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Review article

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The impact of population ageing on the burden of chronic kidney disease

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Abstract

The burden of chronic kidney disease (CKD) and its risk factors are projected to rise in parallel with the rapidly ageing global population. By 2050, the prevalence of CKD category G3–G5 may exceed 10% in some regions, resulting in substantial health and economic burdens that will disproportionately affect lower-income countries. The extent to which the CKD epidemic can be mitigated depends largely on the uptake of prevention efforts to address modifiable risk factors, the implementation of cost-effective screening programmes for early detection of CKD in high-risk individuals and widespread access and affordability of new-generation kidney-protective drugs to prevent the development and delay the progression of CKD. Older patients require a multidisciplinary integrated approach to manage their multimorbidity, polypharmacy, high rates of adverse outcomes, mental health, fatigue and other age-related symptoms. In those who progress to kidney failure, comprehensive conservative management should be offered as a viable option during the shared decision-making process to collaboratively determine a treatment approach that respects the values and wishes of the patient. Interventions that maintain or improve quality of life, including pain management and palliative care services when appropriate, should also be made available.

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Key points

- The global population is rapidly ageing; the proportion of people aged >65 years is expected to rise from around 10% in 2024 to >16% by 2050.
- If the 1990–2016 trend of increasing chronic kidney disease (CKD) prevalence and population ageing continues, the prevalence of CKD category G3–G5 may exceed 10% in many world regions by 2050.
- The global burden of diabetes mellitus and hypertension will continue to rise as the population ages and life expectancy increases, leading to a parallel increase in the burden of CKD.
- The CKD epidemic could be mitigated by scaling up prevention efforts, implementing cost-effective screening programmes and ensuring widespread and affordable access to new kidney-protective drugs.
- Older patients with CKD require an integrated multidisciplinary approach to manage their multimorbidity, polypharmacy, high rates of adverse outcomes, cognitive dysfunction, frailty, fatigue and other age-related complications and symptoms.
- Globally, the increasing demand for kidney replacement therapy will probably further overwhelm the capacity of health-care systems, leaving many more individuals without access to dialysis, particularly in low- and middle-income regions that are already struggling to provide basic renal care.

Introduction

Population growth and ageing are important drivers of the burden of chronic kidney disease (CKD). In November 2022, the global population was estimated to reach 8 billion people[1]. This unparalleled growth is the result of a gradual increase in longevity owing to improvements in public health, nutrition, personal hygiene and medicine as well as persistently high levels of fertility in some countries[1]. Although the global population has increased rapidly over the past few centuries, the rate of growth has more than halved since its peak 60 years ago[2]. Nevertheless, estimates suggest that by 2050, the population will reach 9.7 billion, more than half of whom will live in Asia, and the population of Sub-Saharan Africa will have doubled. By contrast, the populations of many Eastern European countries and Japan are expected to shrink by more than 15% by 2050, mostly owing to record low birth rates in these regions[3].

On average, the world population is ageing at a much faster pace than in the past[4]. Global life expectancy reached 72.8 years in 2019, a nearly 9-year increase from 64.0 years in 1990. Further reductions in mortality are projected to result in an average lifespan of around 77.2 years by 2050 (ref. 3). In 2024, just over 10% of people worldwide were older than 65 years, whereas this age group is expected to account for >16% of the global population by 2050 (ref. 3). However, large regional differences exist (Fig. 1). Japan and Europe are expected to experience the greatest ageing, with 37.5% and 28.9% of their populations being aged >65 years in 2050, respectively, whereas the population of Sub-Saharan Africa will remain much younger, with <5% of people aged >65 years by 2050. Nevertheless, by 2050, two-thirds of people aged >60 years will be living in low- and middle-income countries (LMICs)[4].

Population ageing is associated with an increased burden and duration of non-communicable diseases, including CKD and many of its risk factors such as diabetes mellitus and hypertension. In high-income countries (HICs), population ageing and the resulting increased burden on health-care systems occurs in parallel with a shrinking workforce, an imbalance that could create labour shortages and increase pressure on already strained health-care systems (Supplementary Box 1). To what extent the burden of CKD will be affected by population ageing depends on future trends in risk factors and on ensuring equitable global access to novel and emerging therapeutic interventions[5].

Improved understanding of the growing burden of CKD is crucial to alleviate the health and economic burdens of the ageing population and to build sustainability within the global health system. In this Review, we explore the consequences of the rapidly ageing population for the health and economic burden of CKD and its risk factors. We discuss factors that drive or could mitigate the CKD epidemic and highlight complications and symptoms of CKD that are experienced by older individuals.

The global burden of CKD

A systematic analysis of data from 33 population-based studies estimated that the age-standardized global prevalence of CKD category G1–G5 in adults in 2010 was 10.4% among men and 11.8% among women[6]. Based on these data and the estimated number of patients on kidney replacement therapy (KRT) in 2010 (ref. 7), the total number of individuals with kidney disease worldwide in 2017 was estimated to be almost 850 million people[8,9]. The most comprehensive overview of trends in CKD category G3–G5 burden across world regions and countries to date was provided by an analysis of 1990–2016 data from the Global Burden of Disease (GBD) study[10]. Importantly, these data have some limitations (Supplementary Box 2).

CKD prevalence

From 1990 to 2016, the crude global prevalence of CKD category G3–G5 increased by one-third from 2.8% to 3.7%, with clear increases in most world regions[10] (Fig. 2). The largest relative increases were seen in the high-income Asia Pacific and Central and Tropical Latin America regions, where the prevalence of CKD category G3–G5 increased by 60–80%, whereas it remained relatively stable in Central and Western Sub-Saharan Africa. These increases were mostly attributable to increases in the prevalence of diabetes-related CKD. Although the prevalence of CKD due to hypertension and due to glomerulonephritis decreased, these aetiologies remained the second and third highest causes of CKD, respectively[10].

In 2016, the prevalence of CKD varied substantially with geographical region and level of socioeconomic development. In high-income North America, Central Latin America, Eastern Europe, Southern Sub-Saharan Africa, Central Asia and high-income Asia Pacific regions, the prevalence of CKD was >5%. This finding demonstrates that some regions with relatively young populations such as Southern Sub-Saharan Africa have high CKD prevalence. CKD affects individuals at younger ages in countries with low socio-demographic index (SDI), resulting in a higher prevalence of CKD among adolescents and young adults than in countries with high SDI. In countries with low SDI, the prevalence of CKD is greatest among those aged 60–64 years, whereas in countries with high SDI, the highest prevalence is among those aged 75–79 years[10].

The GBD data reveal a clear increase in CKD prevalence from 1990 to 2016. Increases in CKD prevalence correlate with the rate of population ageing in different geographical regions (Fig. 3). Although the

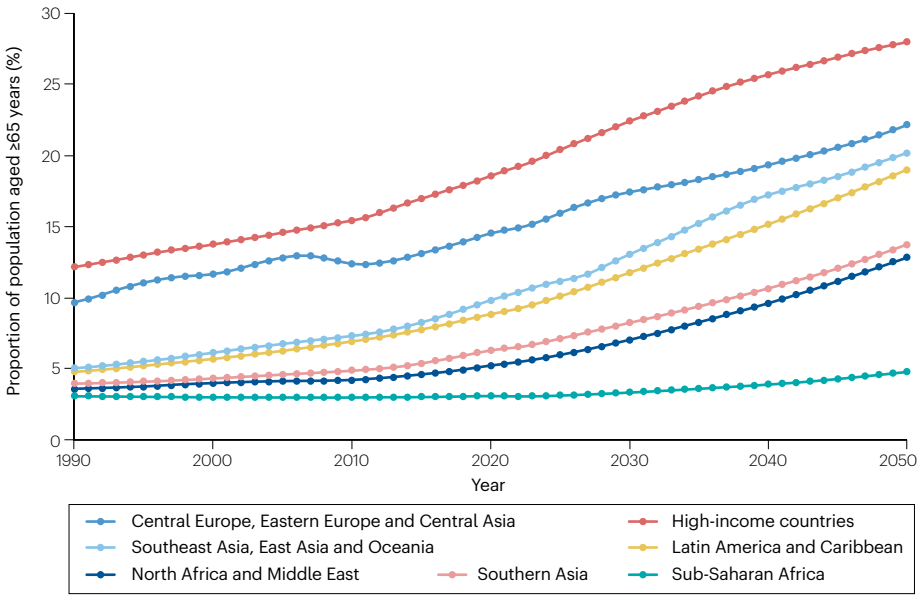

Fig. 1 | Historical and projected ageing of the populations of world regions from 1990 to 2050. In 2024, just over 10% of people worldwide were older than 65 years; this share is expected to surpass 16% by 2050, albeit with large regional differences. By 2050, 80% of older people will be living in low- and middle-income countries. Graph based on data from the United Nations population projections using the 'medium scenario' of population ageing[3].

