not only impact those on KRT. The poor may not even be able to afford simple care to prevent the evolution of early CKD to kidney failure. This intensifies inequities because as disease progresses, higher levels of care and personal expenditure are required[137].

The optimal solution to forestall CKD costs is to reduce disease risk and/or progression, both intimately intertwined with inequities in many places[14,232,233]. However, in most countries investment in initiatives to promote prevention is minimal, in spite of the high value for money compared to the financing of treatment or cure[11,14,190,234,235]. The value for money gained through prevention of illness is not restricted to the health sector. A recent publication from the WHO highlighted the important long-term return on investment of prevention of NCDs. For example, investment of 1 dollar in lower-resource settings to reduce population salt intake in 2018 would yield 13 dollars in return by 2030, given the lower subsequent health expenditures and greater productivity gained with healthier people[236]. Thus, there are also longer-term opportunity costs, which apply especially to many lower-resource settings, where current health budgets are disproportionately channeled to secondary and tertiary care, necessitated by the poor investment into prevention[190,225,237].

Marketing of drugs

A threat to reimbursement systems and costs is the marketing of therapies for specific kidney diseases which are often only available at extremely high prices, either because of patents, or the small market size if a condition mainly affects children (e.g. cysteamine)[238,239]. There is little transparency in the price setting of such drugs (e.g. eculizumab)[240], for which in addition evidence may be low[241]. They are also frequently used off-label for indications for which they are not approved nor evidenced, or used in children and adolescents where they have not been tested (e.g. tolvaptan)[242]. Inflated costs and excessive profits not corresponding to investment[240] initiate and exacerbate inequities among countries and regions[243], and depend on whether countries have orphan drug legislation and reimbursement schemes. Inequities in accessibility of such medications have a negative impact on patient outcomes[244] in low-income but also in high-income settings, as incomplete of absent coverage may necessitate out-of-pocket payments, that are not possible for all.

In summary, the current health-economic model supporting kidney care is flawed. The focus on expensive and/or late stage therapies favors inequity, both across countries and among individuals. Differences in cost of essential therapies between countries, without clear transparency about the prices and the reasons, further exacerbate global inequities[245].

Ethical context

Inequitable accessibility: an ethical dilemma

Clinicians are familiar with the 4 principles of biomedical ethics. The principles of autonomy, beneficence (doing good) and non-maleficence (not doing harm) are readily applicable at the bedside. The principle of justice, however, has implications beyond the bedside and addresses issues of fairness and inequities between individuals. In resource-constrained settings, physicians often realize that autonomy, beneficence and non-maleficence conflict with justice, as an individual patient's needs may be overridden by lack of available therapies, poverty or the needs of others competing for the same treatment[70].
Inequities in nephrology constitute moral dilemmas because patient outcomes are adversely affected by structural injustice and vulnerability, that increase risk of kidney diseases and impact accessibility of care[60]. Although inequity is often thought to begin with a lack of accessibility of healthcare, patients with kidney diseases encounter inequities that extend beyond the healthcare sector, beginning with the conditions in which they are conceived, born, work and live[233]. The social and structural determinants of health include factors like age,

gender, poverty and geographical location in the world and within a country. These factors are inequitably distributed, resulting in vastly different outcomes for patients with the same disease living under different circumstances - highly resourced versus low resource settings, or people who are wealthy versus the poor. These social determinants of health play a large role in pre-determining who lives longer and who dies earlier[246]. Accessibility of kidney care is also inequitably distributed at all levels – from screening, early diagnosis and preventative care up to KRT or comprehensive conservative care for kidney failure.

If inequity in healthcare is inherently ‘unjust’, an ethical dilemma arises for the provider (the principle of justice is violated)[70]. Inequities in kidney care occur in all resource settings and at any stage of disease, but the impact is compounded with worsening kidney function, as life-saving but expensive treatments become necessary. Out-of-pocket costs exacerbate these inequities in low-resource settings, where minorities, women, the poor, elderly and health illiterate, as well as those living remotely, are disproportionately affected. Examples of structural inequities in nephrology are presented as case studies in **Table 3**, highlighting the ethical dilemmas encountered[137,206,217,247-256]. Such moral dilemmas are omnipresent: at the bedside, during shared decision-making, in society, for national governments and at a global level (**Figure 2**).

Responsible stakeholders

In his philosophical approach to health justice, Venkatapuram states that health is not the absence of disease, but a positive ability to be and to do things[257]. People have a moral entitlement to be as healthy as they can, and patients need to be capable of leading productive and quality lives.

Expressing health as a human right is an important complement to advancing health equity because it stresses that the responsibility for care delivery lies with the state, which has an obligation to provide care to whatever extent possible in an equitable manner[230].

The global nephrology community also has an ethical imperative to address/call attention to all the factors underlying inequity, including the social determinants of health, as well as every level of accessibility of kidney care. It is the ethical responsibility of all professionals to reduce inequities in kidney care and improve patient outcomes and to advocate this objective[258]. Governments must be held accountable to acknowledge this and to commit to the progressive realization of the right to kidney care for all.

Solutions

As outlined above, inequities in opportunities to optimize kidney health and to provide accessibility of all forms of kidney care are multiple across the globe. The origin of health inequities can often be narrowed down to both social and systemic injustices[259], related to complex, multisectoral factors. Solutions require leadership, responsibility, and political will. Improvement in accessibility of health care may mitigate the immediate impact of social and systemic injustices to an individual, but lasting progress can only be made through seeking system solutions that prevent the underlying causes at a population level. Accordingly, if medical communities are to make collective progress towards dismantling inequities, the underlying causes must first be acknowledged and understood before they can be solved. This in turn requires collaboration on global, local and individual levels. Suggested actions to tackle the global inequities in kidney health and kidney care per stakeholder group are summarized in table 4 and outlined relative to policy/individual level in what follows.

Global level

Recognize kidney diseases as an important public health problem

Multiple factors have contributed to kidney diseases being relatively overlooked as a public health concern, which include lack of data in many places due to global inequities in accessibility of essential and reliable diagnostics for kidney diseases and rudimentary health information systems which do not track kidney diseases. The focus of global health agendas was initially driven by funding and targets set for infectious diseases and maternal and child health, and subsequently for cardiovascular, cancer, respiratory diseases, diabetes and mental health, but not kidney diseases[28,260]. If the burden of kidney diseases is to be meaningfully impacted, advocacy and strong leadership are required to acknowledge and reduce existing inequities in disease risk and accessibility of care, to strengthen the provision of integrated quality care for NCDs including kidney diseases, to generate robust health-economic evidence on interventions and their impact to guide financing, to improve data capture to identify areas that lag behind, and to track achievement of all sustainable development goals (SDGs), as each SDG impacts kidney health world-wide[233].

Just as health inequities cut across countries, so also do potential solutions. Over the short and medium term, harmonization among countries and classes can be advanced by material, financial or in-kind external support, and by promoting exchange of learning, innovations and best practices[261]. Such initiatives might be optimally managed by umbrella institutions, including governments, supranational political structures (e.g. the European Union), coordinating agencies (e.g. WHO), or non-governmental organizations (e.g. Médecins sans Frontières, European Kidney Health Alliance), but may also result from private initiatives (e.g. Gates Foundation) and professional societies (e.g. International Society of Nephrology, European Renal Association). Over the longer term, countries must be encouraged and supported to finance and deliver sustainable and comprehensive local quality kidney care.

Support affordable innovation to improve kidney care for all

Transparency in investment and in development and production of novel technologies and drugs, especially for orphan kidney diseases, is urgently needed[240]. Structured stakeholder networks, like the virtual European Reference Network on rare diseases of the European Commission, may help to support high quality, sustainable and equitable therapies[262]. Tiered pricing mechanisms adapting the cost of technologies and material to the welfare of a country in mutual agreement between rich and poor countries may improve affordability[263].

Innovation should not only focus on sophisticated technologies, but must also include the development of new approaches to improve uptake of prevention strategies, and accessibility and delivery of primary care for those currently left behind. Implementation and operational research are needed to identify and scale up effective and affordable strategies, including dialysis[264]. Governments, learned societies, clinicians, researchers and patient organizations should work hand in hand to foster innovation at all levels as a means to reduce global inequities.

Country level

Prevention and early detection

The best approach to reduce the burden and cost of NCDs, especially kidney diseases, is prevention[14]. This universal tenet applies to all countries. Unfortunately, only small proportions of healthcare budgets world-wide target prevention[14,56,190]. Timely and appropriate screening for kidney diseases occurs rarely and is often not systematized or harmonized[265].

Prevention is most efficient when risk or disease are identified early. This requires identification of barriers, creating awareness and building trust, especially among vulnerable populations, where the deficiencies in early identification and delivery of evidence-based care are most prominent.

Governments should invest in prevention and screening, especially among high risk groups[51,266] and vulnerable populations[267,268]. Not doing so forces health systems towards more expensive "rescue" solutions like dialysis, which exacerbate inequities[91].

Socio-economic status relates differently to healthy lifestyle across the globe, with higher socio-economic status being related to lower risk of NCDs in high-income settings, but higher NCD risk in lower-income settings as middle classes emerge[73,269] . Modification of these inherent sources of inequity requires a multi-sectoral approach to health and well-being such as that embodied by the SDGs, as well as population education about healthy lifestyle[233,270].

