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Chronic Kidney Disease and the Global Public Health Agenda: An International Consensus

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Abstract

Early detection is a key strategy to prevent kidney disease, its progression, and related complications, but numerous studies show that awareness of kidney disease at the population level is low. Therefore, increasing knowledge and implementing sustainable solutions for early detection of kidney disease are public health priorities. Economic and epidemiological data underscore why kidney disease should be placed on the global public health agenda — kidney disease prevalence is increasing worldwide, and it is now the 7th leading risk factor for mortality worldwide. Moreover, demographic trends, the obesity epidemic and the sequelae of climate change are all likely to increase kidney disease prevalence further, with serious implications for survival, quality-of-life, and healthcare spending worldwide. Importantly, the burden of kidney disease is highest among historically disadvantaged populations that often have limited access to optimal kidney disease therapies, greatly contributing to current socioeconomic disparities in health outcomes. This joint statement from the International Society of Nephrology (ISN), European Renal Association (ERA), and American Society of Nephrology (ASN), supported by three other regional nephrology societies, advocates for the inclusion of kidney disease in the current World Health Organisation (WHO) statement on major NCD drivers of premature mortality.

[H1] INTRODUCTION

In 2015, United Nations member states agreed on the ambitious Sustainable Development Goals (SDGs), with the aim to end poverty and inequality, protect the planet and ensure that all people enjoy health, justice and prosperity. An important health-related target is the reduction of non-communicable disease (NCD)-related mortality by one-third by 2030.[1] The World Health Organization (WHO) has listed heart disease, stroke, cancer, diabetes and chronic lung disease as the five major NCDs driving premature death and disability.[2] Notably absent from this list is kidney disease, either acute kidney injury (AKI) or chronic kidney disease (CKD); of note, AKI increases the risk of CKD and vice versa.[3-6]. Additionally, kidney disease commonly occurs with and enhances the risks of major NCDs such as ischaemic heart disease, stroke and peripheral vascular disease, diabetes and cancer.[7,8]

Approximately 850 million people worldwide are estimated to have kidney disease, most of whom live in low-income and lower-middle-income countries (LICs and LMICs), and a large proportion of these individuals lack access to kidney disease diagnosis, prevention or treatment. [9] As many as 9 out of 10 individuals with CKD in resource-poor settings with weak primary care infrastructure are unaware that they have this condition and therefore do not seek treatment.[10-12] Ageing populations and population growth will translate to large increases in the prevalence of CKD in LICs and LMICs in the coming decades. In contrast to cardiovascular disease, stroke, and respiratory disease, CKD mortality has been rising. Currently, kidney disease is the third fastest-growing cause of death globally and the only NCD to exhibit a continued rise in age-adjusted mortality.[13] By 2040, CKD is projected to be the 5th highest cause of years of life lost (YLL) globally.[14]

Population growth, ageing and the increasing burden of diabetes, heart disease, and hypertension are the best-recognised drivers of CKD incidence, especially in regions with advanced economies. As many as 1 in 3 people with diabetes and 1 in 5 with hypertension in high-income countries (HICs) have CKD, which has led to the suggestion that focusing on the control of diabetes and cardiovascular disease will alleviate the growing burden of CKD.[15] This assumption is based on the premise that screening for CKD is part of the standard of care for these conditions and that no special interventions are required in those

with kidney diseases. However, CKD and AKI have diverse causes, mediators and risk factors beyond diabetes and cardiovascular disease (Figure 1), especially in LICs and LMICs, which account for two-thirds of the global burden of kidney disease.[16] For example, dehydration and infections are leading causes of AKI in LICs and LMICs.[17] Finally, the latest research shows that CKD and AKI require unique treatments and are not merely risk enhancers when they accompany other major NCDs.

In this Consensus Statement, we discuss the unique environmental, social and medical drivers of kidney diseases, highlighting how tackling diabetes and heart disease alone will not target the core drivers of a large proportion of kidney diseases. We also discuss how such an approach worsens global inequities in access to the best attainable standards of health and hinders progress towards targets identified in the SDGs, making the absence of kidney disease from the global NCD health agenda morally indefensible and a substantial challenge to tackling the growing kidney disease burden.

[H1] METHODS

The International Society of Nephrology (ISN), European Renal Association (ERA) and the American Society of Nephrology (ASN) convened a diverse core group of 19 experts representing high and low-income countries in the Americas, Africa, Europe and Asia-Pacific, across adult and paediatric nephrology. Over several meetings, the authorship team discussed current and future challenges, as well as strategies for increasing global awareness of CKD and decreasing its global impact, to develop this Consensus Statement and recommendations. The manuscript was reviewed by various regional representative bodies (ISN Regional Boards), and consensus was attained. The ISN has established a Regional Board in each of its 10 regions — Africa, Eastern and Central Europe, Latin America and the Caribbean, Middle East, New Independent States and Russia, North America and the Caribbean, North and East Asia, Oceania and Southeast Asia, South Asia and Western Europe. The Regional Boards have representation from all affiliated societies within the region and are a major link between the ISN and National Societies of Nephrology.

Endorsement was also provided by other major global and regional societies, namely the Asian Pacific Society of Nephrology (APSN), African Association of Nephrology (AFRAN), Latin American Society of Nephrology and Hypertension (SLANH) and the World Heart Federation (WHF).

[H1] KIDNEY DISEASE IS A GROWING GLOBAL PROBLEM

Kidney disease is an increasing global problem that disproportionately affects poor, vulnerable and marginalised populations, and is associated with high individual, healthcare, and social costs. Approximately 700 million people are estimated to have CKD worldwide. To this must be added the global burden of AKI and kidney failure (including those receiving dialysis and kidney transplant recipients), increasing the global prevalence of kidney disease to around 850 million[7,9], which translates to a global prevalence > 10%. Of note, this prevalence is probably an underestimate owing to the lack of early kidney disease detection and screening programs in many parts of the world, which results in large-scale unawareness of the burden and prevalence of earlier stages of CKD.[11].

AKI affects 7–18% of hospitalized patients and 20–200 per million individuals annually in the community.[18] AKI is most common in LICs and LMICs, where 75% of cases are community-acquired owing to infections, toxins (for example, from animal bites, herbs and medications) and pregnancy complications.[19,20] According to a systematic review, an estimated 13.3 million cases of AKI are recorded worldwide every year, with LICs and LMICs countries contributing 11.3 million.[21] Of the 1.7 million deaths per year from AKI globally, an estimated 1.4 million occur in LICs and LMICs.[18].

Furthermore, the burden of kidney disease is rising worldwide. According to the Global Burden of Disease (GBD) study, the global prevalence of CKD increased by 33% between 1990 and 2017 [7]. Crucially, the greatest growth in the burden of CKD (prevalence and mortality) is concentrated outside of HICs, with almost one-third of all patients with CKD living in India and China alone.[7] Beyond population dynamics, numerous other social, environmental and economic threats increase the global risk of kidney disease. (Figure 1)

Given its increasing prevalence, if CKD remains largely undetected and is consequently not treated, the numbers of people developing kidney failure and requiring expensive kidney replacement therapy (KRT) will naturally increase. In 2010, ~2.6 million people received KRT, and this number is estimated to increase to 5.4 million by 2030.[22] Even in HICs, 15–20% of patients die within 12 months of starting dialysis. [23] Millions more develop kidney failure and require KRT but lack access to therapy and die prematurely.[24,25] Almost all of these people live in LICs and LMICs, which have only 7% of the global KRT population despite comprising 48% of the world population.[24] AKI and progressive CKD are also associated with high mortality even before the development of kidney failure, primarily owing to an increased risk of other major co-morbidities.[7,18] A greater number of people die of cardiovascular disease directly attributable to reduced kidney function than of kidney failure-related deaths [26], with the GBD study attributing ~3.1 million deaths in 2019 to kidney dysfunction.