crude global prevalence of CKD increased by one-third between 1990 and 2016, the age-standardized prevalence remained relatively stable (increasing from 4.04% to 4.06%). Age standardization accounts for changes in population age distribution that occur over time when comparing estimates from different time periods. The discrepancy between changes in crude and age-standardized prevalence of CKD suggests that the increase in global CKD prevalence is almost solely due to the ageing population. If interventions such as lifestyle modifications and novel treatments fail to slow CKD progression, we project that by 2050, population ageing will lead to increases in the prevalence of CKD category G3–G5 to >10% in high-income North America, Central Latin America, Eastern Europe, North Africa and the Middle East, Southern Sub-Saharan Africa, Central Asia and high-income Asia Pacific regions (Fig. 2).

CKD mortality

From 1990 to 2016, worldwide mortality due to CKD increased by 41%, from 11.4 to 16.1 deaths per 100,000 population[10]. In 2016, substantial variation in CKD mortality was reported across the globe, with high levels of >25 deaths per 100,000 population in high-income Asia Pacific, Oceania and Central Latin America[10] (Supplementary Fig. 1). The leading cause of CKD mortality was CKD due to diabetes mellitus, followed by CKD due to hypertension and CKD due to glomerulonephritis. The GBD Consortium forecasts that CKD will be the fifth greatest cause of death worldwide by 2040 (ref. 11).

Similar to the increases in CKD prevalence, the relatively large 41% increase in crude CKD mortality (from 11.4 to 16.1 deaths per 100,000 population) contrasts with the modest 5% increase in age-standardized CKD mortality (17.5 to 18.3 deaths per 100,000 population, primarily attributable to increases in CKD mortality in low-SDI countries) between 1990 and 2016 (ref. 10). These data indicate that population ageing was the primary factor driving increased CKD mortality. This finding suggests that population ageing has led to a higher absolute number of deaths due to CKD over time but may also imply that the underlying risk of CKD-related death at any given age has not changed substantially.

CKD disability-adjusted life-years

One disability-adjusted life-year (DALY) represents the loss of the equivalent of 1 year of full health[12]. Globally, between 1990 and 2016, crude CKD DALYs increased from 410 to 473 per 100,000 population[10]. In 2016, CKD DALYs also varied substantially by geographical region and level of development. Hot spots of DALYs included Central Latin America and Oceania, both of which had CKD DALYs of >900 per 100,000 population in 2016 (Supplementary Fig. 2). CKD due to diabetes mellitus was the primary driver of rising CKD DALYs, accounting for more than half of the increase, followed by CKD due to hypertension, which accounted for nearly a quarter of the increase in DALYs. However, in countries with low SDI, CKD due to other causes, including unknown causes, ranked second after CKD due to diabetes as the major cause of DALYs, and glomerulonephritis ranked third[10]. This finding emphasizes the need for further research on causes of CKD in these countries.

In contrast to the increase in crude global DALYs between 1990 and 2016, age-standardized DALYs decreased from 521 to 500 per 100,000 population during the same period. Decreases in age-standardized DALYs were smaller in low-SDI countries than in high-SDI countries. The contrast between rising crude DALYs and declines in age-standardized DALYs suggests that, despite the increasing number of people affected by CKD, the overall effect of CKD on health has lessened after accounting for population ageing.

Kidney failure

In 2010, 2.6 million people worldwide received KRT and this number is expected to double to 5.4 million by 2030 (refs. 7,13). Alarmingly, estimates suggest that in 2010, only 50% of individuals with kidney failure received KRT, suggesting that more than 2.3 million people may have died due to lack of access to this therapy. Among patients who received KRT in 2010, 93% were living in HICs, with large geographical variation in incidence and prevalence[7,13,14]. In many HICs, the oldest age groups comprised the majority of patients on prevalent KRT. In Europe in 2021, patients aged ≥65 years comprised almost half of the prevalent KRT population[15]. In Australia in 2022, people aged 75–84 years had the highest prevalence of KRT (3,000 per million population (pmp)),