Data required to support decision making

The core social determinants that make up the building blocks of health represent societal injustices in how governments and authorities prioritise the vulnerable, spend resources on those in need, and ensure adequate provision for those affected by ill health. To motivate those who have power to act, knowledge and understanding must be guided by good quality data, moral advice, and a society that holds policymakers to account. Social and healthcare data from real-life practice, research efforts and actions by charities/NGOs should be integrated to improve the availability of meaningful intersectional health. Decision-making and priority setting processes are hampered when incidence, prevalence and health-economic data is lacking[217]. Countries must invest in systematic data collection to permit understanding of disease burden, distribution, costs of care, financial hardships incurred, and to identify and address inequities. Rigorous health technology assessments, based on reliable local evidence of disease burden and costs to the health system and to individuals, are required to support priority setting.

Facilitate fair reimbursement of treatment costs

Universal Health Care (UHC) is a crucial target of the SDG3[271]. True UHC is needed to prevent exclusion of the disadvantaged and reduce inequities[272] (Figure 3). Even if UHC is not currently affordable, governments should commit to its expansion through transparent processes, to progressively realize the right to health for all[230], with stepwise inclusion of expensive therapies, when this becomes possible. Clear societal thresholds should be set regarding the willingness to pay for gain of Quality Adjusted Life Years (QALYs), accounting for the medical need and affordability, also called Value Informed and Affordable Pricing[273]. Such processes should not only include cost and disease burden, but must also take financial hardship and equity into account[274]. For example, two health sector interventions which score highly in terms of equity in the poorest nations are acute dialysis and kidney transplantation for children, but lack of cost-effectiveness data precludes their recommendation for coverage[275]. Cost-effectiveness analyses can however only be based on intervention studies including diasadvantaged groups.

Improve affordable care

Technologic options like hemodialysis should be made affordable and more reliable, accounting for the harsher conditions frequently encountered in low resource situations (e.g. more resistant to heat, humidity, energy-efficient)[276]. Costs for dialysis supplies can be reduced by waiving importation taxes or by local production of PD material[190,228]. In higher-resource settings, home dialysis uptake could be stimulated through financial incentives, policy measures (PD first), fair price setting by industry, patient education, and benchmarking[277]. Health systems should be strengthened to include safe and legal transplantation programs.

Local level

Raise awareness of kidney diseases

All those concerned with kidney health and care (including non-professionals) have a responsibility to be aware of and to create awareness of the problems related to kidney diseases[25]. This includes addressing the causes and consequences of the structural determinants of health which entrench inequities. Healthcare professionals should be trained throughout their studies and continued education to identify and address these problems through advocay and/or concrete measures[278]. Patient associations and NGOs play an important role in this process to improve equity and should engage in training initiatives to optimize their own advocacy skills [31,279]. Patients must raise their voices in holding healthcare planners and leaders to account, activate partnerships for harmonization among regions/countries and expose organizational shortcomings, e.g. calling for availability of specific medication, dialysis or transplantation.

Improve accessibility of equitable quality care

Holistic kidney care requires strong health systems and public health strategies to reduce burden of kidney diseases, and to promote early detection and treatment, integration of kidney care into existing programmes for NCDs and some infectious diseases, and reduction of organ specialty-linked silos. The common diagnostic tools for kidney diseases (serum creatinine and albuminuria) are simple and affordable in many (but not all) countries, and should be made available as much as possible, but also ensuring this is followed by appropriate interpretation and therapeutic intervention. Primary care and non-nephrology physicians and other healthcare workers could play an essential role, but may be insufficiently familiar with kidney diseases and should be educated appropriately[18,280]. Since kidney patients have multiple comorbidities and require multiple healthcare providers, integration of care is quintessential. Capacity building and audit-based education may support implementation of appropriate preventative measures[281]. Accessibility of essential medications should be assured to permit early intervention and stop/delay progression of acute and chronic kidney diseases. Telemedicine and eHealth should be harnessed for remote outreach[282]. Quality assurance activities, including tracking of inequities, should be integrated into clinical routines.

Avoid cherry-picking

In poorly designed pay-for-performance systems, self-interest with utility as the prevailing principle could lead clinicians, hospitals and dialysis units to target high throughput by favoring inclusion of patients with greater resources and more favourable (less complex) clinical characteristics[283]. If applied to the extreme, this morally dubious practice creates an additional disadvantage for the less privileged, as they will start with less favorable conditions and will be driven towards less favorable therapeutic environments[284]. Conflicts of interest may lead to fewer transplantation referrals from private dialysis units[285]. Reporting and monitoring of patient mixes and outcomes is mandatory, especailly in dialysis units where this data is easily obtained.

Individual level

Tackle health illiteracy

To improve health literacy, a coordinated health systems approach informed by consumers and representatives of the concerned groups is needed, with adapted and innovative educational methods to meet various needs. Specific support may be needed for children and families affected by kidney diseases, to optimize adherence and minimize disruptions associated with the high demands of kidney care.

One system level change adopted in other chronic diseases such as diabetes is the introduction of navigators[120,125], who assist patients and caregivers in understanding diseases and treatments and optimize self-care. Such programs have been successful in remote parts of Australia with Indigenous People. In the US, animation has been applied successfully for diabetes education where language barriers exist[286]. Medical professionals need to recognize their own limitations in terms of socal and cultural literacy. Since medical professionals are usually not well-trained in education, advice should be sought from experts in other fields (e.g. pedagogy, animation, telecommunication, health illiteracy)[287-289].

Patient empowerment

A move from paternalistic care (doctors making decisions without patient input) to shared decision making (decisions guided by deliberation between individual patients, their caregivers and practitioners)[290,291] as an approach to enhance equity in therapy choice contributes to more patient satisfaction, adherence and health[292]. All steps should be reported transparently, which helps to avoid imposing therapies for financial or other reasons that may not benefit the patient. Patient organizations may play a central role in facilitating this shift of paradigm. When interacting with patients, decreases in cognitive function should be taken into account, especially in advanced CKD[293], as this common complication affects alertness and hinders fast and accurate decision making. Extra care must be taken in children with kidney diseases and their families to enhance understanding of kidney care and cooperation.

Conclusions

Kidney diseases are associated with significant inequities that increase risk and are imposed by the many social and structural factors, the relative invisibility of the condition as a public health threat, and the time- and resource-intensive therapies required for advanced disease, especially dialysis.
All professionals involved in kidney care should be alert for local inequities and their impact on patient lives, as well as those occurring on a broader, regional, national and international level. Recognition is the first step towards developing actionable solutions.

Inequities include those specific to countries and regions, among social groups, and those related to accessibility of preventive and therapeutic modalities. In addition to adverse clinical outcomes, inequities also raise health economic and ethical concerns, and are heavily compounded by non-medical social and structural determinants such as poverty, social injustice, violence, racism, lack of education, and cultural and religious barriers.

Solutions range from the individual to the global level. Awareness of potential solutions is important to encourage advocacy and action by all stakeholders. Although not all solutions may be universally applicable or implemented, there is a collective need to develop and implement innovative strategies to tackle barriers to equitable kidney health and kidney care. All nephrology professionals should have the conviction to advocate within their communities, armed with local and international data, and to engage with policy makers, administrators and insurers, to raise awareness about inequities in kidney health and to improve kidney care across the globe.

Keypoints:

- Insufficient investment across the spectrum of kidney health and kidney care (from awareness raising, to prevention, diagnosis and treatment) is a fundamental source of inequity. This affects all people at risk of, or living with, kidney diseases.
- Social and structural inequities are major risk factors for, and contribute to, poorer outcomes in kidney diseases both within and between countries.
- There is insufficient accessibility of essential diagnostics and medications to treat kidney diseases and to track their burden. This disadvantages patients in low- and middle-income countries from the very beginning of their disease course.
- Ability to access the entire spectrum of kidney care (from basic medication to dialysis and transplantation) without experiencing financial hardship is very inequitable across the globe. Transplantation is the most equitable form of kidney replacement therapy, but is highly unaccessible in lower income settings. This results in vastly different outcomes and life courses for patients with the same diseases living under different circumstances.
- Novel therapies for rare (orphan) diseases are often only available at extremely high prices, which frequently affects or excludes children and adolescents.
- All nephrology professionals should become skilled at advocating on behalf of their patients to communities, policy makers, administrators and insurers, to develop constructive strategies and collectively reach optimal solutions to improve equity in accessibility of quality kidney care locally and across the globe.

CAPTIONS TO FIGURES

Figure 1: Factors contributing to inequities by increasing risk and by affecting accessibility of preventative measures, care and therapies. The description considers global, national/regional, community-related, health system-related and individual elements.

Figure 2: Ethical dilemmas in inequitable accessibility of kidney care: from global to local.