[H2] Population dynamics will increase the burden of kidney disease

Population dynamics are increasing the numbers of people at high risk of kidney disease but with limited access to kidney care. This effect is driven both by population growth and an ageing population. Population growth is booming in LICs and LMICs (especially in Africa and India) — Central and Southern Asia, Eastern and South-Eastern Asia, and sub-Saharan Africa are expected to hold 70% of the world's population by 2030. [27,28] The age-standardized rate of CKD has already increased by 3–5% between 1990 and 2017 in countries in the lowest three sociodemographic index quintiles.[7] The highest growth in the number of people requiring KRT is projected for Africa, where 23 of the 28 poorest countries in the world are located.[22] Policies aimed at decreasing the burden of other NCDs that do not target CKD in these countries will generate an additional CKD burden. The reasons for the increased risk of CKD in LICs and LMICs are explored further below.

An ageing population faces an inherently increased risk of kidney disease. Current predictions estimate that by 2035, 1.1 billion people will be over 65 years of age, an increase of 60% from 2020 [27], with the largest number of older individuals expected to be in China and India. The controversies with regard to age-adjusted definition of CKD notwithstanding,

the rising prevalence of CKD translates to an increased risk of adverse outcomes in individuals in all age groups.[29-31] The loss of kidney reserve with ageing also exacerbates the bidirectional interplay between AKI and progressive CKD risk.[32] Moreover, CKD is associated with inflammation and accelerated whole-body ageing, particularly of the cardiovascular system, thereby increasing the burden of ageing-associated health decline even in younger patients.[33] [22]

[H2] Environmental and social threats to kidney health continue to rise

The burden of CKD risk factors that traditionally drive disease in HICs, such as diabetes, hypertension and obesity, is growing most rapidly in LICs and LMICs. Moreover, LICs and LMICs face a constellation of additional risks that translate to a greater kidney disease burden than that seen in HICs.[16] Risks related to environmental change, including global warming, environmental toxins, air pollution and declining biodiversity are global. However, the lack of capacity and resources for mitigation and adaptation makes LIC and LMIC populations particularly vulnerable to such risks. These populations also continue to have high rates of infectious diseases, many of which affect the kidneys.[19,34,35]. The lack of resources in these countries means that the contribution of local CKD risk factors is not as well-studied as those related to diabetes or cardiovascular disease that were first recognised in HICs, which leads to their continued under-recognition. Superimposed on this background, limited public health architecture and high poverty levels create life-course threats to kidney health, with a particular impact on pregnancy and childhood.

Fragile and underfunded health systems struggle to cope with the burden of kidney disease, leading to high and increasing mortality. Regional variations in the distribution of risk factors and the ability to implement adaptation measures mean that, in some places, CKD is an even bigger threat than that observed at a global level. For example, in Central America, CKD is the second most common cause of death.[7] Even in HICs, social determinants of health and factors such as gender, race or ethnicity influence the risk of kidney disease and underscore many health outcome disparities.[36-39] Race, for example, is increasingly recognized as a social construct, highlighting that its impact on kidney health is potentially modifiable.[40]

Environmental factors and climate instability contribute to the increased risk of kidney disease globally.[41] The GBD team estimated that in 2019, as many as 8% of deaths due to CKD were attributable to non-optimal (high or low) ambient temperatures.[42] For example, persistent exposure to high temperatures, particularly for agricultural and outdoor workers in LICs and LMICs who lack access to adaptation interventions, increase heat stress, which exacerbates the risk of kidney disease [43-46]. Heat stress is a potential contributor to CKD of unknown cause (CKDu) in agricultural communities, which is increasingly recognized as a major global cause of CKD. This condition is characterized by the presence of a benign urinary sediment and tubulointerstitial changes on biopsy.[47] Proposed mechanisms include recurrent heat stress with repeated episodes of AKI and exposure to environmental toxins, including pesticides and heavy metals.[48-51] Also known as CKD of non-traditional cause (CKD-NT), chronic interstitial nephritis in agricultural communities (CINAC), Mesoamerican nephropathy and Uddanam Nephropathy, CKDu has been seen largely in the Global South, including India, Sri Lanka, parts of Africa and Central and South America. [49,51,52] One study of people with CKDu in India found worsening of metabolic acidosis and hypertension in Summer compared with Winter, supporting the hypothesis that a warming planet also threatens kidney health.[50] Increasing salinity of drinking water in coastal areas of Bangladesh affected by rising sea levels has also been linked to increased rates of preeclampsia and gestational hypertension, in addition to hypertension and albuminuria in the general population, all of which are risk factors for subsequent kidney disease. [53-55] Furthermore, large population studies suggest rises in fine particulate matter in the air are associated with an increased risk of AKI, as well as CKD prevalence and progression. [56-58]

Climate change will also affect water availability. Since 2000, the global frequency and duration of drought have increased by nearly 30%.[59]. In the context of profound drought, current haemodialysis options are not environmentally sustainable, as the average haemodialysis treatment uses >500 litres of water.[60] Emergencies such as extreme climate events (drought, snowstorms, floods and fires), natural disasters such as the earthquakes in Turkey and Syria, and floods in Pakistan, and man-made disasters like wars and conflicts all impact the ability of patients with kidney disease to access and receive lifesaving treatment

such as haemodialysis or kidney transplantation, thereby endangering lives.[61-63] Notably, extreme events can also directly cause kidney injury, such as mass rhabdomyolysis from crush injuries caused by earthquakes.[64]

Threats to kidney health vary across the lifespan. In low-resource and underprivileged settings, maternal factors such as malnutrition, poor health literacy and comorbidity burden contribute to an adverse uterine environment.[65] Mothers in low-resource settings are more likely to give birth to children who are small for gestational age (SGA), have low birth weight (LBW) and or are born prematurely than those in high-resource settings.[66] Importantly, numerous large population studies show that SGA, LBW and prematurity increase the risk for the infant developing proteinuria, hypertension, CKD and kidney failure in later life.[67-73] This risk seems to be mediated through multiple mechanisms, with low nephron endowment owing to suboptimal growth in utero increasing susceptibility to kidney injury later in life.[74] Poor maternal nutrition, which despite improvements remains substantially prevalent in large parts of the world, also increases the risk of gestational diabetes and hypertension, both of which are known risk factors for CKD.[65] Poor infant and childhood nutrition, as well as childhood AKI events related to infections, superimpose additional layers of risk to kidney health across the lifespan.[65]

Although kidney diseases are commonly grouped with other NCDs, infections are also important causes of AKI in LICs and LMICs, either through direct kidney involvement (for example in cases of leptospirosis or HIV infection) or indirectly through haemodynamic mechanisms, systemic inflammatory responses or infection-related glomerulonephritis.[19,35,75] The adverse kidney effects of infections in LICs and LMICs are exacerbated by decreased access to specialized care, especially in areas endemic for diseases such as malaria, leptospirosis, scrub typhus, hemorrhagic fevers, or dengue, and for children or adults with severe gastrointestinal fluid loss.[76,77]. AKI is associated with increased morbidity and mortality and affects all age groups, from neonates to older individuals. Continued high mortality due to childhood AKI in the absence of dialysis prompted the ISN to introduce the

Saving Young Lives Program in collaboration with the International Society of Peritoneal Dialysis (ISPD), European Peritoneal Dialysis (EuroPD), and the International Pediatric Nephrology Association (IPNA) to promote peritoneal dialysis in Africa, later expanded to Asia and Latin America [78] However, this program is just scratching the surface with regard to addressing the KRT needs of people with AKI in these regions.