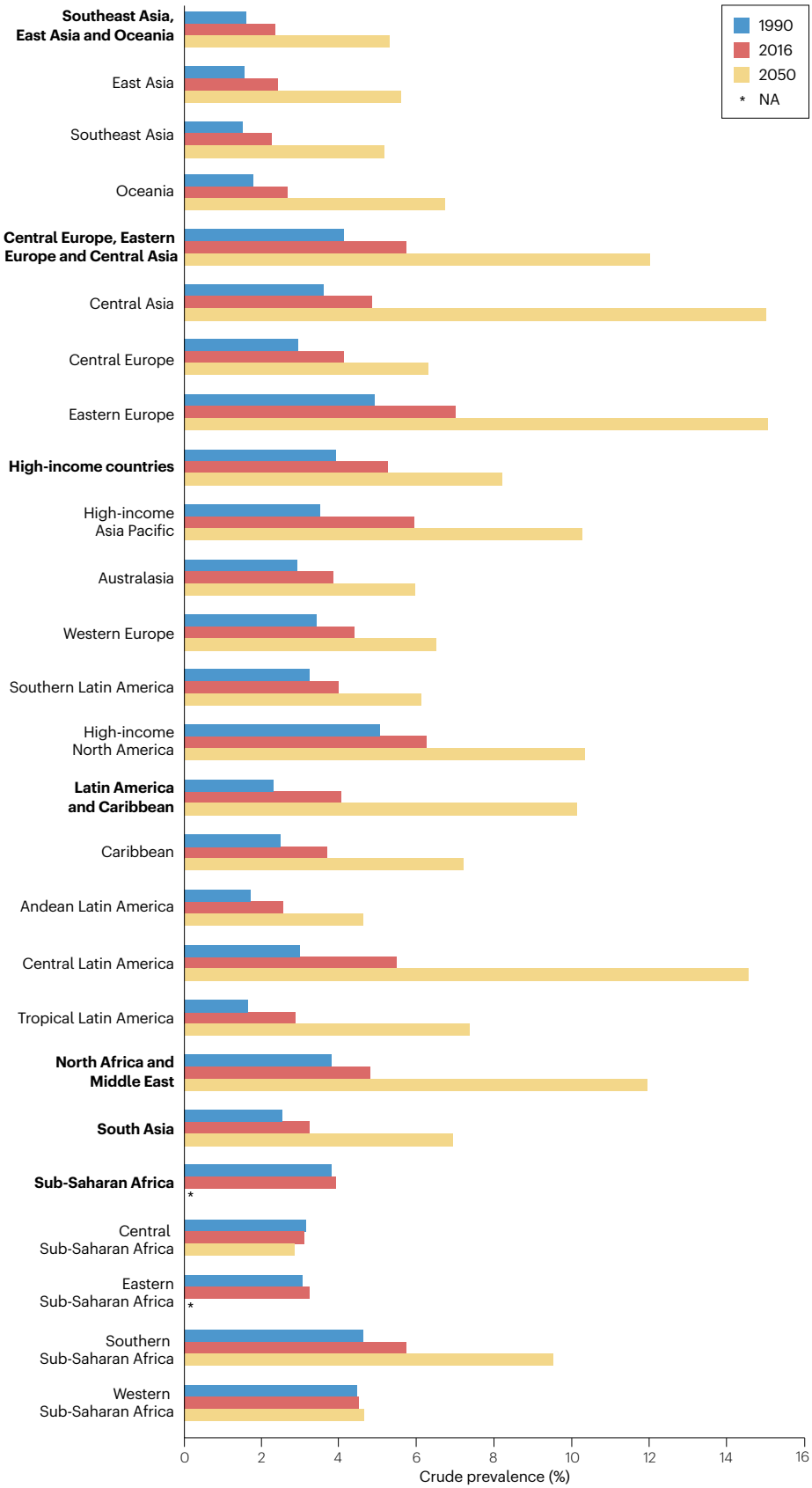

Fig. 2 | The historical and projected crude prevalence of CKD in world regions in 1990, 2016 and 2050. From 1990 to 2016, the prevalence of chronic kidney disease (CKD) increased in most world regions, with the largest relative increases in the high-income Asia Pacific and Central and Tropical Latin America regions, whereas it remained relatively stable in Central and Western Sub-Saharan Africa. Projections suggest that by 2050, the prevalence of CKD will increase to >10% in the high-income North America, Central Latin America, Eastern Europe, North Africa and the Middle East, Central Asia and high-income Asia Pacific regions. Data on CKD prevalence in 1990 and 2016 were obtained from the Global Burden of Disease Study[10]. CKD prevalence in 2050 was extrapolated based on the assumption that the effect of population ageing between 1990 and 2016 was solely responsible for the increase in CKD prevalence between 1990 and 2016. Population ageing was extrapolated to 2050 using the 'medium scenario' United Nations population projections of the percentage of people aged >65 years in 2050 (ref. 3). This method was not applicable (NA) to the Sub-Saharan Africa and Eastern Sub-Saharan Africa regions owing to the decreasing percentage of people aged >65 years between 1990 and 2016 in these regions, which resulted in a negative projected prevalence of CKD in 2050.

which was almost double that of people aged 45–54 years (1,547 pmp)[16]. In the USA in 2021, people aged >75 years had the highest prevalence of KRT (7,744 pmp), which was more than tenfold higher than that of individuals aged 45–64 years (593 pmp)[13].

The prevalence of KRT is steadily increasing worldwide[17,18]. In the USA, for example, the number of patients on prevalent KRT increased by 29% from 596,000 in 2010 to 808,000 in 2019 (ref. 19). Notably, this increase was disproportionately steeper among older age groups, with patients aged 18–44 years experiencing an 11% increase, those aged 45–64 years experiencing a 27% increase and those aged >65 years experiencing a 58% increase. Similar patterns have been observed across other HICs[20–22]. The increase in KRT prevalence was driven primarily by improved survival among older patients and an increasing incidence of KRT (Fig. 4). In most HICs, the overall incidence of KRT has plateaued over the past two decades, but in some countries it continues to rise in the oldest age groups[20,23,24]. The increase in KRT incidence is probably attributable to improved life expectancy, delayed progression of CKD, a resultant increase in the average age at which individuals start KRT and more relaxed criteria for acceptance onto dialysis[23].

As renal registries collect information only on patients who undergo dialysis or kidney transplantation, the true incidence of kidney failure remains largely unknown. Data on people with kidney failure who do not receive KRT are generally not available. Comprehensive conservative management (CCM) of kidney failure, defined as non-dialytic management that is chosen through a process of shared decision-making, focuses on maintaining quality of life (QoL) through symptom management. A Global Kidney Health Atlas (GKHA) study estimated that in 2022, CCM was offered as a treatment option in only 87 of 165 (53%) countries, whereas haemodialysis was available in 162 of 165 (98%) countries[25]. However, in HICs where CCM is available, estimates suggest that approximately equal numbers of patients with kidney failure are treated with KRT versus CCM and the odds of receiving CCM instead of KRT increase exponentially with age[26,27]. In Australia, in 2003–2007, more than 90% of patients aged 5–60 years with kidney failure received dialysis or underwent transplantation, compared with only 4% of those aged ≥85 years[26,27]. Consequently, ageing of the population is expected to lead to a greater increase in the number of patients with kidney failure who receive CCM than those who receive KRT. Researchers should therefore not rely solely on KRT data when estimating the extent of the kidney failure burden caused by ageing of the population.

Diagnosis of CKD in older patients

Diagnosing CKD in older individuals presents unique challenges. The KDIGO criteria has been criticized as it defines CKD as a persistent estimated glomerular filtration rate (eGFR) of <60 ml/min/1.73 m^2, regardless of age[28]. This fixed threshold approach does not account for the normal decline in kidney function that occurs with age[29], so could potentially lead to overdiagnosis and inappropriate treatment of CKD in otherwise healthy older adults without disease-related kidney impairment. The fixed threshold could also lead to overestimation of CKD prevalence among older people and underestimation