Figure 3: The Universal Health Coverage cube: expanding universal healthcare coverage for kidney diseases in low resource settings. The health needs of the population are depicted by the larger transparent box, the funds available for health financing are depicted in the blue box. In many high-income countries the size of the blue and the transparent boxes are very similar (almost all health needs are covered), whereas in low resource settings the blue box is considerably smaller than the transparent box, meaning that many health needs that do not fall within the blue box are not covered by the health system and must be provided/paid for by individuals. As countries set health priorities and expand their health coverage they must consider the impact across all 3 dimensions: who should be covered, which services should be provided and how much of the costs can be covered by the health system. KRT falls outside of the blue box in most low-resource settings. Suggestions here include how accessibility of kidney care can be progressively expanded under universal heath coverage. Priority setting must consider prevalence of a condition, cost of therapeutic options and available resources. AKI: acute kidney injury; CKD: chronic kidney disease; KRT: kidney replacement therapy; CHE: catastrophic health expenditure. *: data on disease burden missing in many places. Reprinted from Publication

“Making fair choices on the path to universal health coverage: final report of the WHO consultative group on equity and universal health coverage. https://apps.who.int/iris/bitstream/handle/10665/112671/9789241507158_eng.pdf?sequence=1&isAllowed=y Figure 1.1, page 5, Copyright (2014)."

Box 1: Motivating scenarios for inequitable care specific groups of people

Social and economic position

“When you enter through the emergency department, you arrive in bad shape...you need to have a high potassium or they send you home even though you feel you are dying. Sometimes, you crawl out when they decide to not do dialysis. You eat a banana because it is high in potassium even though you may die and you go back and wait and hope that they will do dialysis so that you don’t feel like you are drowning and so that the anxiety goes away.”
(An undocumented immigrant in the USA receiving only emergency dialysis services)[123]

"We have a population of about 30 million people and have less than 20 trained nephrologists. Unfortunately, due to lack of knowledge about kidney disease and its management, over 70% of patients report late to the teaching hospital with kidney failure and since care is not reimbursed by the National Health Insurance scheme, about a third of patients with kidney disease die on admission for which we have to sign death certificates and this does not include those who are stable enough to be discharged home with no hope of sustaining themselves on dialysis. It’s really sad. Without money you die when you have kidney failure."
(A health professional’s perspective on kidney care in Ghana)[126]

Discrimination

“In my doctors they used to have this thing that when you signed in it was on a screen and you had to select in front of everyone in the waiting room whether you were male or female. Even that half a second just breaks my brain every time and I’m like, I kind of don’t want to go to this appointment now”.
(An LGBTQ+ patient on attending their appointment)[127]

“My doctor[s]... be shocked when I asked them, well why is there so many Black people on dialysis and they don't have no real answer for me. I really don't like that. And so then on top of that he only spends ninety seconds with me... I'm like wow, I feel like cattle.”
(A patient receiving dialysis discussing mistrust in their nephrologists connected with race)[122]

Inequity within algorithms and guidelines

A 54 year old woman of mixed race is opportunistically found to have a low eGFR when attending hospital with a minor injury. She is advised that this is probably due to muscle mass and goes home. Several months later she reattends hospital in need of emergency dialysis.

“The insights about sexist and racist biases... are important because information organizations, from libraries to schools and universities to governmental agencies, are increasingly reliant on being displaced by a variety of web-based "tools" as if there are no political, social, or economic consequences of doing so.”
(Safiya Umoja Noble, on reinforcing structural discrimination by use of algorithms)[294]

Health literacy

“I'd say about the hardest part was when he was on the prednisolone when he's on a high dosage, it's very lunatic. And then we went to the doctor to what's going on. Oh, it's the prednisolone. It causes anger and stress. So, more information and education of the carers as to what possible side effects could be and talk to you about this is what's going to happen.”
(A caregiver’s perspectives on kidney transplant aftercare and education)[115]

“I would have really liked to have sat and talked with somebody who had gone the journey before me, and to give me a heads up on about what I'm going to experience from the importance of taking the medication, understanding what the kidney function is in my body, understanding about my fluids, my nutrition, all of those coming together of the importance, because as a primary school teacher, you're having to say it at least 20 times before it clicks.”
(A care partner)[125]

“All the patient navigators that I've met, have been on dialysis and going through transplant and their second transplant. They know exactly what it's like to sit in that chair, and have treatment for hours on end, the restrictions that you're on, the medications that your body must handle after transplant. And although someone can sit and tell you about this importance, I think it comes at another level with someone else who's experienced that and been successful, and that you can draw on and build a relationship with, and it's kind of upskilling.”
(A patient’s perspective of lay navigators)[128]

Geography and accessibility of care

J lives in a town with no dialysis services, the closest is 175kms away. He is ineligible for a transplant or home dialysis. His only choice is to move or receive conservative care.

“Just the understanding, like if you're having a transplant, you've got to deal with the city hospital and they say, "Okay, I'll book you in 8:00 in the morning, tomorrow morning, can you make it?" Well, I live in XXX. All right, well can you travel? Well, it's six hours away and I've got a family to organize and I'm on dialysis so it's like they don't get it. And then they'll say, "Come back next week and see me." Like, you're kidding. Can't you have

the one stop thing?"
(A patient experience of lack of accessible care due to remoteness)[125]

Abbreviations: LGBTQ+, lesbian, gay, bisexual, transgender, queer, and other

Acknowledgements

The European Kidney Health Alliance (EKHA) is a not-for-profit organization defending the case of the kidney patients and the nephrological community at the level of the European Commission. The EKHA network has five full members (the European Renal Association, the International Society of Nephrology, the European Kidney Patients Federation, the European Dialysis and Transplant Nurses Association-European Renal Care Association and the Dutch Kidney Foundation) next to 27 National or Regional Societies as affiliated members.

European Kidney Health Alliance is the recipient of support by the European Union in the context of the Annual Work Program 2022 on prevention of non-communicable diseases of EU4Health, topic ID EU4H-2022-PJ02, project # 101101220 PREVENTCKD

Disclosures: RV is advisor to AstraZeneca, Glaxo Smith Kline, Fresenius Kabi, Novartis, Kibow, Baxter, Nipro, Fresenius Medical Care and Nextkidney.

VL receives royalties as a co-editor of “The Kidney” textbook. LA is advisor to AstraZeneca and Baxter. BS received grant support from GSK, Fresenius Medical Care and Boehringer Ingelheim as part of the CKD-REIN study. EB is advisor to Baxter, IiberDi and AWAK and received speaker fees from Baxter and Vifor. All other authors declared no conflict.

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Table 1 – Barriers to optimal kidney care

	Patient level (inherent to kidney diseases and care)	**Health system level (inherent to organisation of healthcare)**	**Population level (inherent to environment)**
Chronic Kidney Disease*	• Lack of symptoms in early stage kidney diseases • Lack of awareness of symptoms of kidney diseases • Late diagnosis of kidney disease due to lack of appropriate screening of those at risk • Late diagnosis of kidney disease due to long asymptomatic phase • Late start of measures to prevent kidney disease progression • Inadequate monitoring, surveillance and treatment • Poor health literacy associated with lower concordance with medications, clinical plans, dietary requirements • Instability of living environment (financial resources, housing, recreation facilities, freedom of persecution or war)	• Inadequate screening for kidney disease in at risk populations • Lack of funding of prevention • Unavailability or lack of reimbursement of kidney function tests • Shortage and brain drain of nephrologists and shortage of kidney centres • Lack of healthcare funding for expensive drugs • Limitation of healthcare provision or reimbursement to certain groups or certain therapeutic options • Lack of education of primary and secondary healthcare professionals regarding early signs of kidney disease and when to refer to specialist teams • No consideration of priorities and outcomes that matter to patients	• Lack of accessibility of healthy food, clean water, health facilities • Healthy diet and lifestyle may be unaffordable for some people • No financial incentives to stimulate healthy diet and lifestyle • Unhealthy or polluted living areas or working conditions • Working conditions in conflict with health needs (e.g. to attend check-up appointments) • Population burden of diabetes, obesity and hypertension is exacerbated by social dterminants of health • Inadequate dietary information for population, e.g., on salt intake • Religion, culture or tradition may interfere with optimal solutions for kidney health • Discrimination of race or minorities

	• Distrust, fear and misunderstanding of health professionals • Language barriers • Follow-up by (too) many healthcare providers due to multimorbidity • Competing complications and outcomes may disturb decision making • Difficult to treat symptoms (fatigue, itching) may disturb confidence in care providers • Chronic stress without sufficient adaptive oping strategies • Cognitive dysfunction, visual and hearing impairment, learning difficulties, mental illness) hamper decision making • Inability to pay for drugs • Expensive special diets • Potential loss of income attending outpatient clinics • Complexity of required decisions • Distrust of healthcare system • Fear of stigmatisation • Unavailability of personal health insurance	• Lack of training of healthcare professionals on how to provide culturally appropriate care and how to deal with discrimination, unconscious bias or health illiteracy • Lack of research and research funding on kidney health and care • Unavailability of structural health insurance (universal health insurance coverage)	• Lack of education of general population on kidney health and care