Climate change and loss of global biodiversity are also increasing the risk of infectious diseases that predispose to AKI and CKD outside of current tropical areas as the climate becomes more conducive to the survival of parasites (for example, those causing malaria or schistosomiasis) and/or their vectors (for example, mosquitoes or ticks).[41] Of note, although the association between certain infections and AKI is well known, the role of infections in the development and/or progression of CKD is not well studied. However, emerging data suggest that leptospirosis might contribute to the development of CKDu or increase susceptibility to triggers such as heat stress.[79-81]

Globally, multifactorial social determinants of health influence kidney health profoundly. Indigenous populations, people living in rural areas, migrants, older individuals or those affected by poverty, homelessness and food insecurity are more likely to be affected by kidney disease and develop its worst manifestations [36-38,82,83]. For example, underprivileged people with CKD are more likely to experience rapid progression of disease.[84] Importantly, progressive CKD can also exacerbate poverty (see later discussion). Sex and gender also influence the causes of CKD, the profile of comorbidities and disease evolution over time.[39] These differences are probably driven by complex biological, social and system-level factors. For example, women are 29% more likely to have CKD than men, but men are more likely to die from CKD than women.[7,85] Notably, despite the increased competing risk of death, men are 47% more likely than women to access dialysis or to have a kidney transplant.[7] In older general population cohorts, women had a lower baseline glomerular filtration rate (GFR), although men had a steeper rate of GFR decline over time.[86,87] This complex interplay of age, and sex or gender needs to be better understood to allow the development of appropriate health system-level responses.

[H2] Lack of health system response to kidney disease and global health

Despite being the third fastest-growing cause of death,[13] kidney disease has not received the attention it deserves from governments, multilateral organizations such as the WHO, the lay press, or health systems. Failure to diagnose CKD rests on the silent nature of the disease, lack of awareness of the devastating consequences of opportunities missed owing to lack of timely detection (including through coordinated screening programs), referral to nephrologists, and management. Even when treatment is sought, the quality of care might be poor. Information asymmetry is evident in the lay press for kidney disease. In an analysis of US newspapers, kidney disease was 11-fold underrepresented in the media as a discussed versus actual cause of death.[88] Diagnosis is further hampered by the limited availability or lack of tests needed to assess kidney function in many LICs or LMICs.[89]

Globally, health systems and governments have failed to create robust systems for generating data on the burden of kidney disease and its drivers. Data registries are vital for understanding disease epidemiology, tracking progress and developing cost-effective intervention targets. Kidney disease registries are sparse in LICs and LMICs, which is where they are most needed.[90] A 2022 review of dialysis registries found none in large Asian countries.[91] The AFRAN registry has been established in Africa, but so far only involves seven countries (Botswana, Burundi, Ghana, Kenya, Nigeria, South Africa and Zambia.)[92] Latin America is served by the Latin America Dialysis and Transplant Registry.[93] Of note, CKD registries are rare in both HICs and LICs.

Data from the 2023 Global Kidney Health Atlas revealed that the availability of national strategies to address CKD correlates positively with income level — LIC 11%, LMIC 23%, UMIC 22% and HIC 33%.[94] Despite the immense healthcare costs, only 48% of national governments recognise CKD and/or its treatment and prevention as a health priority.[94] In 2016, 50% of countries had no national health system oversight of kidney care.[95] Even in HICs, coordinated multi-agency approaches are lacking.[96] For example, the 2022–2027 European Commission “Healthier Together – European Union Non-Communicable Diseases Initiative” does not address CKD.[97] [98]

[H2] Targeting current WHO major NCDs will not solve the growing global kidney disease problem

CKD is often caused by pre-existing major NCDs that have been acknowledged by the WHO as priority conditions, such as diabetes, or by risk factors common to heart disease and stroke, such as hypertension. The WHO further reports that one-third of kidney mortality is caused by diabetic kidney disease.[99] However, glomerulonephritis, infection, malnutrition, environmental stressors and other toxins, pollution, climate change and obstetric catastrophes are all major causes of AKI and CKD, which are not addressed in the current list of major NCDs. CKD due to causes other than diabetes and hypertension already accounts for the highest global age-standardised rate of disability-adjusted life years (DALYs)[7]. Crucially, a common cause of kidney failure, even in HICs, is 'kidney failure where the cause cannot be ascertained'. In a recent report of the European Renal Association, the cause of kidney failure was unknown in 28% of participants.[100] This finding emphasizes the need for research that can advance understanding of underlying causes of kidney disease and enable the development of cause-specific therapies. Failing to address kidney disease risk factors and mediators will fail to curb its devastating health, economic and psychosocial consequences.

[H1] KIDNEY DISEASES HAVE MULTIPLE ADVERSE CONSEQUENCES

Kidney disease causes premature mortality, disability, reduced quality of life and other psychosocial harms, and incurs high costs to governments, healthcare systems, and patients and their families. (Box 1) The burden of this harm disproportionately affects those living in LICs and LMICs. Progressive CKD is a systemic disease and contributes to the evolution and progression of other major NCDs, most notably cardiovascular disease.[101]

[H2] Kidney disease carries high morbidity and mortality

The overall global age-standardised DALY rate declined sharply from 1990 to 2019.[102] In particular, the age-standardised DALY rate for WHO-recognised major NCDs such as ischaemic heart disease and stroke decreased by 28% and 35%, respectively.[102] By contrast, the age-standardised DALY rate for CKD increased by 6% (with an absolute increase of 62%)

over the last 30 years, causing CKD to rise from the 29th to the 18th leading cause of global disability.[102,103] In 2017 alone, CKD resulted in 36 million DALYs.[7] Nearly 75% of DALYs occurred in countries within the lowest three sociodemographic index quintiles.[7] Current population demographic trajectories and the increase in kidney disease risk factors mean that, without urgent action, CKD will continue to rise through the league table of global causes of death and disability.

The symptom burden of CKD is profound, and patients with kidney failure experience a similar or greater symptom burden (including fatigue, itch and pain) than those with terminal malignancies.[104] Kidney disease has multiple adverse psychosocial consequences, including reduced quality of life, poor life participation and mental illness. A 2022 meta-analysis of nearly 200,000 patients demonstrated that CKD reduced quality of life, especially for those on dialysis, for whom the pooled 36-item Short Form Health Survey (SF-36) physical component summary score was 36 out of 100.[105] Even among patients who were not on KRT (that is, dialysis or transplantation), many reported high symptom burden. At least 45% reported fatigue, poor mobility, bone and/or joint pain, drowsiness, insomnia and/or poor sleep, anxiety, pain, sexual dysfunction, muscle cramps, gastrointestinal distress, dyspnoea, itching, heartburn or oedema.[105] Children with CKD also have worse quality of life reported than those with type 1 diabetes or survivors of childhood cancer.[106] In older individuals, who typically have lower access to KRT than the younger adults, quality of life decreases and symptom burden increases for years before starting KRT and, in those starting KRT, symptom burden might stabilize but does not improve.[107-109] Of note, in advanced CKD, quality of life is worse in women than in men.[107] Moreover, having a person with CKD in the family adversely impacts the mental health of caregivers, 30–50% of whom report symptoms of anxiety or depression.[110-113]

The burden from kidney disease naturally extends to mortality. The global mortality from all kidney diseases likely ranges between 5–11 million per year[114] and kidney dysfunction is currently the 7th leading risk factor for death.[99] AKI contributes to an estimated additional 1.7 million deaths per year.[21] Deaths due to kidney disease increased by 50% from 2000 to 2019, and even mild CKD increases the risk of morbidity and mortality. [115,116] In 2019, CKD in

LICs led to ~600 YLL per age-standardised 100,000 population and around ~560 YLL per 100,000 in LMICs, compared with 200 YLL per 100,000 in HICs.[102] Increasing prevalence and the relatively young age at death mean that overall deaths and YLL due to kidney disease are predicted to escalate dramatically at a global level (Figure 2 and 3). In 2040, kidney disease is predicted to cause 52 million YLL, moving from the 16th most common cause of YLL (in 2016) to the 5th, surpassing other major NCD drivers of early mortality listed by the WHO such as diabetes (Figure 3).[14] In 2040, CKD is expected to account for 5% of YLL .[14] (Figure 4) [18]

CKD also increases the risk of developing severe acute and chronic infections (such as COVID-19 and tuberculosis), which are major causes of death in LICs and LMICs. [117,118] Hence, decreasing the incidence and severity of CKD will have beneficial effects on other NCDs and communicable diseases.