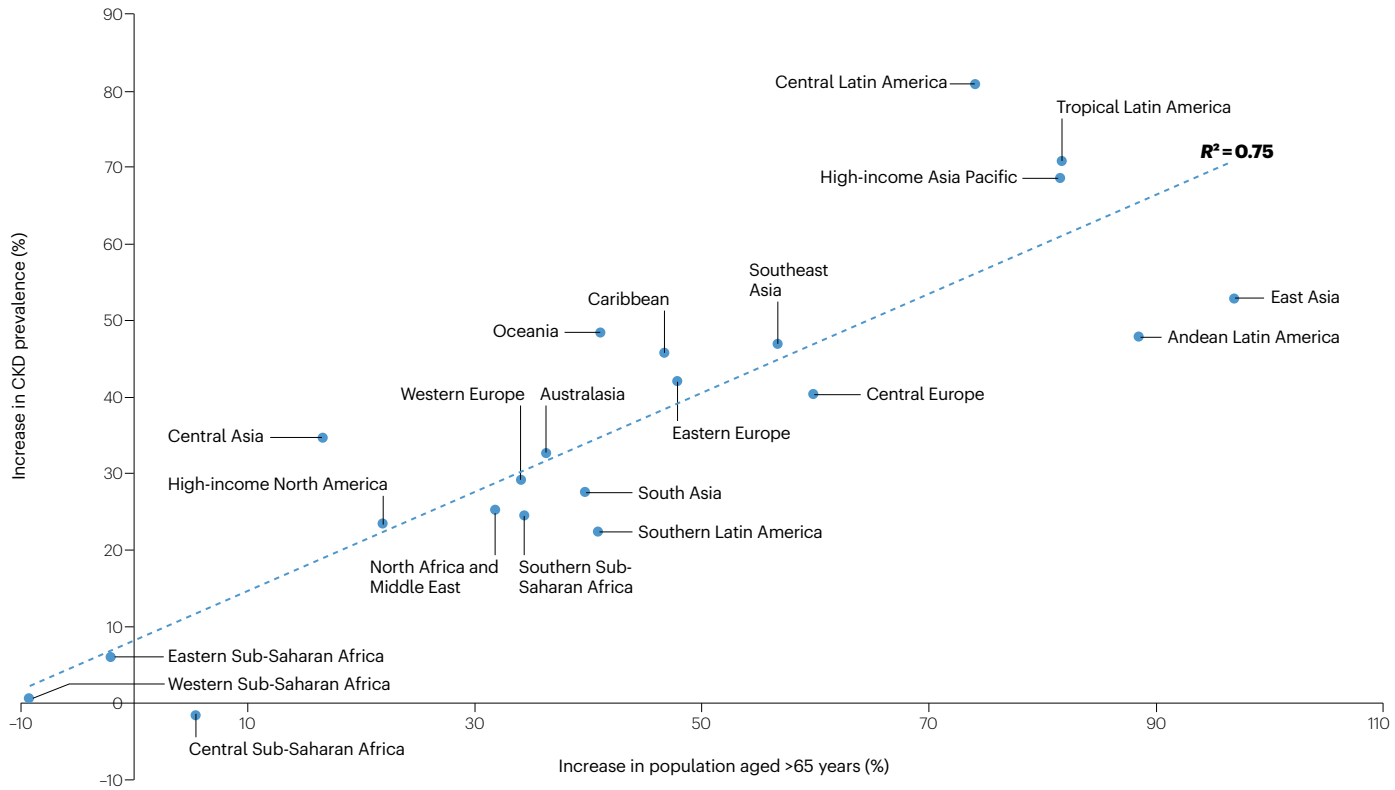

Fig. 3 | The rate of population ageing correlates with the increase in CKD prevalence between 1990 and 2016. The rate of population ageing, defined as the increase in the percentage of the population aged >65 years, strongly correlates with the percentage increase in crude chronic kidney disease (CKD) prevalence in various world regions between 1990 and 2016. Data on CKD prevalence were obtained from the Global Burden of Disease Study[10] and data on population ageing were obtained from the United Nations population projections using the 'medium scenario' (ref. 3).

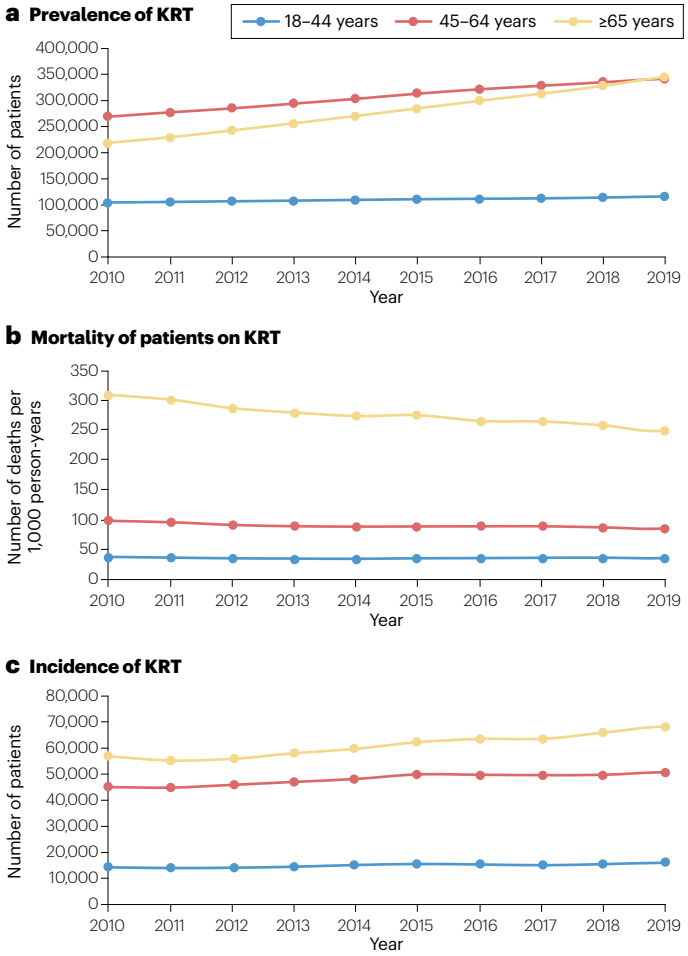

Fig. 4 | The epidemiology of KRT in the USA, 2010–2019. a, The prevalence of kidney replacement therapy (KRT) was stable among people aged 18–44 years, increased steadily among those aged 45–64 years and increased more dramatically among those aged ≥65 years. **b**, The mortality of patients on KRT was stable among those aged 18–44 years and 45–64 years, but decreased among those aged ≥65 years. **c**, The incidence of KRT increased among patients aged ≥65 years but was fairly stable in the other two age groups. These data suggest that the rising prevalence of KRT in the USA is driven primarily by improved survival and an increasing incidence among the oldest patients[19]. Data were extracted from the United States Renal Data System[19].

among younger people[30]. To address these issues, age-adapted eGFR thresholds for CKD diagnosis have been proposed but their use is still debated[30,31]. These age-adapted eGFR thresholds were chosen on the basis of their associations with adverse outcomes rather than their frequency in the population.

The 2024 KDIGO guidelines support continued use of the current CKD staging system in younger (<65 years) and older (>65 years) adults[32,33] based on 1980–2021 data from the CKD Prognosis Consortium[34]. These data showed that although the relative risks for various adverse outcomes, including kidney failure requiring KRT and all-cause mortality, were slightly smaller in older (≥65 years) than in younger (<65 years) adults, the patterns of risk association across eGFR and urinary albumin-to-creatinine ratio (UACR) categories remained consistent regardless of age. In both age groups, individuals with eGFR <60 ml/min/1.73 m^2 and albuminuria <30 mg/g (CKD category G3, A1) had consistently elevated relative risks of adverse outcomes compared with individuals with normal kidney function[34]. Despite the slightly lower relative risks of adverse outcomes in older adults, their absolute increase in risk when eGFR is lower is far higher than that of younger individuals. This discrepancy means that even a small increase in relative risk can translate into a substantial increase in the overall likelihood of adverse outcomes, which may justify a CKD diagnosis and subsequent treatment in older individuals using the current threshold definition. To estimate the absolute risk of progression to kidney failure in individuals with CKD G3–G5, KDIGO recommends using an externally validated risk equation such as the Kidney Failure Risk Equation[32,35].

In addition to diagnosis of CKD, monitoring of kidney function in older patients is crucial, not only to guide kidney-protective therapy, but also to optimize medication safety and efficacy by adjusting dosages of renally cleared drugs[36]. Isotope dilution mass spectrometry is the gold standard for measuring creatinine as it ensures accuracy and consistency across laboratories. Serum creatinine values depend on muscle mass, which often decreases with age owing to sarcopenia[37], potentially leading to overestimation of eGFR, particularly in older adults. The 2024 KDIGO guidelines list specific clinical conditions in which non-GFR determinants of serum creatinine, such as reduced muscle mass, may affect the accuracy of creatinine-based eGFR equations[32]. In these conditions, use of cystatin C is indicated as it provides a more accurate alternative to creatinine. The frequently used CKD-EPI 2009 equation has been criticized for not being adequately validated in older populations and tends to overestimate eGFR in older individuals[38]. Equations such as the Berlin Initiative Study (BIS) equation[39], which was developed based on data from a cohort of participants aged >70 years, and the European Kidney Function Consortium (EKFC) equation, which was developed based on data from cohorts of diverse ages, have been shown to have better performance that the CKD-EPI 2009 equation in older individuals[40,41]. The 2024 KDIGO guidelines recommend using an eGFR equation that has been validated in the population of interest and includes the EKFC equation as one of their recommended validated equations[32].

CKD risk factors

As the world population ages, the prevalence of risk factors for CKD is likely to increase. Unless these risk factors are identified and mitigated at an early stage, this increase will in turn lead to an increase in the prevalence of CKD. Many risk factors for CKD exist, some of which are intertwined, including genetic background, physical inactivity, salt intake and smoking. Here, we focus on risk factors that have a clear relationship with age, namely diabetes, hypertension, obesity, cardiovascular disease (CVD) and acute kidney injury (AKI).

Ageing

As kidney function declines with age even in healthy people, age is considered to be a risk factor for CKD. Age-related loss of kidney function at the cellular level causes a decline in GFR[42,43]. Ageing of the kidney is characterized by macroscopic and microscopic structural changes as well as functional changes that are also found in CKD. These structural changes include reductions in kidney size and weight, a decrease in nephron number owing to nephrosclerosis, compensatory hypertrophy of the remaining nephrons, an increase in the number of (benign) kidney cysts and renovascular changes. Functional changes include

reduced GFR, impaired tubular function and decreased endocrine function[42,44,45]. As people age, a complex interaction between genetic predisposition[46], nephron number at birth[47,48] and environmental factors[49] can contribute to a decline in kidney function even in the absence of a specific cause of kidney disease. This finding suggests that in the absence of traditional CKD risk factors in otherwise healthy individuals, rising life expectancy will coincide with an increase in CKD prevalence.