	• Non-adherence augmented in adolescents • Stigmatization		
Dialysis	• Inadequate accessibility of pre-dialysis nephrology care • Inability to engage in decision making regarding choices / health illiteracy • Ageing and frailty • Dependence on family and social support which is not always available • Inability to pay out-of-pocket expenses • Distance from kidney centre • Certain options (home hemodialysis, peritoneal dialysis, self-care) not available • Long-term dependence on life-saving treatment as cause of lack of adherence • Accesibility problems in humanitarian crises (wars, refugees, undocumented migrants) • Child size limits dialysis possibilities	• Availability of dialysis facilities • Government funding • Education of healthcare providers about dialysis options • Number of nephrologists and specialist dialysis nurses • Availability of multi-professional teams for psychosocial support • Availability of dialysis-related drugs e.g., erythropoietin • Insufficient possibilities to diagnose, prevent and treat acute kidney injury • Unconscious/structural biases of healthcare providers, favouring patients of their own age, sex, and social and ethnic background • Limitation in availability of dialysis modalities – PD and HD variably accessible	• Lack of awareness of dialysis options • Lack of medical support for comorbidities • Lack of welfare support for patients • Urban vs. rural living area • Geographic distribution of dialysis centers

Conservative care	• Inadequate accessibility of pre-dialysis nephrology care • Inability to engage in decision making regarding choices / health literacy • Dependence on family and social support which is not always available • Cultural / religious beliefs perturbing decision making • Lack of training of health care workers	• Lack of respect for patient autonomy and shared decision making • Lack of government funding • Lack of training in decision making related to frailty • Lack of vision or know-how on person-centred care • Unavailability of palliative care • Unavailability of community / primary care	• Skewed healthcare beliefs regarding end-of-life decision • Religion, philosophy, culture or tradition interfere with decision making • Family members or acquaintances may impose their views
Transplantation	• Perturbing inaccurate knowledge and beliefs • Socio-economic situation and inability to afford long-term medications • Racial/ ethnic/gender/ cultural inequities and differences • Concern for living donor (hesitancy to ask) • Dependence of caregivers and family support • Co-morbidities • Risk of recurrence of primary disease (e.g. aHUS) • Availability limited by need for matching • Child size limits transplantation possibilities	• Lack of government funding • Unavailability of transplant program • Unavailability of immunosuppression • Delayed nephrology referral and referral for transplantation • Lack of health literacy support for education regarding transplantation • Systemic racism • Lack of transplantation workup tests and protocols • Certain options (e.g. pediatric transplantation, living donation, organ exchange programs, cross-over	• Lack of awareness and community education regarding organ donation • Opt-in versus opt-out deceased organ donation policy • Inadequate organ allocation algorithms • Population disease burden • Centralisation of transplantation services to major metropolitan areas. • Government policies for financial support of living donors and recipients insufficient • Unavailability of transplantation registry • Cultural and legal restrictions

		programs, altruistic donation) not available • Presence of co-payments • Lack of transparent centralised organ allocation service • Unconscious/structural biases of healthcare providers, favouring patients of their own age, sex, and social and ethnic background	

*: Applies to all CKD care (also dialysis, transplantation, conservative care)

Table 2: Health-economic sources of inequity, depending on the country's financial status

Higher income countries*	Lower income countries
Selection bias in favor of health literate for home dialysis and transplantation leaving those remaining in-center at high risk of certain complications (e.g. COVID-19)	Countries with lower incomes invest proportionally more of their healthcare budget in (in-center) hemodialysis, making less funds available for measures that would benefit more people (e.g. prevention of CKD)
Higher uptake of peritoneal dialysis and home hemodialysis in wealthier countries	Unavailability of the therapeutic options with the lowest societal or out-of-pocket cost (prevention, transplantation, home dialysis) because of organizational or infrastructural problems
Lack of adequate screening and prevention programs creates a disadvantage for the deprived, health illiterate and minoritized communities who face barriers in obtaining health care	No or inadequate screening and prevention and no or inadequate education will cause large groups or regions to be missed out
Educational initiatives, if any, are not adapted to health illiteracy, culture, language	Educational initiatives, if any, are not adapted to health illiteracy, culture, language
Higher risk for employment loss and financial disadvantage for less educated and deprived if they suffer from NCDs including CKD	High risk of employment loss and financial disadvantage for less educated and deprived if they suffer from NCDs including CKD
Even if KRT is fully reimbursed, if there are remaining out-of-pocket costs these will be more problematic for the deprived (e.g. for transportation, medication co-payments) potentially leading to abandoning KRT	If KRT is not reimbursed, risk of impoverishment for patients and their families until all resources are exhausted and treatment must be abandoned
Even if KRT is fully reimbursed, if there is no global educational and financial support for approaches for early diagnosis and prevention of progression towards kidney failure, including preventive	Insufficient resources to pay or reimburse basic preventive medication (antihypertensives, antidiabetics) will especially harm the deprived

medication. Accordingly, deprived populations may be at higher risk of progression, because of fewer opportunities to make healthy choices	
Shortage of workforce for delivery of care will especially be felt by financially deprived	Shortage of workforce for delivery of care may be more substantial in lower income countries
	Medical technology (dialysis) not adapted to local conditions (heat, humidity), no possibilities for repair, no financial resources
	Two-tiered health care systems (public for the poor and private for the rich) are a basic form of inequity although not necessarily resulting in unequal quality of therapy)
	If no universal health care insurance, only the rich, the employed and certain classes (e.g. government officials) will be covered
	Money invested in reimbursement of dialysis cannot be invested in prevention
	The poor in lower income countries may be forced to sell their kidneys, and as a consequence may be victim of criminal, unethical or harmful practices

*: the dichotomy between higher and lower income country is artificial and only for illustrative reasons. There may also be exceptions to these general principles.

NCDs: non-communicable diseases; CKD: chronic kidney disease; KRT: kidney replacement therapy

Table 3: Examples of ethical dilemmas caused by structural inequities in nephrology

Case – by Level of Care	Sources of Inequity	Ethical Dilemmas Arising from Inequity
Primary Level		
Poor accesibility of primary care and preventative kidney care A 35-year-old mother of 3 from a poor rural farming background in a LIC was diagnosed with gestational diabetes, pre-eclampsia and proteinuria during her third pregnancy. At her postnatal check fingerstick blood glucose and BP were still elevated. She was advised to get HbA1c, urine albumin creatinine ratio and kidney function testing but these were not available in the primary healthcare center nearby. The woman’s family, not wanting to spend money on travel to a nearby city for care, instead took her to a traditional medicine practitioner. When the woman became too fatigued to carry out her household duties, she was brought to a referral hospital where diabetes, hypertension and proteinuria were confirmed. In addition to ACE inhibitors, SGLT2 inhibitors were considered. The medical team contemplated on enrolling her in a clinical trial of SGLT2 inhibitors but all studies required frequent clinic visits that were considered too burdensome for the family. The woman’s family decided to continue whatever care was available at the primary care center and in addition resumed traditional medicine.	• Poverty • Poor primary healthcare • Low health literacy • Discrimination against women • Effective medications too expensive • Inequitable inclusion in clinical trials • Cultural mistrust of regular medicine • Lack of universal health care	Adverse effect of Social Determinants of Health on Outcomes and the principle of Justice: • The woman’s social determinants of health (low socioeconomic status, sex and geographic location) very likely affected her possibilities to obtain primary care and prevention of progression of kidney disease. • Are these differences avoidable through better governance or change in circumstances (would a woman with the same disease living in a wealthy urban educated family have had better possibilities to obtainpreventative care?). If yes, then the inequality in outcome is unfair, and addressing this inequity is a moral imperative. Gender Discrimination • inclusion into clinical research and thus determination of efficacy of important preventive medications are unfairly biased against women who are pregnant or breastfeeding. This inequity must be addressed to improve outcomes.
Secondary Level		
Poor accesibility of early diagnosis and treatment		Poor prioritization of pediatric kidney disease

During an antenatal ultrasound of a 20-year-old woman's first pregnancy in an LMIC, a kidney and bladder anomaly of the fetus was suspected. Unable to travel to the maternal-fetal referral center 250 km away, she delivered a low birth weight male at home. The infant did not feed well, had a poor urinary stream and became progressively lethargic. At the primary health center, he received some antibiotics, improved and was discharged. After multiple similar admissions and persistent failure to thrive, at the age of one, he was referred to a private pediatric nephrology center 300 km away where the parents had to pay out-of-pocket for care. The possibilities for an effective treatment in the private center in that country were considered minimal. By this time the child already had growth failure, rickets, blood urea of 200mg/dL and a serum creatinine of 4mg/dL. At work-up a diagnosis of posterior urtheral valves (PUV) was made. The family was told about the need for expensive surgery to treat the PUV to salvage some kidney function and possibility of dialysis. Unable to afford care, they left against medical advice.	• Geographic remoteness • Poverty • Inadequate accessibility of effective maternal screening • Low awareness of pediatric kidney disease • Inadequate pediatric kidney care services • Poor public-private partnership rendering treatment unaffordable • Poor social services support for children • No accessibility of UHC	• In low resource settings, funding pediatric kidney disease detection (by good perinatal follow-up of structural anomalies) is of low priority for governments. Thus accessible public sector care is inadequate, resulting in late diagnosis, high morbidity and poor outcomes. Where UHC is absent, ability to pay determines outcomes • When specialized pediatric care is only available in the private sector, life-saving therapy is accessible only for those who can afford to pay. This violates the ethical principle of justice Parental refusal of treatment • Refusal of treatment by the parents is undoubtedly against the best interest of the child. However, given the expense to family should we consider the interests of the family as well? Patient families in LIC and LMIC often exhaust all their financial resources without reaching positive outcomes (no cure and no transplantation). This morally distressing question results from inequitable accessibility of care.
Tertiary Level		
Case 1: Rationing Dialysis A 50-year-old father of 3 with kidney failure due to type 2 diabetes in a MIC was assessed by the healthcare team for eligibility for the single remaining spot for government-funded maintenance dialysis. He was not considered a candidate for kidney transplantation due to his diabetes complications and was denied dialysis.	• Rationed availability of free or low cost dialysis • Age-based discrimination • Disease-based discrimination • Rationing policies favoring those with	Ethical challenges of rationing life-saving therapy • Rationing access to dialysis may result in biased unethical decisions based on prejudices related to age, sex, race or socioeconomic status • The patient's ability to exercise his autonomy to make treatment choices is constrained by (lack of) policy