[H2] Kidney disease increases the risk of other major NCDs

Beyond the directly attributable toll of kidney disease, CKD contributes to and exacerbates other major NCDs. Uraemic toxins and systemic inflammation have profound effects on other organ systems, and extensive kidney–heart, kidney–brain, and kidney–lung interactions underscore the high co-morbidity burden of CKD.[119-121] In 2017, the GBD study estimated that 1.4 million cardiovascular disease-related deaths and 25 million cardiovascular DALYs were lost owing to kidney disease. [7] Accordingly, the 2021 European Society of Cardiology cardiovascular disease prevention guidelines suggest screening people with CKD for atherosclerotic cardiovascular disease [122]. These guidelines also advocate for albuminuria screening in those with high cholesterol or diabetes, acknowledging the importance of CKD as risk factor for cardiovascular disease.[123] Recognition of the role of CKD in increasing the risk of other major NCDs is essential to reducing overall NCD burden.

[H2] Kidney disease imposes unacceptably high costs on economies, healthcare systems and individuals

The direct healthcare costs of kidney disease are relevant at the global, country, health system and individual levels. Patients with CKD are complex to manage and account for a disproportionately large amount of national economic expenditure.

Most countries use a mix of public and private funding to provide kidney care. In 2016, only 19% of countries had completely publicly funded kidney care.[95] In the USA, kidney failure qualifies adults for Medicare benefits regardless of age. Of note, although <1% of Medicare beneficiaries have kidney failure, expenditures for kidney failure accounted for over 6% of Medicare spending in 2020, exceeding $50 billion.[23] US federal costs for people with CKD are > $85.4 billion annually, representing 23.5% of Medicare fee-for-service spending. [23] Similarly, in the UK, half of the National Health Service (NHS) budget spent on CKD care went to those with kidney failure, who comprise only 2% of patients with CKD stage 3–5.[124] In a range of other HICs and MICs, 2–4% of the healthcare budget is spent on the 0.1–0.2% of the population with kidney failure.[125,126] Moreover, the costs of CKD care are rising given the increased prevalence of CKD and the complexity of patients with CKD. Inflation-adjusted spending in the USA on people with kidney failure in 2021 had increased 20% over the preceding decade.[23] Notably, US expenditure on people with CKD rose faster than that for the general population or even patients with diabetes or heart failure.[23] A large Canadian general population study also found that patients with kidney disease had the highest comorbidity burden, number of medications, death rate and need for placement in long-term care facilities.[127] In Europe, aggregated annual healthcare costs of CKD are estimated to be higher than those of cancer or diabetes mellitus.[128] The average length of hospital stay in the UK is 35% longer for people with CKD compared to people without CKD.[124] Higher healthcare costs are also incurred from the increased rates of diseases such as cardiovascular disease in people with CKD. In the UK in 2010, a cost of £174 million was incurred from excess stroke and myocardial infarction in people with CKD.[124]

Health systems in LICs and LMICs will need increased funding to manage the rising burden of kidney disease. The prohibitive cost of dialysis likely explains the nearly 30-fold difference in the reported rates of kidney failure treated with dialysis between the country with highest rate (Taiwan) and the lowest (Bangladesh).[125] In 2016, 40% of LIC and 22% of LMIC reported

poor to extremely poor healthcare infrastructure for CKD care.[95] In Africa, where AKI is more common than in the rest of the world, 50% of countries reported poor to extremely poor AKI care infrastructure.[95] The negative impact of this lack of infrastructure is exacerbated by poor population coverage by nephrologists (0.2 nephrologists per million population in LICs, compared with 23 per million in HICs).[129] For children, the situation is even more dire. In the 2018 Global Health Kidney Atlas, nearly 40% of LICs and LMICs reported absent or extremely limited access to a paediatric nephrologist.[130]

At the individual level, the costs of kidney care can be staggering. In LICs and LMICs the burden of meeting healthcare costs is largely placed on the individual. Only 13% of LICs and 19% of LMICs cover the cost of KRT for adults.[95] A World Bank report highlighted that out of all the disease groups, CKD is responsible for the largest number of people (188 million annually in LICs and LMICS) suffering catastrophic healthcare expenditures worldwide.[131] Even in the USA, where Medicare covers people with kidney failure, younger adults with CKD are not covered unless they have private health insurance, leading to massive out-of-pocket costs.

Kidney disease also has many indirect economic costs. The individual patient faces decreased earning potential, and educational and vocational outcomes are compromised in children with kidney disease.[132,133] In the USA, >75% of patients initiating dialysis were unemployed.[134] Caregivers face similar lost earning opportunities, and the state receives less taxation revenue.

With increasing prevalence, the overall global cost of providing kidney care is likely to rise. Moreover, with an ageing global population, the global tax base to fund health care will shrink over the next 30 years, emphasizing the crucial need to prevent kidney failure and its associated high health care costs (such as KRT costs).[135] The recognition of kidney disease as a major global driver of mortality is, therefore, essential to focus efforts on improving kidney health and decreasing the massive healthcare costs associated with kidney disease.

[H1] THE MORAL CASE FOR KIDNEY HEALTH PRIORITISATION

It is unacceptable that the only NCD consistently witnessing an increase in the number of deaths year-on-year is not identified as a priority for policy action. Kidney diseases disproportionately affect the poor and disadvantaged, globally and within each country. Moreover, kidney disease not only has a profound negative impact on patients owing to its debilitating symptom burden, but it also increases their risk of developing other major NCDs, restricts their ability to work and care for family members, and is cripplingly expensive for individuals, families, health systems, and governments.

The changing population dynamics predicted over the next 20 years will translate to an increase in the number of people with kidney disease in LICs and LMICs, who are the least able to access kidney care. Arguments have been made that prioritizing kidney disease is not necessary in health systems without the resources to pay for the care of people with kidney disease. This approach will perpetuate and exacerbate the current global inequities in the care of patients with kidney disease, represents a pressing moral quandary to the world and is contrary to the Sustainable Development Agenda of leaving no one behind. Acceptance of such a situation by using the framing of cost-effectiveness as the primary metric further deprioritizes these patients leading to the outright denial of care. The status quo perpetuates this injustice.

[H2] When kidney healthcare costs cannot be met, people die

Most people access care in community or secondary health care settings in LICs and LMICs. However, less than a third of LIC or LMIC community health care settings can access essential diagnostics such as those measuring kidney function (for example, estimated GFR and/or albuminuria testing).[136] Medicines that can decrease albuminuria, or treat glomerulonephritis and the complications of CKD (such as anaemia or CKD–mineral and bone disorder (CKD–MBD)) are crucial to slow disease progression and limit the burden of its complications (for example, cardiovascular disease).[137,138] However, in a recent survey of the nephrology workforce in LICs and LMICs, only a third of respondents reported that essential kidney medicines (such as angiotensin-converting enzyme (ACE) inhibitors, anti-hypertensives, medications to treat acid–base and electrolyte disturbances or for CKD–MBD) were mostly available in community settings. [139] This finding highlights the avoidable

progress to kidney failure and death faced by many patients in low-resource settings. Newer, paradigm-shifting medications, such as sodium–glucose cotransporter 2 (SGLT2) inhibitors and mineralocorticoid receptor antagonists are even less accessible.