Diabetes mellitus

Diabetes continues to be the leading cause of CKD worldwide[50–52] (Fig. 5). Data primarily from HICs suggest a stabilization or even decline in new diabetes diagnoses since the mid-2000s, even in older age groups[53]. This trend could be linked to preventive measures, public health education efforts and increased awareness campaigns. However, the prevalence of diabetes continues to rise worldwide, suggesting that the effects of population ageing and increases in life expectancy are outpacing the effects of preventive efforts to stabilize the incidence of diabetes. In 2019, global diabetes prevalence was estimated to be 9.3% (463 million people), representing a 62% increase from 2009 (285 million people). This prevalence is projected to increase to 10.2% (578 million people) by 2030 and 10.9% (700 million people) by 2045 (ref. 54). LMICs bear a disproportionate burden of diabetes, with the prevalence increasing at a much faster rate than in HICs[10,55–58]. This disparity may be due to limited resources for the implementation of preventive measures to stabilize the incidence of diabetes in these regions. Notably, in many LMICs, the crude prevalence of diabetes almost doubled between 1990 and 2014. For example, the prevalence of diabetes rose from 4.7% to 8.1% in Brazil and from 5.2% to 9.8% in South Africa; in Egypt the prevalence more than doubled from 8.0% to 16.2%[51].

The prevalence of diabetes increases with age. In 2019, nearly one in five people (19.9% or an estimated 111.2 million) aged 65–79 years had diabetes[54]. As diabetes mainly affects older individuals[59] and kidney damage typically occurs 5–15 years after diabetes onset, the rise in the burden of diabetes is expected to lead to a parallel rise in the burden of CKD, unless the implementation of preventive measures is substantially increased.

Hypertension

Hypertension and declining kidney function create a harmful cycle; high blood pressure can damage kidney blood vessels over time, and impaired kidney function worsens blood pressure control[60]. The prevalence of hypertension increases with age[61–64]. In Australia and the USA, the prevalence of hypertension among older age groups was strikingly high; nearly half of all individuals aged >75 years in Australia[65], and almost three-quarters of adults aged >60 years in the USA, had hypertension[63]. Effective antihypertensive therapy has reduced the prevalence of raised blood pressure, especially in HICs[66], and has probably had a substantial role in stabilizing the prevalence of CKD over time in countries such as Norway (from 1996 to 2007) and the UK (from 2010 to 2016)[67]. Nevertheless, ageing of the population together with the high prevalence of hypertension in older adults, is expected to outpace (pharmaceutical) measures to reduce high blood pressure, inevitably causing a higher prevalence of hypertension worldwide[68]. As, after age standardization, hypertension ranked as the second leading cause of prevalent CKD[10], an increasing prevalence of hypertension is expected to result in an increasing prevalence of CKD, particularly in Latin America and the Caribbean, Central and Eastern Europe and Central Asia and Sub-Saharan Africa (Fig. 5).

Obesity

Obesity, defined as BMI ≥30 kg/m^2, is associated with haemodynamic, structural and histological renal changes and has been identified as one of the main risk factors for CKD[69–71]. Obesity is also a major risk factor for diabetes and most individuals with type 2 diabetes mellitus (T2DM) also have obesity. The prevalence of obesity is highest in the USA, where the crude prevalence has doubled in less than two decades, rising from 18.7% in 1990 to 37.3% in 2016 (ref. 72). Similar trends have been observed in other HICs. Notably, several low-income countries (LICs) have also experienced a substantial increase in the prevalence of obesity. For example, Brazil and Malaysia, which historically had low prevalence of obesity, have seen large increases. In Malaysia, the prevalence of obesity rose from 3.4% in 1990 to 15.4% in 2016, and in Brazil it rose from 9.1% to 22.3% in the same period[72].

In most regions, obesity is associated with age. For example, in England in 2021, the prevalence of obesity was 8% among adults aged 16–24 years, 32% among those aged 65–74 years and 26% among those aged ≥75 years[62]. By contrast, the prevalence of obesity in the USA is consistently high and shows little variation across age groups. Data from January 2017 to March 2020 indicates that the prevalence of obesity in the USA was 39.8% among adults aged 20–39 years, 44.3% among those aged 40–59 years and 41.5% among those aged ≥60 years[73]. This pattern may reflect a ceiling effect as the prevalence of obesity is high in younger age groups. Nonetheless, ageing of the population is expected to coincide with increasing trends in obesity prevalence, which in turn is expected to contribute to a rise in the prevalence of CKD.

Cardiovascular diseases

CVDs, including heart failure, coronary artery disease, atrial fibrillation and stroke, remain the greatest health burden worldwide. These diseases have been the leading cause of death since 1980 and affected 620 million people in 2021 (refs. 74,75). Older people are particularly susceptible to CVD, with a prevalence of approximately 50% among

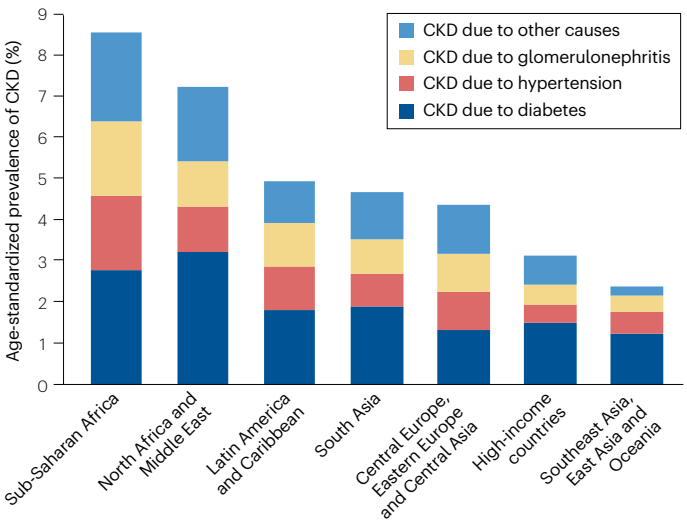

Fig. 5 | The age-standardized prevalence of CKD in 2016 by aetiology and region. In 2016, diabetes continued to be the leading cause of chronic kidney disease (CKD) followed by hypertension. Sub-Saharan Africa showed the highest age-standardized prevalence of CKD, followed by North Africa and the Middle East, and Latin America and the Caribbean. Data obtained from the Global Burden of Disease Study[10].

those aged >75 years in low-, middle- and high-SDI countries[76]. According to GBD data, the crude prevalence of CVD was highest in high-SDI countries, rising from 9.1% in 1990 to 12.2% in 2021. Conversely, in LICs, the crude prevalence of CVD remained relatively low and stable, rising from 3.9% in 1990 to 4.2% in 2021. Middle-income countries experienced the highest relative increase, with the crude prevalence of CVD rising from 4.3% in 1990 to 7.6% in 2021 (ref. 76). However, the age-standardized prevalence of CVD decreased in HICs and stabilized in middle-income countries between 1990 and 2021 (refs. 76,77). This contrast between crude and age-standardized prevalence indicates that population ageing is the primary factor driving increases in CVD prevalence over the past three decades. It also suggests that the CVD risk at any given age has either declined or remained stable, probably as a consequence of successful public health interventions aimed at preventing CVD and managing its risk factors. As CKD and CVD are closely related and share common risk factors, including diabetes, hypertension and obesity, such efforts probably also contributed to the decline in age-standardized CKD DALYs discussed above. Despite these improvements, the combined effects of the ageing population and the high prevalence of CVD and its shared risk factors in older adults is expected to outpace prevention efforts, in turn contributing to a higher overall burden of CKD[74,78–80].