Unable to pay for dialysis in the private sector, he was forced to accept palliative care. By policy, a younger patient with no comorbidities was deemed eligible instead.	highest likelihood of survival (utilitarianism)	- Forced rationing decisions result in moral distress amongst physicians forced to deny life-saving care to patients - Ensuring distributive justice (a fair, transparent, equitable priority-setting process with stakeholder input) is essential for policy makers but is rarely applied
Case 2: Inequitable global accessiblility of transplantation A 50-year-old wealthy man with kidney failure in a MIC desired kidney transplantation. There were no compatible living donors in his family and his native country had no deceased donor transplant program. He travelled to a private sector, for-profit hospital in a LMIC accompanied by a 50-year-old woman, from a lower socioeconomic background. The patient claimed she was a distant cousin. He requested living donor transplantation be performed and furnished a government certificate giving clearance for altruistic kidney donation. Communicating with the recipient and his donor was limited and required an interpreter. Paid donation was suspected but could not be proven. After the transplantation, the patient returned for care to his native country. The donor was never seen with the patient again and did not show up for follow-up care.	- Poor accessibility of deceased donor transplantation - Necessity for physicians to rely on living donation as only option for transplantation - Inadequate surveillance process and legal framework to prevent organ trafficking	Inequitable accessibilty of donor transplantation drives people to organ trade and unjustly exploits donors - Without UHC, transplantation is largely inaccessible to the poor - Although paying for donor evaluation and surgery to ensure financial neutrality is acceptable, offering donors financial gain is unethical and illegal - Trafficked donors have poor health and economic outcomes - Trafficked donors are often unfairly exploited by intermediary persons Organ trafficking remains a serious and prevalent problem despite global condemnation. - Nations may have a moral obligation to provide deceased donor transplantation services to their citizens - Nations have a major obligation to combat paid donation via legal and judiciary means, but this is often neglected - Preventing organ trafficking is a global responsibility but the burden of decision making unfairly falls most on healthcare providers.

Case 3: Caregiver burden A 15-year-old boy with PUV in a rural area of a HIC was initiated on PD in a city 450 km from his home. The indigenous family had owned a farm for 3 generations. His parents incurred high out-of-pocket costs for travel to a pediatric nephro-urology centre and lost income during monthly clinic visits. When his mother initiated work-up for a living donor transplantation, the hospital visits became more frequent. The family decided to sell their farm to move closer to the city where they had no family or friends. The mother stayed home to be the primary caregiver. The father relied on daily odd jobs, the family's income plunged and the existence of all centered around keeping the boy alive.	• Inadequate accesibility of pediatric focused KRT • Geographic remoteness reduces accessibilily of care • Poor support for living donor indirect costs • Caregivers not provided with enough social support	Caregiver burden worsened by socioeconomic and demographic factors • Patients in remote areas face unfair obstacles to accessing care and a greater financial burden. • It is unfair that caregivers of kidney failure patients be expected to shoulder these burdens • To satisfy the principle of justice and non-maleficence, clinicians might consider discussing these burdens with caregivers before beginning dialysis but this may lead to a difficult and uneasy conversation • The inequitable accessibility of care unfairly burdens indigenous populations, minorities and immigrants

HIC: high income country; LIC: Low income country; LMIC: low middle income country; MIC: middle income country; BP: blood pressure; HbA1C: hemoglobin A1C; PUV: posterior urethral valves; UHC: universal health care; PD: peritoneal dialysis; KRT: kidney replacement therapy

Case stories are based on the clinical experience of the authors.

Table 4: Opportunities for stakeholders to mitigate inequities

STAKEHOLDER GROUP	ATTENTION POINTS
Patients, patient organizations	- Raise patient voices - Raise awareness of CKD - Advocate for fair therapeutic price setting - Advocate to combat inequities - Facilitate empowerment and communication training - Include people from all origins and social classes in their activities
Nephrology professionals	- Self-awareness of own socio-cultural knowledge/communication limitations - Listen to patient voices - Favour patient empowerment - Increase advocacy efforts to draw appropriate attention to kidney diseases - Embed structural competency in the training process, including inequities and their mechanisms, and apply approaches to avoid those, e.g. by shunning racism and paying special attention to health illiteracy - Steer clear of therapeutic cherry picking - Use language translation - Increase diversity among nephrology work force - Share equipment and expertise with emerging countries
Nephrology societies	- Lead by example, ensure diverse and equitable global representation - Include local experts in guideline committees, decision-making, research calls - Include sessions devoted to equity in their meetings and congresses - Collect reliable data on disease burden, costs and inequities related to CKD - Generate a shift of mind from cure to screening and prevention, by engaging with policy makers, those involved in healthcare design, and funders - Achieve harmonization among countries by support and exchange of information - Create patient education materials adapted for language and culture - Advocate at regional and global level
General educators	- Ensure all children, both boys and girls, have access to quality education - Include health in education - Promote healthy lifestyle through education about food, exercise, smoking, alcohol etc - Provide healthful food and sport opportunities in schools

Medical educators	- Ensure diversity among educators - Include inequities in the educational curricula - Improve teaching about kidney diseases and especially their diagnosis and prevention - Consciously act as role models
Researchers, developers	- Develop therapeutic options that are affordable for all - Ensure that newly promoted approaches are made available and evaluated across subsets where inequities may occur - Prioritize research that focuses on equity and accessibility of kidney care in disadvantaged populations - Prioritize research on health illiteracy - Develop and study approaches to prevent CKD or progression of CKD - Be conscious of the risks of research in exacerbating inequities - Include patients with kidney diseases in clinical trials, including in non-kidney areas (e.g. cardiology, oncology) - Ensure diverse representation of patients included in clinical trials - Consider ethnic and sex/gender aspects in clinical trials, drug metabolism, patient reported outcomes
Pharmacological and medical technology sectors	- Develop therapeutic options that are affordable for all - Develop and study approaches to prevent CKD or progression of CKD - Being transparent on investments in therapy development and real cost of therapies - Apply fair prices and fair profit principles - Register and distribute therapeutic products (e.g. peritoneal dialysis fluids) in all countries
Governments, administrations, insurers	- Acknowledge CKD as a public health problem - Collect reliable data on disease burden, costs and inequities related to CKD to support priority setting - Negotiate fair price setting of medications - Favour affordable therapies and therapies with high value-for-money, without further exacerbation of inequities - Aim for progressive expansion of universal health coverage - Generate a shift of paradigm from focus on cure towards focus on screening and prevention - Achieve harmonization among countries by support and exchange of information - Apply reimbursement models that disincentivize cherry picking - Stimulate and finance research on health inequities and health illiteracy

Table 1 – Barriers to optimal kidney care

	Patient level (inherent to kidney diseases and care)	Health system level (inherent to organisation of healthcare)	Population level (inherent to environment)
Chronic Kidney Disease*	• Lack of symptoms in early stage kidney diseases • Lack of awareness of symptoms of kidney diseases • Late diagnosis of kidney disease due to lack of appropriate screening of those at risk • Late diagnosis of kidney disease due to long asymptomatic phase • Late start of measures to prevent kidney disease progression • Inadequate monitoring, surveillance and treatment • Poor health literacy associated with lower concordance with medications, clinical plans, dietary requirements • Instability of living environment (financial resources, housing, recreation facilities, freedom of persecution or war)	• Inadequate screening for kidney disease in at risk populations • Lack of funding of prevention • Unavailability or lack of reimbursement of kidney function tests • Shortage and brain drain of nephrologists and shortage of kidney centres • Lack of healthcare funding for expensive drugs • Limitation of healthcare provision or reimbursement to certain groups or certain therapeutic options • Lack of education of primary and secondary healthcare professionals regarding early signs of kidney disease and when to refer to specialist teams • No consideration of priorities and outcomes that matter to patients	• Lack of accessibility of healthy food, clean water, health facilities • Healthy diet and lifestyle may be unaffordable for some people • No financial incentives to stimulate healthy diet and lifestyle • Unhealthy or polluted living areas or working conditions • Working conditions in conflict with health needs (e.g. to attend check-up appointments) • Population burden of diabetes, obesity and hypertension is exacerbated by social dterminants of health • Inadequate dietary information for population, e.g., on salt intake • Religion, culture or tradition may interfere with optimal solutions for kidney health • Discrimination of race or minorities