Globally, <50% of all people requiring KRT can access it, with vast discrepancies in access between HICs and LICs.[24,140,141 22] Up to 98% of people with kidney failure in LICs do not receive KRT, compared with up to 30% in HICs. Of those patients unable to access KRT, 88% reside in Africa or Asia. The great disparity in wealth and availability of nephrologists greatly impact KRT funding and outcomes.[142] Approximately 93% of the world population receiving KRT lives in HICs or upper-middle-income countries (UMICs), who comprise only 52% of the world population. Women, children, socially marginalized groups, migrants, and refugees are particularly disadvantaged.[140,143] Even those who access KRT often cease quickly owing to cost constraints. In sub-Saharan Africa, only ~10% of adults and 35% of children who managed to access KRT were still on therapy by three months.[144] In a report from India that evaluated a state-funded dialysis program, the number of patients accessing the service increased over time, but about two-thirds of patients discontinued dialysis in less than one year and likely died because they could not afford the substantial out-of-pocket payments needed to meet the indirect costs of care.[126]

Access to dialysis for AKI is similarly poor in LICs. Up to 85% of people with AKI live in the Global South.[21] In the ISN *0by25* global snapshot of AKI, nearly 50% of people who required dialysis in LICs and LMICs were unable to receive it owing to resource constraints or inability to pay. [17] A systematic review of AKI outcomes in sub-Saharan Africa found that only 64% of children and 33% of adults could access dialysis when needed.[19] In those unable to access dialysis, mortality was ~80%.[19]

[H1] EXPECTED IMPACT OF PLACING KIDNEY DISEASE IN THE WHO LIST OF NCD DRIVERS OF EARLY DEATH

The ISN, ASN and ERA and nephrology communities worldwide unite in calling for kidney health to become a core part of the global health agenda. A crucial first step is the official

recognition by the WHO that kidney disease is a major NCD driver of early mortality. The significance of prioritising CKD by an important multilateral organization such as the WHO in strengthening the fight against CKD cannot be overstated. Specifically, prioritization by the WHO will help to raise awareness and demand for care, develop and implement guidelines and standards, improve implementation of locally appropriate surveillance and monitoring mechanisms, coordinate international efforts, and allocate resources more efficiently. In addition to enhanced efforts to prevent the development and progression of kidney disease, prioritization will foster investment towards the development of sorely needed new therapies. (Box 2)

Firstly, placing kidney disease on the WHO list of major NCD causes of premature mortality will enable a cohesive and targeted global campaign to decrease the harm caused by kidney disease, especially in emerging economies. Failure to spotlight kidney disease will undo or substantially slow progress towards the 2015 United Nations Sustainable Development Goal 3.4 of reducing premature mortality from NCDs by a third by 2030.[145] Combating kidney disease will also contribute to action on many other Sustainable Development Goals, including SDG 1 (no poverty), 2 (gender equity), 6 (water security), 8 (work and economic growth), 10 (inequalities), and 13 (climate action). Adding kidney disease to the WHO major NCD list will translate to better health outcomes across the world and enhance the ability to address pervasive inequities that place disadvantaged populations at increased risk of kidney disease.

Previous successful collaborations between Latin American Society of Nephrology and Hypertension (SLANH) and the Pan American Health Organization (PAHO), which is a specialized agency of the United Nations, exemplify the progress that can be made by multilateral organisational collaboration. This joint initiative has been pivotal in implementing and developing dialysis and transplantation registries, increasing knowledge of CKD and AKI among primary care health personnel, establishing a clinical and epidemiological definition of CKD of non-traditional causes, prioritising individuals with kidney disease for COVID vaccination, and establishing a direct line of action with local ministries of health.[146] The ongoing evolution of digital health technologies as a lever to

improve the detection and monitoring of kidney disease will accelerate these programs and improve their implementation. Recognition of kidney disease as a major NCD driver of mortality is crucial to translating these gains to a global stage.

Early disease detection and a life course approach are cornerstones for reducing CKD-related morbidity and mortality worldwide. CKD meets the WHO principles for screening as early stages are asymptomatic, and there are effective early interventions.[98,147] In 2021, the Kidney Disease Improving Global Outcomes (KDIGO) global multidisciplinary expert panel recommended screening high-risk groups (for example, individuals with diabetes or hypertension) for CKD.[98]

One of the main historical arguments against CKD screening has been the lack of effective therapies to slow disease progression, but this landscape has changed radically in the past 5 years. The advent of new therapeutic agents such as SGLT2 inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, endothelin receptor antagonists, selective mineralocorticoid receptor antagonists, and new glomerulonephritis-targeted therapies, means that early recognition of disease can translate to massive health improvements. For example, a 2021 meta-analysis revealed that SGLT2 inhibitor use decreased the risk of CKD progression by 37% in people with and without diabetes.[128] Consensus-based expert opinion recommends case detection in individuals with known risk factors such as diabetes, hypertension and cardiovascular disease.[98] As discussed above, the list of relevant risk factors is likely longer and poorly studied in LIC and LMICs. [16,148] Prioritization by the WHO will spur studies to more accurately document disease burden and risk factors in these geographic areas. Failure to identify people at high risk of kidney disease development and/or progression is a missed opportunity to intervene and prevent kidney failure and its stratospheric health, economic and psychosocial costs.[138]

Prioritising kidney disease will also facilitate the development and expansion of kidney disease registries. Accurate registry data are crucial to understanding trends and risk factors and to inform cost-effective and equitable resource delivery. The ISN, through its Share-RR program, is providing support for the setting up of registries but such initiatives are unlikely

to be sustainable without embedment in local health systems.[149] Registries are already highlighting global hotspots of kidney failure, enabling investigation of disease causes and improving the understanding of new disease entities such as CKDu.[93,150]

Greater attention to kidney health and disease will also translate to increased investment by governments, the private sector and research funders, which will spur innovation and new therapies. Despite spending disproportionate amounts of money on funding KRT, governments worldwide have not prioritised innovation in these areas. Professional societies have been trying to fill this gap, with exciting results. The Affordable Dialysis Prize co-funded by the ISN, the Asian Pacific Society of Nephrology, the Farrell Family Foundation and the George Institute for Global Health and has led to the development of a prototype of a low-cost dialysis machine. The KidneyX project in the USA is a public–private partnership that has raised tens of millions of dollars to foster innovations in dialysis care, including an artificial kidney prize .

New therapies that focus on the prevention of kidney disease development and progression will result in major health and socio-economic benefits. Finally, highlighting kidney disease will enable kidney health societies to expand advocacy for appropriate access to care for patients with kidney disease, increasing access to diagnosis and treatment and including medications needed to treat kidney disease in the WHO essential medicines list.