Importantly, the relationship between CKD and CVD is bidirectional. In older people, CKD is associated with a very high risk of cardiovascular complications[81–84], including coronary artery disease, heart failure, arrhythmias, sudden cardiac death and peripheral artery disease. Patients with CKD have a unique tendency towards calcification and vascular stiffness, which underlies their increased risk of arterial disease. Left ventricular hypertrophy, which is significantly associated with heart failure, develops in the early stages of CKD and affects 70–80% of patients with kidney failure[85]. Notably, CKD is associated with an increased risk of all-cause and cardiovascular death, which is related to accelerated biological ageing in all age groups, with the greatest absolute increase in risk in those aged >75 years[86]. Owing to high levels of CVD mortality, most individuals with progressive CKD do not survive to reach kidney failure.

Acute kidney injury

AKI is a heterogeneous condition characterized by an acute loss of kidney function[87]. In HICs, AKI affects approximately 20% of hospitalized adults and nearly 50% of those in intensive care units[88]. The risk of AKI hospitalization increases with age. Among US Medicare beneficiaries aged >66 years in 2021, hospitalization rates for AKI among those aged ≥85 years were three times higher than those aged 66–69 years[13]. Outcomes in this population were poor. At discharge, 17% of patients had either died or entered hospice care, with this figure rising to 42% for those requiring dialysis. Within 3 months after discharge, one in six survivors of AKI had died and one in eight were newly diagnosed with CKD[13]. Moreover, patients with AKI and pre-existing CKD had a 41-fold higher risk of kidney failure and patients with AKI who did not have pre-existing CKD had a 13-fold higher risk of kidney failure than patients without kidney disease[89].

Age-related structural and functional changes that reduce kidney function and kidney reserve result in increased susceptibility to AKI and the subsequent development of CKD[90], as well as poorer AKI recovery[91,92]. Furthermore, the prevalence of comorbidities such as diabetes, hypertension and CVD increases with age. These comorbidities also reduce kidney reserve and often result in polypharmacy, increasing the risk of nephrotoxic drug exposure and drug–drug interactions that may adversely affect kidney function, further predisposing to AKI and subsequent CKD. In addition, older individuals are more likely than younger individuals to undergo (cardiac) surgery and other procedures that require diagnostic radiography, which exposes them to nephrotoxic contrast medium — an important risk factor for AKI[93].

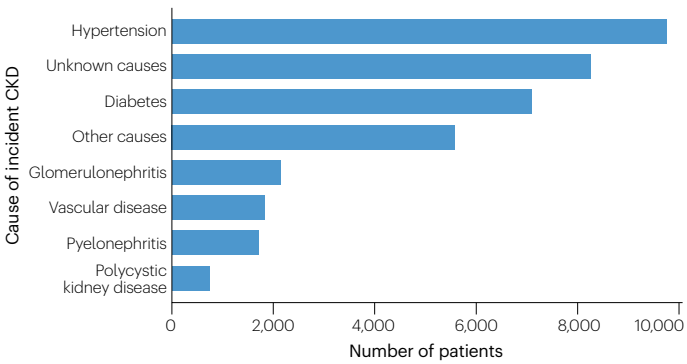

Fig. 6 | Causes of incident CKD in older patients starting kidney replacement therapy in European countries in 2010–2013. The three main causes of incident chronic kidney disease (CKD) in patients aged ≥75 years initiating kidney replacement therapy were hypertension, unknown causes and diabetes. Data obtained from the European Renal Association Registry[104].

Slowing the increase in CKD prevalence

The ageing-associated increase in the prevalence of CKD may be slowed by focusing on CKD prevention with interventions at younger ages. This approach requires characterization of the main causes of CKD in older individuals, the development of tools to identify those at higher risk of developing CKD and the development of interventions that target the drivers of CKD. Additional measures include early diagnosis and treatment of CKD to prevent CKD-associated premature death and progression to more advanced stages of CKD or kidney failure. Clinical guidelines specify high-risk populations that should be screened for CKD[94–101] (Supplementary Table 1). However, implementation of screening, particularly assessment of albuminuria, is suboptimal[102]. Although many strategies for primary prevention of non-communicable diseases exist, none has been specifically developed for the prevention of CKD in high-risk individuals.

Causes of CKD in older people

Understanding of the underlying causes of kidney disease in older people is essential to enable effective interventions to mitigate the increasing prevalence of CKD in ageing populations. Large European registries reported that the three main causes of kidney failure requiring incident KRT in people aged ≥75 years were hypertension, unknown causes and diabetes[103,104] (Fig. 6). However, the role of hypertension as a major cause rather than a consequence of CKD has been questioned[105]. Even young patients with primary hypertension may meet the KDIGO histological diagnostic criteria for CKD[106] and a dissociation exists between the burden of hypertension and the incidence of KRT attributed to kidney failure owing to hypertension in various countries[105]. Moreover, *APOL1* risk variants have been shown to underlie the increased risk of CKD among African American individuals, which was previously attributed to hypertension[107]. In 2023, a small-molecule inhibitor of APOL channel function was shown to reduce proteinuria in patients with biopsy-proven focal segmental glomerulosclerosis and two *APOL1* risk variants[108,109].

Thus, the cause of CKD in most older patients should be considered unknown[30,32,105–112]. Unknown causes of CKD may represent suboptimal diagnostic work-ups or simply the absence of a specific cause of disease, which could represent one end of the spectrum of age-associated kidney function decline. Biological ageing is heterogeneous between and within individuals[113,114]. The interaction between genetic background and environment may modulate the rate of organ ageing in those who are free of disease. Indeed, polygenic risk scores may identify people at birth with up to eightfold increased risk of developing CKD[115]. This baseline risk may interact with environmental factors (for example, intrauterine growth, prematurity, environmental toxins, diet and lifestyle) to modify the baseline number of nephrons or the rate of nephron loss.

Delaying kidney ageing

The rate of age-associated GFR loss has been estimated as 1 ml/min/1.73 m^2 per year[116]. However, this rate is variable and accelerates nearly threefold in healthy men aged 60–65 years[117]. Preclinical evidence suggests that age-associated CKD can be prevented. In mice, administration of renin–angiotensin system (RAS) blockers from weaning led to a 3.8-fold higher nephron number in old age compared with controls[110]. Whether this finding can be translated to humans, at what age the intervention should be initiated and the optimal therapeutic regime remains unclear.

Specific interventions such as SGLT2 inhibitors have been shown to stabilize eGFR loss (to as little as ≈0 ml/min/1.73 m^2 per year) and prevent the development of CKD in people with T2DM and high CVD risk[107]. Similar stabilization of eGFR with SGLT2 inhibitors was observed in patients with CKD owing to diverse causes and albuminuria <30 mg/g[100,101,107,111,112,117,118] (Fig. 7a). If loss of kidney function in patients with CKD risk factors can be stopped or slowed to a rate lower than that of age-associated eGFR loss, at least for the 2–3-year duration of a clinical trial, it is reasonable to speculate that age-associated eGFR loss could also be slowed in healthy people. Such an approach might be beneficial for prevention of CKD in high-risk individuals. This hypothesis should not be considered an argument for the prescription of SGLT2 inhibitors to delay kidney ageing in individuals with normal kidney function, but instead a consideration for the design of future clinical studies that should include assessment of the effect of these drugs on eGFR in younger individuals with CKD risk factors and normal kidney function. The implementation of such prevention approaches would probably be more cost-effective than setting up dialysis centres for the increasing numbers of individuals who require KRT in countries that cannot currently offer such therapy, even for their younger citizens.