	• Distrust, fear and misunderstanding of health professionals • Language barriers • Follow-up by (too) many healthcare providers due to multimorbidity • Competing complications and outcomes may disturb decision making • Difficult to treat symptoms (fatigue, itching) may disturb confidence in care providers • Chronic stress without sufficient adaptive oping strategies • Cognitive dysfunction, visual and hearing impairment, learning difficulties, mental illness) hamper decision making • Inability to pay for drugs • Expensive special diets • Potential loss of income attending outpatient clinics • Complexity of required decisions • Distrust of healthcare system • Fear of stigmatisation • Unavailability of personal health insurance	• Lack of training of healthcare professionals on how to provide culturally appropriate care and how to deal with discrimination, unconscious bias or health illiteracy • Lack of research and research funding on kidney health and care • Unavailability of structural health insurance (universal health insurance coverage)	• Lack of education of general population on kidney health and care

	• Non-adherence augmented in adolescents • Stigmatization		
Dialysis	• Inadequate accessibility of pre-dialysis nephrology care • Inability to engage in decision making regarding choices / health illiteracy • Ageing and frailty • Dependence on family and social support which is not always available • Inability to pay out-of-pocket expenses • Distance from kidney centre • Certain options (home hemodialysis, peritoneal dialysis, self-care) not available • Long-term dependence on life-saving treatment as cause of lack of adherence • Accesibility problems in humanitarian crises (wars, refugees, undocumented migrants) • Child size limits dialysis possibilities	• Availability of dialysis facilities • Government funding • Education of healthcare providers about dialysis options • Number of nephrologists and specialist dialysis nurses • Availability of multi-professional teams for psychosocial support • Availability of dialysis-related drugs e.g., erythropoietin • Insufficient possibilities to diagnose, prevent and treat acute kidney injury • Unconscious/structural biases of healthcare providers, favouring patients of their own age, sex, and social and ethnic background • Limitation in availability of dialysis modalities – PD and HD variably accessible	• Lack of awareness of dialysis options • Lack of medical support for comorbidities • Lack of welfare support for patients • Urban vs. rural living area • Geographic distribution of dialysis centers

Conservative care	• Inadequate accessibility of pre-dialysis nephrology care • Inability to engage in decision making regarding choices / health literacy • Dependence on family and social support which is not always available • Cultural / religious beliefs perturbing decision making • Lack of training of health care workers	• Lack of respect for patient autonomy and shared decision making • Lack of government funding • Lack of training in decision making related to frailty • Lack of vision or know-how on person-centred care • Unavailability of palliative care • Unavailability of community / primary care	• Skewed healthcare beliefs regarding end-of-life decision • Religion, philosophy, culture or tradition interfere with decision making • Family members or acquaintances may impose their views
Transplantation	• Perturbing inaccurate knowledge and beliefs • Socio-economic situation and inability to afford long-term medications • Racial/ ethnic/gender/ cultural inequities and differences • Concern for living donor (hesitancy to ask) • Dependence of caregivers and family support • Co-morbidities • Risk of recurrence of primary disease (e.g. aHUS) • Availability limited by need for matching • Child size limits transplantation possibilities	• Lack of government funding • Unavailability of transplant program • Unavailability of immunosuppression • Delayed nephrology referral and referral for transplantation • Lack of health literacy support for education regarding transplantation • Systemic racism • Lack of transplantation workup tests and protocols • Certain options (e.g. pediatric transplantation, living donation, organ exchange programs, cross-over	• Lack of awareness and community education regarding organ donation • Opt-in versus opt-out deceased organ donation policy • Inadequate organ allocation algorithms • Population disease burden • Centralisation of transplantation services to major metropolitan areas. • Government policies for financial support of living donors and recipients insufficient • Unavailability of transplantation registry • Cultural and legal restrictions

		programs, altruistic donation) not available • Presence of co-payments • Lack of transparent centralised organ allocation service • Unconscious/structural biases of healthcare providers, favouring patients of their own age, sex, and social and ethnic background	

*: Applies to all CKD care (also dialysis, transplantation, conservative care)

Table 2: Health-economic sources of inequity, depending on the country's financial status

Higher income countries*	Lower income countries
Selection bias in favor of health literate for home dialysis and transplantation leaving those remaining in-center at high risk of certain complications (e.g. COVID-19)	Countries with lower incomes invest proportionally more of their healthcare budget in (in-center) hemodialysis, making less funds available for measures that would benefit more people (e.g. prevention of CKD)
Higher uptake of peritoneal dialysis and home hemodialysis in wealthier countries	Unavailability of the therapeutic options with the lowest societal or out-of-pocket cost (prevention, transplantation, home dialysis) because of organizational or infrastructural problems
Lack of adequate screening and prevention programs creates a disadvantage for the deprived, health illiterate and minoritized communities who face barriers in obtaining health care	No or inadequate screening and prevention and no or inadequate education will cause large groups or regions to be missed out
Educational initiatives, if any, are not adapted to health illiteracy, culture, language	Educational initiatives, if any, are not adapted to health illiteracy, culture, language
Higher risk for employment loss and financial disadvantage for less educated and deprived if they suffer from NCDs including CKD	High risk of employment loss and financial disadvantage for less educated and deprived if they suffer from NCDs including CKD
Even if KRT is fully reimbursed, if there are remaining out-of-pocket costs these will be more problematic for the deprived (e.g. for transportation, medication co-payments) potentially leading to abandoning KRT	If KRT is not reimbursed, risk of impoverishment for patients and their families until all resources are exhausted and treatment must be abandoned
Even if KRT is fully reimbursed, if there is no global educational and financial support for approaches for early diagnosis and prevention of progression towards kidney failure, including preventive	Insufficient resources to pay or reimburse basic preventive medication (antihypertensives, antidiabetics) will especially harm the deprived

medication. Accordingly, deprived populations may be at higher risk of progression, because of fewer opportunities to make healthy choices	
Shortage of workforce for delivery of care will especially be felt by financially deprived	Shortage of workforce for delivery of care may be more substantial in lower income countries
	Medical technology (dialysis) not adapted to local conditions (heat, humidity), no possibilities for repair, no financial resources
	Two-tiered health care systems (public for the poor and private for the rich) are a basic form of inequity although not necessarily resulting in unequal quality of therapy)
	If no universal health care insurance, only the rich, the employed and certain classes (e.g. government officials) will be covered
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*: the dichotomy between higher and lower income country is artificial and only for illustrative reasons. There may also be exceptions to these general principles.

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Table 3: Examples of ethical dilemmas caused by structural inequities in nephrology

Case – by Level of Care	Sources of Inequity	Ethical Dilemmas Arising from Inequity
Primary Level		
<u>Poor accesibility of primary care and preventative kidney care</u> A 35-year-old mother of 3 from a poor rural farming background in a LIC was diagnosed with gestational diabetes, pre-eclampsia and proteinuria during her third pregnancy. At her postnatal check fingerstick blood glucose and BP were still elevated. She was advised to get HbA1c, urine albumin creatinine ratio and kidney function testing but these were not available in the primary healthcare center nearby. The woman's family, not wanting to spend money on travel to a nearby city for care, instead took her to a traditional medicine practitioner. When the woman became too fatigued to carry out her household duties, she was brought to a referral hospital where diabetes, hypertension and proteinuria were confirmed. In addition to ACE inhibitors, SGLT2 inhibitors were considered. The medical team contemplated on enrolling her in a clinical trial of SGLT2 inhibitors but all studies required frequent clinic visits that were considered too burdensome for the family. The woman's family decided to continue whatever care was available at the primary care center and in addition resumed traditional medicine.	• Poverty • Poor primary healthcare • Low health literacy • Discrimination against women • Effective medications too expensive • Inequitable inclusion in clinical trials • Cultural mistrust of regular medicine • Lack of universal health care	<u>Adverse effect of Social Determinants of Health on Outcomes and the principle of Justice:</u> • The woman's social determinants of health (low socioeconomic status, sex and geographic location) very likely affected her possibilities to obtain primary care and prevention of progression of kidney disease. • Are these differences avoidable through better governance or change in circumstances (would a woman with the same disease living in a wealthy urban educated family have had better possibilities to obtainpreventative care?). If yes, then the inequality in outcome is unfair, and addressing this inequity is a moral imperative. <u>Gender Discrimination</u> • inclusion into clinical research and thus determination of efficacy of important preventive medications are unfairly biased against women who are pregnant or breastfeeding. This inequity must be addressed to improve outcomes.
Secondary Level		
<u>Poor accesibility of early diagnosis and treatment</u>		<u>Poor prioritization of pediatric kidney disease</u>