Shining a spotlight on kidney disease will not only result in decreased numbers of people needing resource-intensive kidney treatment but also empower programs to reduce waste in dialysis. More sustainable dialysis modalities and technologies are urgently needed. Haemodialysis, the most common form of KRT, uses hundreds of litres of water per session.[60] In drought-affected areas, this demand poses a profound challenge. Decreasing the amount of people on dialysis by disease prevention will improve water security and reduce waste. Dialysis also produces >900,000 tonnes of plastic waste a year, rendering it one of the highest emitters of carbon emissions in healthcare.[151] In the USA, annual emissions per haemodialysis facility are estimated at nearly 770,000 kg of CO_2 equivalents.[152] Nearly 38,000,000 kg of recyclable plastic waste is generated annually from

peritoneal dialysis globally, but limited recycling options exist.[153] Encouragingly, programs to monitor electricity and water use in dialysis facilities have resulted in 30–50% savings despite increasing patient numbers in France.[154]

[H1] Grand challenges for kidney health

Several major unmet policy, advocacy and implementation needs (Box 3) must be tackled to alleviate the global burden of kidney disease. We call for the global health community to address the following urgent public health needs to meet the needs of those at risk of, and with kidney diseases:

1. *Improved access to care:* Many people with CKD do not have access to adequate diagnostic and treatment (including preventive) services, particularly in LICs and LMICs. Similarly, >1 million people with potentially reversible AKI die yearly owing to lack of access to timely therapies, including dialysis. These gaps must be addressed by increasing the availability of affordable and accessible healthcare services.
2. *Better prevention:* More effective strategies are needed to prevent the development of CKD and AKI. Kidney disease risk factors need to be better understood, especially in LICs and LMICs, through appropriately designed studies using a multi-disciplinary approach, interpreting the results in the context of the study population and its limitations, and considering their implications for the community and public health. In a recent White Paper, an ISN Working Group suggested points that countries should consider before developing a CKD case finding and management program, and put forward an evidence-based, resource-sensitive framework that can be adjusted to suit the local contexts. (139)
3. *Developing, testing and scaling up novel balanced models of care:* Implementing affordable, scalable and sustainable models of care requires co-development with stakeholder communities. Balanced models should also outline a systematic but flexible approach to planning treatment and care within the overall context of strengthened primary health care services. In low-resource settings, this approach might include a combination of task-sharing between physicians and non-physician healthcare workers in a locally appropriate way for diagnosis and follow-up care (facilitated by digital mobile

technology and the use of clinical decision support systems with regional supervision), the use of online platforms to deliver competency training and facilitate supervision, and the use of peers for quality assurance. Potential risks of such approaches should be recognised and addressed by implementing policies that ensure the equitable delivery of safe, effective and high-quality care. In high-resource settings, care delivery needs to be refined across all levels of healthcare with the addition of an extended range of services in terms of coverage and degree of specialisation.

4. *Greater awareness and education:* Many people with CKD are not aware that they have the disease, and many more are not aware of the steps that they can take to slow its progression. Similarly, a large proportion of the primary care community does not fully appreciate the adverse consequences of early-stage CKD. Greater awareness and education campaigns are needed to help people understand the importance of early diagnosis and management of CKD.
5. *Addressing social determinants of kidney health:* As kidney diseases disproportionately affect impoverished and marginalized communities, addressing social determinants of health, such as poverty, poor housing and lack of access to healthy food and clean water, is essential to address the burden of kidney diseases.
6. *Increased funding for research and development:* More funding is needed to support the development of new treatments and therapies for kidney diseases, and to improve understanding of these diseases and their underlying causes in different parts of the world.
7. *International cooperation and coordination:* International cooperation and coordination are needed to promote the development and implementation of effective policies and programs for the prevention, early detection, and management of kidney diseases and to share knowledge and best practices.
8. *Greater engagement with patient communities:* The demand for meaningful participation by community members in shaping health policies and in planning, delivering, quality assurance, and evaluation of services has increased steadily. Greater engagement with patient communities is needed to ensure that policies and programs address the needs and priorities of people living with kidney diseases effectively. Community involvement can range from consultation and collaboration to leadership.

CONCLUSION

The 2015 United Nations Sustainable Development Goal 3.4 aims to reduce premature mortality from NCDs by a third by 2030.[145] To tackle this goal, the WHO has recognised cancer, heart disease, stroke, chronic lung disease and diabetes as the major NCD drivers of early mortality. Failure to include kidney disease in this initiative misses the opportunity to address a major contributor to premature and preventable mortality. Changing population dynamics and evolving risk accumulation mean that the global burden of kidney disease is increasing relentlessly to become the 5th most common NCD driver of mortality by 2040. Kidney disease increases the risk of mortality, morbidity, and disability, decreases quality of life and has profound individual and health system level economic consequences, as well as dire environmental impacts. Kidney disease is under-recognised and under-resourced. Recognising kidney disease as a major driver of NCD-related mortality will translate to coordinated global efforts to minimise the burden of kidney disease and will save lives.

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Author contributions

A.F. and V.J. researched data for the article. A.C.MO., S.L.T., A.O., A.B.F., D.F., P.R.-C., M.F., M.N., C.W., C.M. L.S., I.U. and V.J. made substantial contributions to discussions of the content. A.F., M.N.H., V.J. wrote the manuscript. A.H., D.A., S.B., A.C., L.S., I.U. and V.J. reviewed or edited the manuscript before submission.

Competing interests

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Peer review information

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Related links

Prototype of a low-cost dialysis machine: https://www.ellenmedical.com/

KidneyX project: kidneyx.org

Figure Legends :

Figure 1. Many risk factors for chronic kidney disease will not be addressed by targeting the current WHO recognised major non-communicable diseases.

A Venn diagram of risk factors for kidney disease and other major NCDs reveals separate major risk factors for CKD which will not be addressed by targeting WHO-recognized major NCDs.

Figure 2. Predicted change in deaths due to chronic kidney disease from 1990 to 2040

Legend. Modelling of Global Burden of Disease data reveals an increase in predicted deaths due to CKD each year from 1990 to 2040. Blue spectrum = less deaths, red spectrum= more deaths

Source: Institute for Health Metrics and Evaluation, University of Washington; open access under the Creative Commons Attribution, Non-Commercial, No Derivatives 4.0 International License

Figure 3. Predicted change in years of life lost to chronic kidney disease from 1990 to 2040

Legend. Modelling of Global Burden of Disease data reveals an increase in predicted years of life lost due to CKD each year from 1990 to 2040. Blue spectrum = less years of life lost, red spectrum= more years of life lost

Source: Institute for Health Metrics and Evaluation, University of Washington; open access under the Creative Commons Attribution, Non-Commercial, No Derivatives 4.0 International License

Figure 4. Predicted years of life lost from chronic kidney disease by 2040 is similar to other WHO recognised major non-communicable diseases.

Legend. By 2040, CKD is expected to surpass diabetes as a cause of years of life lost. Adapted from data from Foreman KJ et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative

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Box 1: The burden of kidney disease

- Premature mortality
- Disability
- Reduced quality of life
- Other psychosocial harms
- High costs to governments and health care systems
- High costs to individuals and families, in part due to lost productivity

Box 2: The impact of WHO recognition of CKD as a major driver of NCD-related early mortality

- Rise in global awareness of CKD
- Further development of guidelines and standards for the care of people with CKD
- Improved implementation of locally appropriate surveillance and monitoring mechanisms
- Facilitated coordination of international efforts to understand disease burden and develop evidence-based prevention approaches
- Improved resource allocation
- Fostering of investment for new therapies

Box 3: A path to developing sustainable patient-centered kidney care services to achieve SDG targets

- Improved access to care by integrating kidney care services into routine primary care and restructure care pathways away from hospitals and into community settings
- A staged approach to understanding and responding to kidney disease, with focus on region-specific risk factors, comorbidity and multimorbidity
- Task-sharing of integrated preventive, diagnostic and management interventions for kidney disease with non-specialised workers in the overall context of NCD care
- Adoption of technological solutions, such as digital platforms and point of care tests, to facilitate the delivery of interventions across the continuum of care
- Development of a continuum of care pathway by integrating primary preventive care with specialist care
- Commitment to involving patients and family members in planning and providing services
- Implementation of community-based interventions to enhance the demand for preventive care

Figure 1

A Venn diagram of risk factors for kidney disease and other major NCDs reveals separate major risk factors for CKD which will not be addressed by targeting WHO recognized major NCD's