Lifestyle interventions

CKD and its risk factors can be prevented by healthy lifestyle practices. Health education and lifestyle interventions include not smoking, regular exercise, good sleep hygiene and healthy diets. Avoiding processed foods with excess salt or phosphate is key and should be recommended from an early age and throughout the life course, as emphasized by the American Heart Association Presidential Advisory on cardiovascular–kidney–metabolic health[119–122]. These lifestyle measures also reduce the development of risk factors for the development and progression of CKD, such as obesity, diabetes, hyperlipidaemia, hypertension and CVD. However, compliance with lifestyle interventions is limited owing to multiple factors, including socioeconomic issues[121]. Achieving broad adoption of healthy lifestyle behaviours is challenging and requires multi-stakeholder action involving governments, educational institutions, health-care systems, media and the food and health and fitness industries[123].

Management of CKD risk factors

Effective management of diabetes, hypertension, obesity and CVD through medical and lifestyle interventions reduces diverse risks, including the risk of developing CKD. However, CKD outcomes in patients with these risk factors remain suboptimal. The diabetes complication that showed the smallest decline in incidence between 1990 and 2010 was kidney failure[124]. From 2015 to 2020, the overall incidence of CKD among patients with T2DM declined by 22% to 64.0

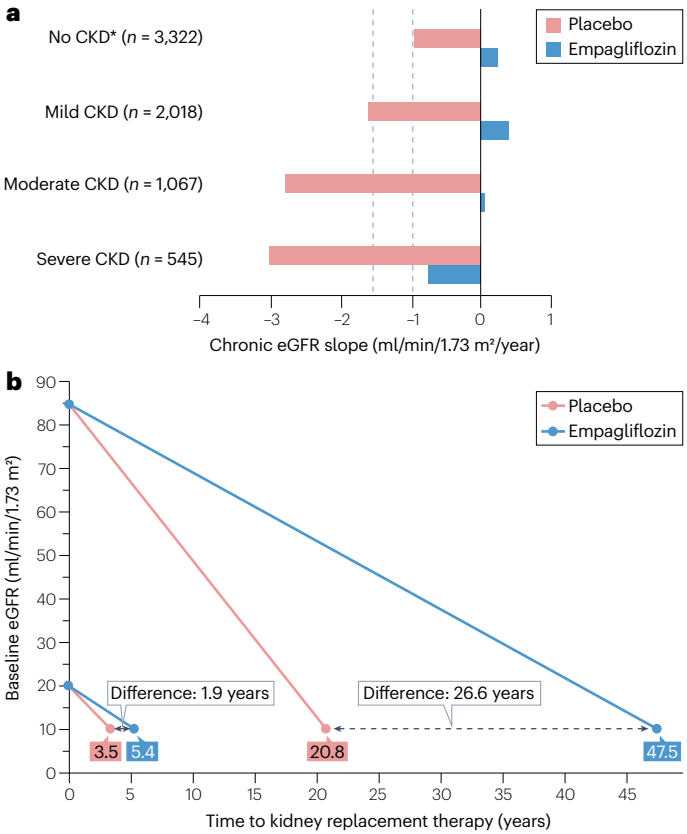

Fig. 7 | Effect of SGLT2 inhibitors on chronic eGFR slopes and time to need for KRT. a, Chronic estimated glomerular filtration rate (eGFR) slopes in participants with different categories of chronic kidney disease (CKD) in the EMPA-REG outcome cardiovascular safety trial of empagliflozin. This trial enrolled participants with type 2 diabetes mellitus and high cardiovascular risk, most of whom did not meet the KDIGO eGFR and albuminuria thresholds for diagnosis of CKD[107]. The CKD categories were based on the 2021 ESC guideline on cardiovascular disease prevention nomenclature[100,101]. Values for *n* are the number of participants in each CKD category at baseline. The vertical discontinuous lines at −1.0 and −1.5 ml/min/1.73 m^2 indicate the widely accepted age-associated eGFR slope and measured GFR slope for men older than 65 years, respectively[117]. **b**, Conceptual model of the potential effect of initiation of SGLT2 inhibitor therapy at different levels of baseline GFR on time to kidney replacement therapy (KRT) in patients with CKD of various causes. Adapted with permission from ref. 161, OUP, which used observed data on chronic eGFR slopes at different baseline levels of eGFR in the placebo and SGLT2 inhibitor groups of the EMPA-KIDNEY trial of empagliflozin in participants with CKD[118]. This model assumes that the chronic eGFR slope observed in the clinical trial is maintained over time and that the individual survives long enough to start KRT.

cases per 1,000 person-years (95% CI 62.2–65.9)[125]. However, the long-term cumulative incidence of CKD in people with T2DM may be as high as 54%[126].

Lack of CKD-specific prevention efforts in individuals with risk factors may contribute to suboptimal CKD outcomes[98]. Guidelines for the management of hypertension and diabetes recommend medications to achieve good blood pressure and metabolic control, but not specifically to prevent CKD[127–130]. The optimal blood pressure target, especially for older individuals, remains controversial, and recommended targets differ between guidelines[127,128]. Intensive blood pressure control has been associated with an increased incidence of CKD, highlighting the need to understand the long-term consequences of antihypertensive treatment-related decreases in eGFR[131].

A clinical trial in participants with T2DM showed no differences between the effect of the glucose-lowering drugs insulin glargine, glimepiride, liraglutide or sitagliptin combined with metformin on albuminuria or kidney impairment during a mean follow-up of 5 years[132]. GLP1 receptor agonists (GLP1RAs) have been shown to lower body weight, improve blood glucose and blood pressure control and reduce the risk of cardiovascular events in patients with overweight, obesity or diabetes, and at least some GLP1RAs might prevent CKD in people with diabetes[133–136]. A post hoc analysis of three cardiovascular safety trials that included >20,000 participants with T2DM who were at high risk of CVD and did not have CKD according to KDIGO criteria (eGFR >60 ml/min/1.73 m^2 and albuminuria category A1), reported that SGLT2 inhibitors reduced the risk of new onset CKD or kidney events by 33–60% compared with placebo[98,107,112] (Supplementary Table 2). Implementing measures for CKD prevention from mid-life may reduce the prevalence of CKD among older people. However, in the absence of specific trials with primary end points of kidney events that enrol participants with T2DM who are at high risk of CKD but do not have CKD at baseline, estimating the long-term effect of CKD prevention strategies involving SGLT2 inhibitors or GLP1RAs on the future prevalence of CKD and KRT is difficult. Whether these strategies could also be beneficial for prevention of CKD among individuals without T2DM is also unclear.

Effective prevention strategies require the development of tools for the sufficiently early identification of people at high risk of developing CKD (beyond classical risk factors) and of environmental factors that must be avoided, which may be specific to the genetic background of the individual. In addition to complex tools that could potentially be used to identify high-risk individuals, such as genomics, imaging and urinary peptidomics, currently available biomarkers such as increasing levels of albuminuria or accelerated decreases in eGFR slopes that do not yet reach the diagnostic thresholds for CKD, might identify a high risk of CKD among people with or without T2DM[137–139].

Early diagnosis of CKD

The 2024 KDIGO guideline states that CKD can be diagnosed at an early stage before loss of >50% of the functional kidney mass (eGFR <60 ml/min/1.73 m^2) by assessing markers of kidney damage such as UACR >30 mg/g[32]. Population-wide or targeted screening for biomarkers of CKD has been implemented in some countries[140]. For example, urinalysis screening of Japanese schoolchildren and Israeli military recruits may detect glomerular haematuria or proteinuria[141,142]. Similar screening programmes for adults are scarce, perhaps because general population screening for CKD is often not deemed to be cost-effective. However, this situation may change depending on the cost and availability of new kidney-protective drugs such as SGLT2 inhibitors[143,144].