During an antenatal ultrasound of a 20-year-old woman's first pregnancy in an LMIC, a kidney and bladder anomaly of the fetus was suspected. Unable to travel to the maternal-fetal referral center 250 km away, she delivered a low birth weight male at home. The infant did not feed well, had a poor urinary stream and became progressively lethargic. At the primary health center, he received some antibiotics, improved and was discharged. After multiple similar admissions and persistent failure to thrive, at the age of one, he was referred to a private pediatric nephrology center 300 km away where the parents had to pay out-of-pocket for care. The possibilities for an effective treatment in the private center in that country were considered minimal. By this time the child already had growth failure, rickets, blood urea of 200mg/dL and a serum creatinine of 4mg/dL. At work-up a diagnosis of posterior urtheral valves (PUV) was made. The family was told about the need for expensive surgery to treat the PUV to salvage some kidney function and possibility of dialysis. Unable to afford care, they left against medical advice.	• Geographic remoteness • Poverty • Inadequate accessibility of effective maternal screening • Low awareness of pediatric kidney disease • Inadequate pediatric kidney care services • Poor public-private partnership rendering treatment unaffordable • Poor social services support for children • No accessibility of UHC	• In low resource settings, funding pediatric kidney disease detection (by good perinatal follow-up of structural anomalies) is of low priority for governments. Thus accessible public sector care is inadequate, resulting in late diagnosis, high morbidity and poor outcomes. Where UHC is absent, ability to pay determines outcomes • When specialized pediatric care is only available in the private sector, life-saving therapy is accessible only for those who can afford to pay. This violates the ethical principle of justice Parental refusal of treatment • Refusal of treatment by the parents is undoubtedly against the best interest of the child. However, given the expense to family should we consider the interests of the family as well? Patient families in LIC and LMIC often exhaust all their financial resources without reaching positive outcomes (no cure and no transplantation). This morally distressing question results from inequitable accessibility of care.
Tertiary Level		
Case 1: Rationing Dialysis A 50-year-old father of 3 with kidney failure due to type 2 diabetes in a MIC was assessed by the healthcare team for eligibility for the single remaining spot for government-funded maintenance dialysis. He was not considered a candidate for kidney transplantation due to his diabetes complications and was denied dialysis.	• Rationed availability of free or low cost dialysis • Age-based discrimination • Disease-based discrimination • Rationing policies favoring those with	Ethical challenges of rationing life-saving therapy • Rationing access to dialysis may result in biased unethical decisions based on prejudices related to age, sex, race or socioeconomic status • The patient's ability to exercise his autonomy to make treatment choices is constrained by (lack of) policy

Unable to pay for dialysis in the private sector, he was forced to accept palliative care. By policy, a younger patient with no comorbidities was deemed eligible instead.	highest likelihood of survival (utilitarianism)	• Forced rationing decisions result in moral distress amongst physicians forced to deny life-saving care to patients • Ensuring distributive justice (a fair, transparent, equitable priority-setting process with stakeholder input) is essential for policy makers but is rarely applied
Case 2: Inequitable global accessiblility of transplantation A 50-year-old wealthy man with kidney failure in a MIC desired kidney transplantation. There were no compatible living donors in his family and his native country had no deceased donor transplant program. He travelled to a private sector, for-profit hospital in a LMIC accompanied by a 50-year-old woman, from a lower socioeconomic background. The patient claimed she was a distant cousin. He requested living donor transplantation be performed and furnished a government certificate giving clearance for altruistic kidney donation. Communicating with the recipient and his donor was limited and required an interpreter. Paid donation was suspected but could not be proven. After the transplantation, the patient returned for care to his native country. The donor was never seen with the patient again and did not show up for follow-up care.	• Poor accessibility of deceased donor transplantation • Necessity for physicians to rely on living donation as only option for transplantation • Inadequate surveillance process and legal framework to prevent organ trafficking	Inequitable accessibilty of donor transplantation drives people to organ trade and unjustly exploits donors • Without UHC, transplantation is largely inaccessible to the poor • Although paying for donor evaluation and surgery to ensure financial neutrality is acceptable, offering donors financial gain is unethical and illegal • Trafficked donors have poor health and economic outcomes • Trafficked donors are often unfairly exploited by intermediary persons Organ trafficking remains a serious and prevalent problem despite global condemnation. • Nations may have a moral obligation to provide deceased donor transplantation services to their citizens • Nations have a major obligation to combat paid donation via legal and judiciary means, but this is often neglected • Preventing organ trafficking is a global responsibility but the burden of decision making unfairly falls most on healthcare providers.

Case 3: Caregiver burden A 15-year-old boy with PUV in a rural area of a HIC was initiated on PD in a city 450 km from his home. The indigenous family had owned a farm for 3 generations. His parents incurred high out-of-pocket costs for travel to a pediatric nephro-urology centre and lost income during monthly clinic visits. When his mother initiated work-up for a living donor transplantation, the hospital visits became more frequent. The family decided to sell their farm to move closer to the city where they had no family or friends. The mother stayed home to be the primary caregiver. The father relied on daily odd jobs, the family's income plunged and the existence of all centered around keeping the boy alive.	• Inadequate accesibility of pediatric focused KRT • Geographic remoteness reduces accessibilily of care • Poor support for living donor indirect costs • Caregivers not provided with enough social support	Caregiver burden worsened by socioeconomic and demographic factors • Patients in remote areas face unfair obstacles to accessing care and a greater financial burden. • It is unfair that caregivers of kidney failure patients be expected to shoulder these burdens • To satisfy the principle of justice and non-maleficence, clinicians might consider discussing these burdens with caregivers before beginning dialysis but this may lead to a difficult and uneasy conversation • The inequitable accessibility of care unfairly burdens indigenous populations, minorities and immigrants

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Case stories are based on the clinical experience of the authors.

Table 4: Opportunities for stakeholders to mitigate inequities

STAKEHOLDER GROUP	**ATTENTION POINTS**
Patients, patient organizations	- Raise patient voices - Raise awareness of CKD - Advocate for fair therapeutic price setting - Advocate to combat inequities - Facilitate empowerment and communication training - Include people from all origins and social classes in their activities
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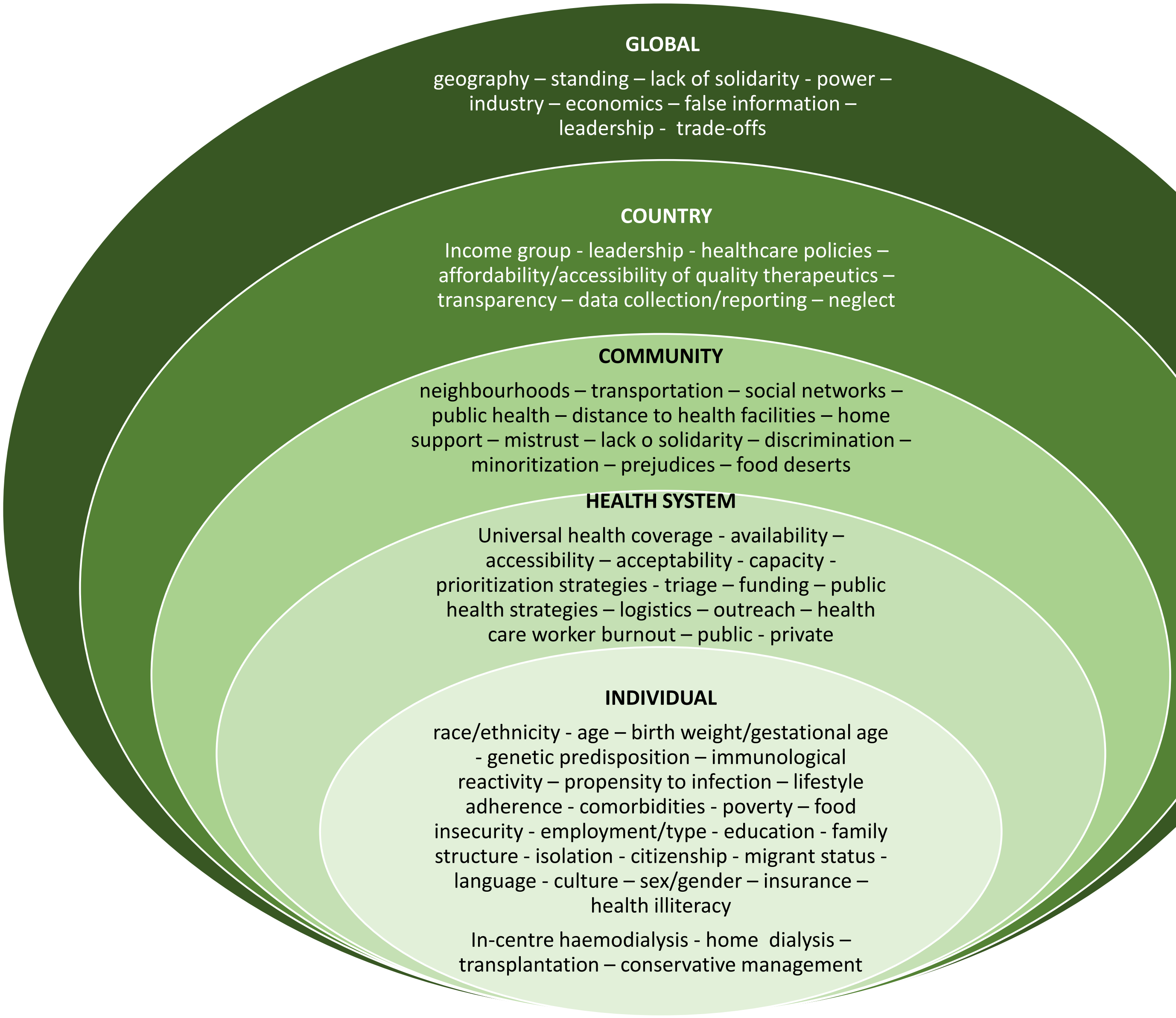
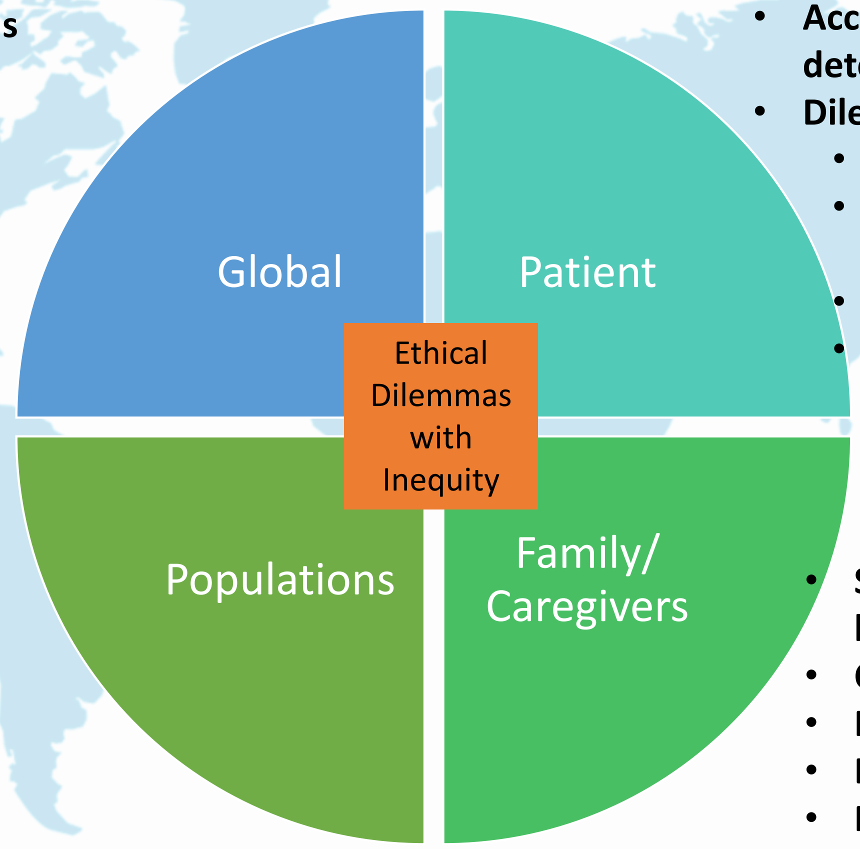
Nephrology societies	- Lead by example, ensure diverse and equitable global representation - Include local experts in guideline committees, decision-making, research calls - Include sessions devoted to equity in their meetings and congresses - Collect reliable data on disease burden, costs and inequities related to CKD - Generate a shift of mind from cure to screening and prevention, by engaging with policy makers, those involved in healthcare design, and funders - Achieve harmonization among countries by support and exchange of information - Create patient education materials adapted for language and culture - Advocate at regional and global level
General educators	- Ensure all children, both boys and girls, have access to quality education - Include health in education - Promote healthy lifestyle through education about food, exercise, smoking, alcohol etc - Provide healthful food and sport opportunities in schools