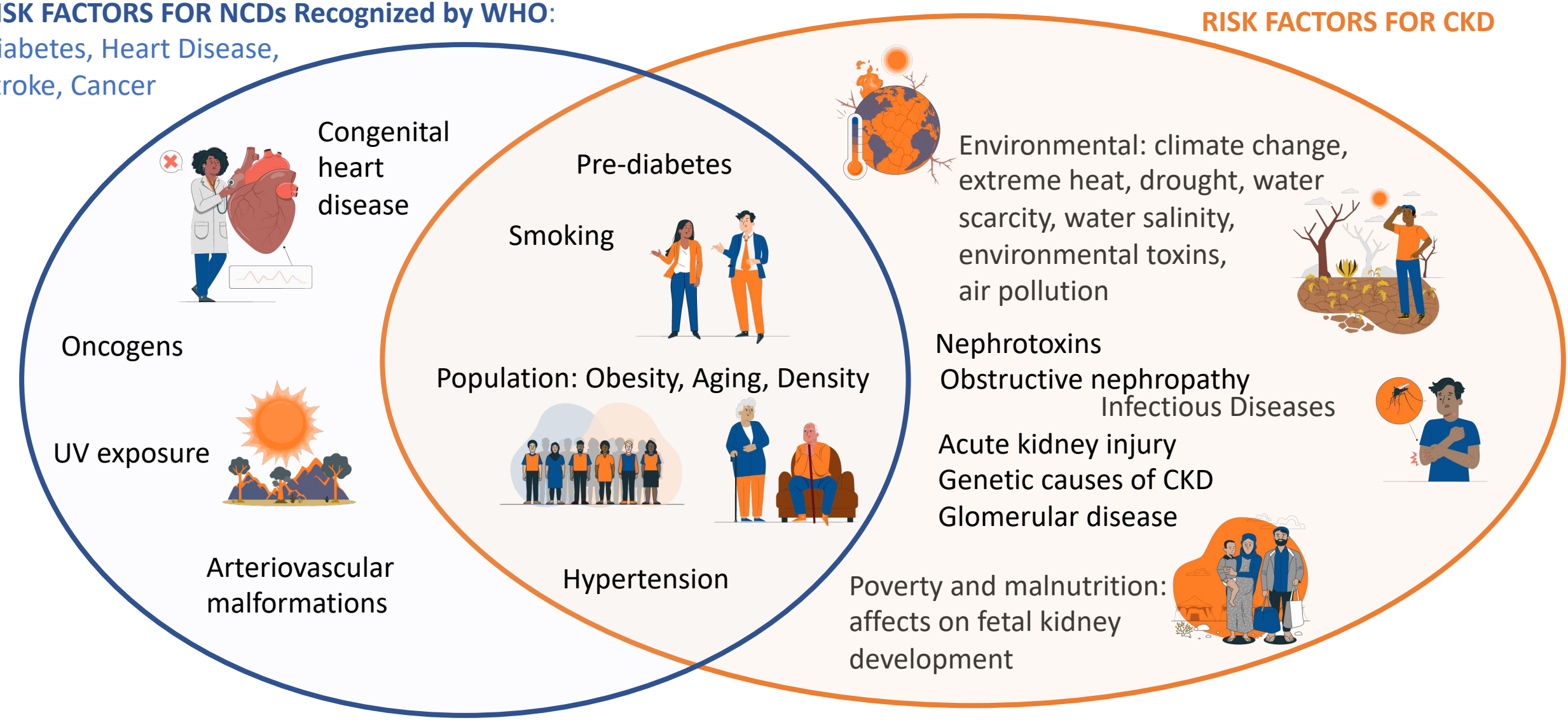


Figure 2a. Predicted change in deaths due to CKD 1990 to 2040

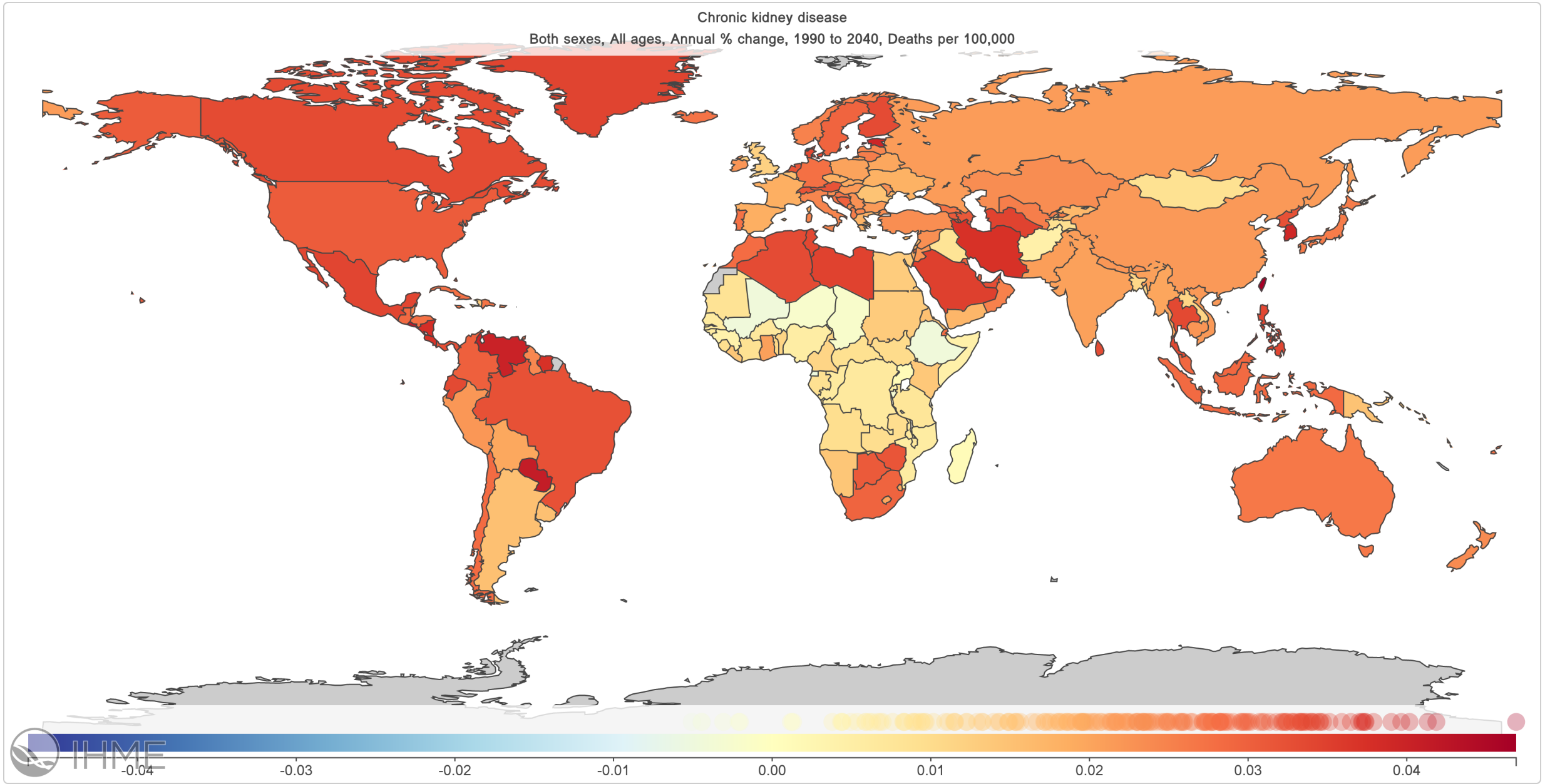


Figure 2b. Predicted change in years of life lost due to CKD 1990 to 2040

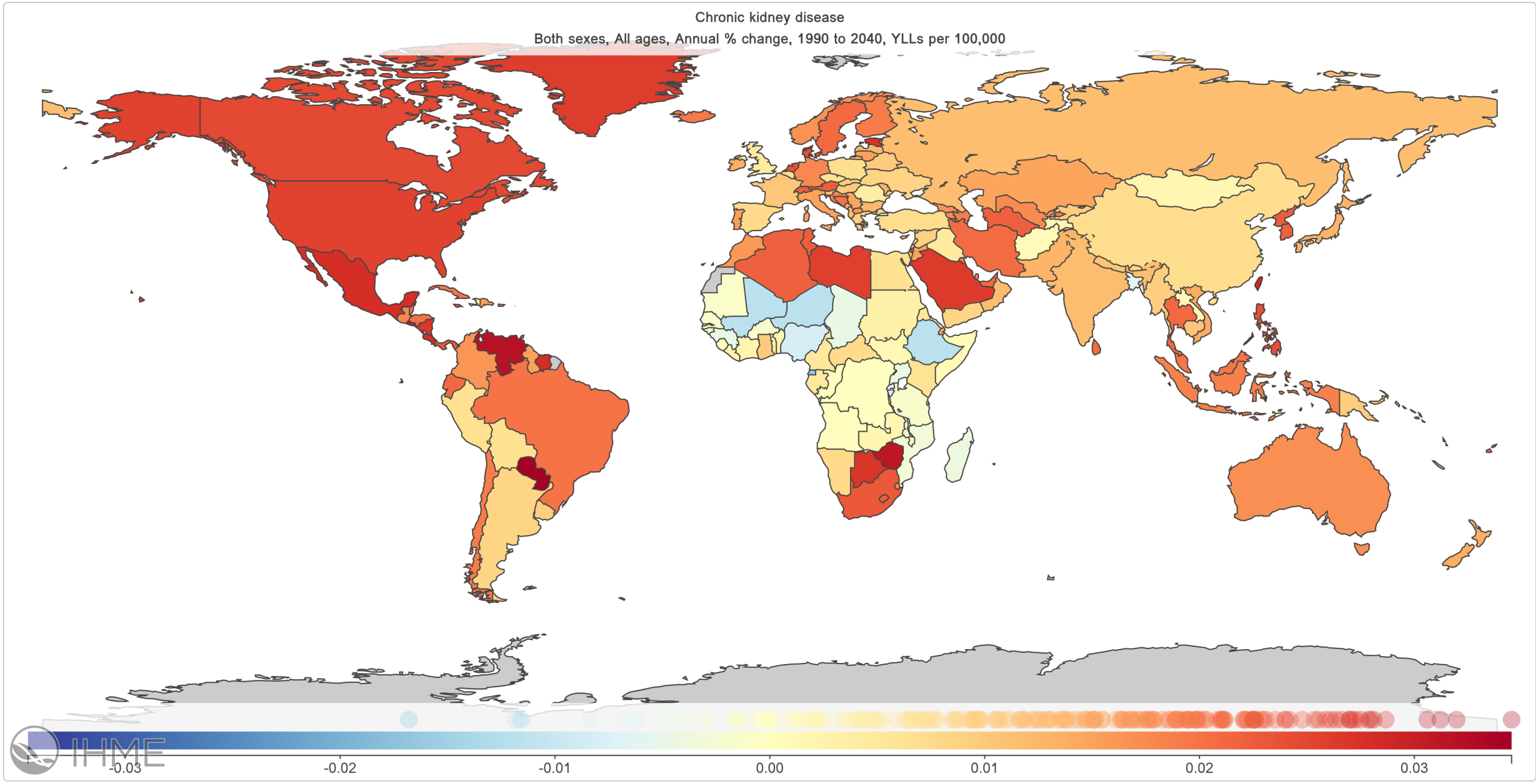
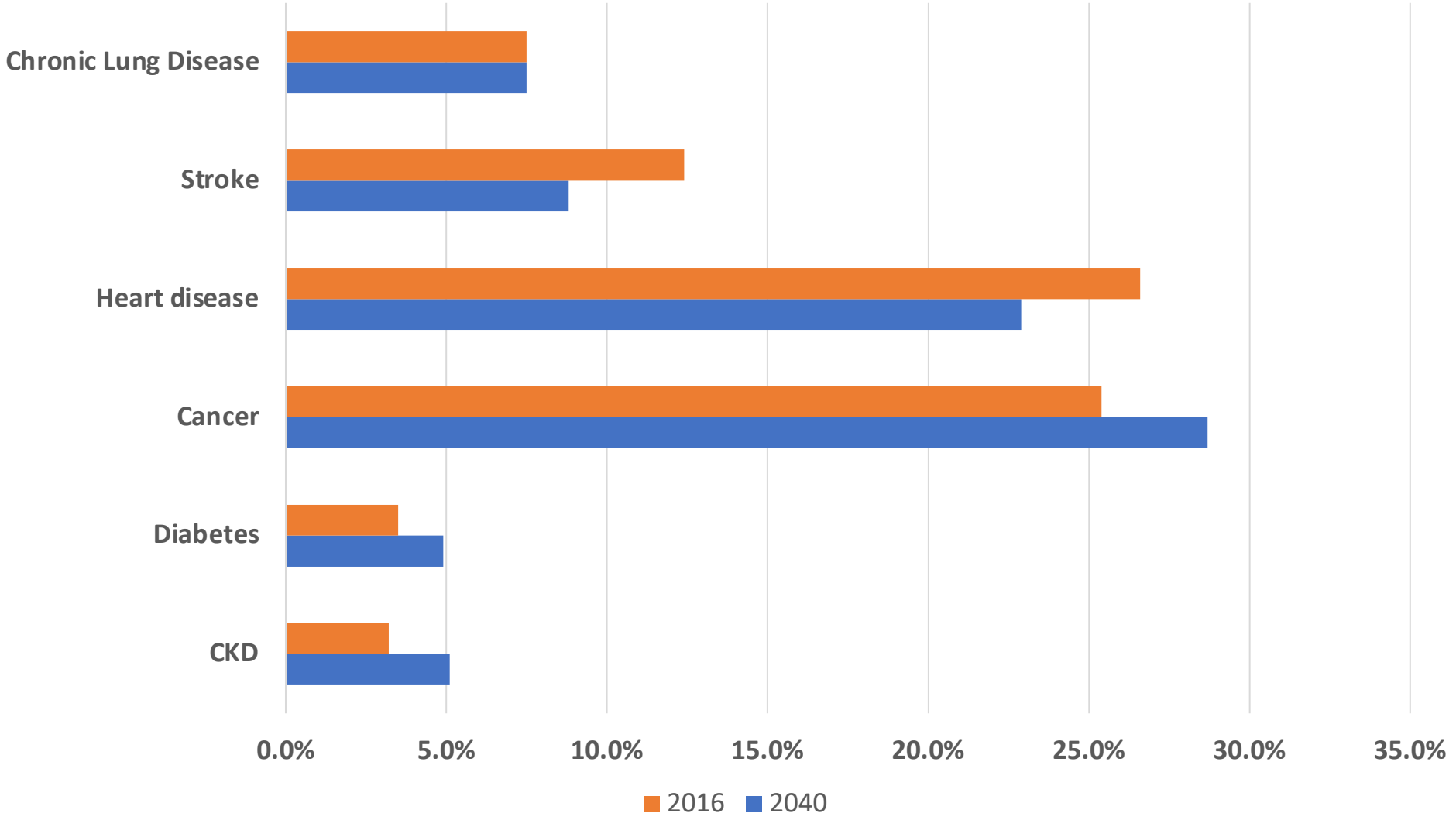


Figure 3. By 2040, kidney disease will account for a larger percentage of years of life lost globally due to non-communicable disease than diabetes.



Adapted from data from oreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016 -2040 for 195 countries and territories. The Lancet. 2018;392(10159):2052-90.