Medical educators	- Ensure diversity among educators - Include inequities in the educational curricula - Improve teaching about kidney diseases and especially their diagnosis and prevention - Consciously act as role models
Researchers, developers	- Develop therapeutic options that are affordable for all - Ensure that newly promoted approaches are made available and evaluated across subsets where inequities may occur - Prioritize research that focuses on equity and accessibility of kidney care in disadvantaged populations - Prioritize research on health illiteracy - Develop and study approaches to prevent CKD or progression of CKD - Be conscious of the risks of research in exacerbating inequities - Include patients with kidney diseases in clinical trials, including in non-kidney areas (e.g. cardiology, oncology) - Ensure diverse representation of patients included in clinical trials - Consider ethnic and sex/gender aspects in clinical trials, drug metabolism, patient reported outcomes
Pharmacological and medical technology sectors	- Develop therapeutic options that are affordable for all - Develop and study approaches to prevent CKD or progression of CKD - Being transparent on investments in therapy development and real cost of therapies - Apply fair prices and fair profit principles - Register and distribute therapeutic products (e.g. peritoneal dialysis fluids) in all countries
Governments, administrations, insurers	- Acknowledge CKD as a public health problem - Collect reliable data on disease burden, costs and inequities related to CKD to support priority setting - Negotiate fair price setting of medications - Favour affordable therapies and therapies with high value-for-money, without further exacerbation of inequities - Aim for progressive expansion of universal health coverage - Generate a shift of paradigm from focus on cure towards focus on screening and prevention - Achieve harmonization among countries by support and exchange of information - Apply reimbursement models that disincentivize cherry picking - Stimulate and finance research on health inequities and health illiteracy


GLOBAL
geography – standing – lack of solidarity - power – industry – economics – false information – leadership - trade-offs
COUNTRY
Income group - leadership - healthcare policies – affordability/accessibility of quality therapeutics – transparency – data collection/reporting – neglect
COMMUNITY
neighbourhoods – transportation – social networks – public health – distance to health facilities – home support – mistrust – lack o solidarity – discrimination – minoritization – prejudices – food deserts
HEALTH SYSTEM
Universal health coverage - availability – accessibility – acceptability - capacity - prioritization strategies - triage – funding – public health strategies – logistics – outreach – health care worker burnout – public - private
INDIVIDUAL
race/ethnicity - age – birth weight/gestational age - genetic predisposition – immunological reactivity – propensity to infection – lifestyle adherence - comorbidities - poverty – food insecurity - employment/type - education - family structure - isolation - citizenship - migrant status - language - culture – sex/gender – insurance – health illiteracy
In-centre haemodialysis - home dialysis – transplantation – conservative management

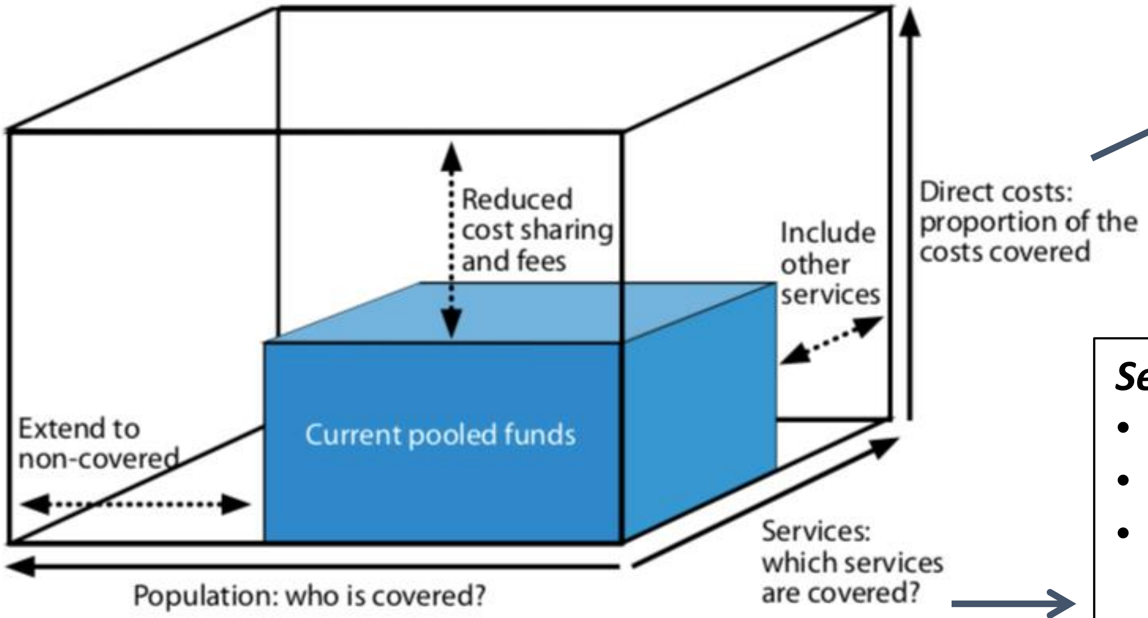
- Recognition of kidney disease as important NCD
- Need for moral responsibility
    - Global solidarity amongst patients and providers
    - Prevent brain drain
    - Develop a ‘global’ moral theory of kidney care?



- Accessibility
  determines
- Dilemmas in
    - Benefic
    - Real wo
      autono
    - Shared
    - Palliativ

- Inequitable distribution of risk factors for kidney disease
- Decision-making driven by healthcare systems
    - National expenditure on health
    - Social, distributive justice
    - Moral Distress with rationing

- Social det
  burden
- CHE leads
- Family fac
- Disparate
- Need for



Financing?
- **Priority settin**
  - **Transpare**
  - **Accounta**
- **Sustainability**
- **Quality of car**

Services to be provided?
- **Prevention - YES**
- **Primary care – YES**
- **Dialysis – YES/NO?**
  - Moral dilemmas i
    - AKI vs. CKD v
    - Adult vs. Chi
    - No comorbic
    - Employed or
    - Transplantab
    - Transparent
  - **Transplantation -**
    - If financially

Is kidney disease a priority*?
- **AKI – probably**
- **CKD not on KRT - probably**
- **KRT – if sustainable, yes, but currently expensive and technically difficult; risk of CHE high if not reimbursed**