The UACR is a non-expensive measurement that can diagnose CKD even in individuals with normal proteinuria and GFR. UACR-based diagnoses of CKD are actionable as clinical guidelines recommend treatment for CKD based on albuminuria levels[32,98]. Current high-throughput methods can be used to assess UACR semi-quantitatively for less than €0.2 per sample. However, a positive UACR result need to be confirmed using quantitative UACR. Unfortunately, UACR measurement is not available in some settings even though European and national guidelines have expanded the indication of albuminuria screening for individuals at high risk of either CKD or CVD[96,97,100,145] (Supplementary Table 1). For example, measurement of albuminuria is not currently reimbursed in Belgium for people who do not have diabetes[146]. This situation limits access to early diagnosis and treatment of CKD, which does not help efforts to decrease the extremely high incidence of KRT in Belgium[15]. In the Netherlands, a pilot home-based albuminuria screening programme identified pathological albuminuria in 1.7% of participants (aged 45–80 years)[147]. Among participants who were referred to primary care physicians on the basis of their screening results, those from areas of low socioeconomic status were less likely to visit their primary care physicians, highlighting socioeconomic disparities in health care and compliance.

Suboptimal awareness of CKD among physicians and the general population also needs to be addressed to improve early diagnosis. Evidence suggests that CKD may be undiagnosed and untreated even in patients with persistently low eGFR. An analysis of a Swedish cohort that included 57,880 adults with persistent eGFR <60 ml/min/1.73 m^2, reported that nearly 80% had not been diagnosed with CKD and this lack of diagnosis was associated with an increased risk of prescription of nephrotoxic drugs[148,149].

Slowing CKD progression

RAS blockade with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) has been used for the treatment of CKD in patients with proteinuria or hypertension for several decades[28]. Novel families of kidney-protective drugs are also now available or have shown beneficial effects on CKD outcomes in clinical trials[107,109,111,112,115,118,150–160] (Supplementary Table 2). To date, however, only SGLT2 inhibitors have been shown to consistently slow CKD progression across different agents and aetiologies of CKD[150,154]. Dapagliflozin and empagliflozin slowed eGFR loss and reduced the incidence of a combined primary end point of kidney events and cardiovascular death in patients with CKD and a wide range of eGFR and UACR values, independently of cause of CKD[118,154]. The chronic eGFR slopes reported in these trials suggest that SGLT2 inhibitors may delay KRT by up to 28 years when baseline eGFR is ~80–90 ml/min/1.73 m^2 and CKD is diagnosed based on albuminuria, assuming that the patients survive and the reported benefits of these agents are maintained long term[118,161] (Fig. 7b). If SGLT2 inhibitor therapy is initiated in patients aged 60–70 years, they may not require dialysis until they reach the age of 107–117 years (instead of 81–91 years), assuming that they survive to such an advanced age. As survival to >105 years is unlikely, SGLT2 inhibitors (and other interventions) that slow CKD progression are expected to reduce the need for KRT or CCM in older patients. If SGLT2 inhibitors are initiated in patients with eGFR 20 ml/min/1.73 m^2, KRT might be delayed for 1.9 years, potentially avoiding 296 haemodialysis sessions and the associated societal costs and environmental impact[161]. In patients with CKD, SGLT2 inhibitors were shown to reduce the risk of CVD death or heart failure hospitalization from the first month after treatment initiation, indicating early benefit of these

therapies[154]. The mean age of participants in the kidney-protective trials was around 65 years, suggesting that older individuals were adequately represented in these studies. In EMPA-KIDNEY for example, the mean age of those in the empagliflozin group was 63.9 years with a standard deviation of 13.9 years, meaning that >15.8% of participants were older than 77.8 years[118]. In some countries, generic SGLT2 inhibitors are already available, potentially making these drugs affordable outside high-income settings.

Other new agents have been tested only for certain aetiologies of CKD[109,133,155,156,159,162] (Supplementary Table 2). The FLOW trial of semaglutide in participants with CKD (UACR >100 mg/g) and T2DM was stopped prematurely owing to efficacy for kidney, cardiovascular and all-cause mortality outcomes[160,163,164]. The nonsteroidal mineralocorticoid receptor antagonist (nsMRA) finerenone, improved kidney and cardiovascular outcomes in patients with diabetic kidney disease and albuminuria >30 mg/g (refs. 133,162). In post hoc analyses, the combination of SGLT2 inhibitor plus finerenone halved the incidence of kidney events compared with SGLT2 inhibitor alone[158]. The ongoing FIND-CKD trial is evaluating kidney protection by finerenone in participants with non-diabetic CKD[165]. Interestingly, SGLT2 inhibitors, RAS blockers and MRAs preserve the expression of Klotho, which is predominantly expressed in the kidney and has anti-ageing properties[166–168].

Competing risks

CKD is associated with an increased risk of all-cause death, which remains high for patients on KRT[169–171]. This competing risk of death may reduce the prevalence of CKD and KRT[172]. As novel kidney-protective drugs reduce the risk of CVD and/or all-cause death[150,154], their widespread therapeutic use could potentially increase the prevalence of CKD by improving patient survival. However, such an effect is unlikely. An analysis of data for participants with diabetic kidney disease in trials of new kidney-protective drugs suggested a larger effect on CKD progression than on risk of death; combination therapy with SGLT2 inhibitors, GLP1RAs and the nsMRA may delay all-cause death by 2.4 years (95% CI 1.4–3.4), major adverse cardiovascular events by 3.2 years (95% CI 2.1–4.3) and CKD progression by 5.5 years (95% CI 4.0–6.7), compared with conventional therapy[173].

CKD complications in older patients

CKD in older individuals is an inherently complex medical condition with a multitude of interconnected complications and symptoms that can substantially affect QoL[174,175]. Patient complexity is an interaction between the "personal, social, and clinical aspects of the patient's experience" that affects patient care[176]. Increasing age and multiple comorbid conditions, social factors such as low income and low education, a high number of drugs and background factors, such as long-term care environments, affect perceived patient complexity[177]. The complexity of patients varies substantially across medical specialties but is particularly high in nephrology owing to the multimorbid nature of CKD, the requirement for multidisciplinary care, the high frequency of polypharmacy and the high rates of hospitalization and death[176].

Hospitalizations are common in patients with CKD, especially older patients with multimorbidities. Among 4,766 participants of the Atherosclerosis Risk in Communities study, older adults with very-high-risk stages of CKD had hospitalization rates of >50 per 100 person-years[178]. In the Chronic Renal Insufficiency Cohort study, participants had an unadjusted overall hospitalization rate of 35 per 100 person-years and an unadjusted hospitalization rate for cardiovascular-related causes of 11 per 100 person-years. All-cause, non-cardiovascular and cardiovascular hospitalizations were all associated with older age[179].

Fatigue affects about 70% of patients with CKD, and the prevalence of this symptom increases with age and CKD stage[180,181]. Fatigue is often a result of anaemia or a general state of ill health and affects not only physical well-being and functioning but also emotional well-being and social participation[180]. CKD compromises nutritional status and muscle function, and sarcopenia and frailty, which are associated with a wide range of adverse health outcomes, are highly prevalent in the older CKD population[182]. Although no recommended pharmacological treatments exist, exercise training and nutritional supplementation are widely accepted to be key interventions to maintain skeletal muscle mass and strength in patients with sarcopenia[183].

The prevalence of skeletal fractures in the general population and in individuals with CKD has increased over the past decade owing to population ageing and associated bone loss[184]. Longitudinal studies showed that the incidence of fractures increases with worsening CKD stage, with the highest risk in individuals with eGFR <15 ml/min/1.73 m^2 (ref. 185). Patients with CKD aged >65 years had the highest rate of fractures, with 1 in 10 women and 1 in 20 men experiencing at least one fracture within 3 years[186]. In particular, hip fractures are more common among patients with CKD than in the general population. The incidence of hip fractures is four times higher in patients on dialysis than in the general population[187]. Risk factors for hip fractures include older age, low BMI, long dialysis vintage and a history of previous hip fracture. Although the risk of subsequent major non-hip fractures following a hip fracture is not increased in patients with CKD, hip fracture and non-hip fracture mortality is increased in patients with advanced-stage CKD[188].

Cognitive dysfunction and dementia are strongly associated with advanced age[189] and are common in patients with CKD[190]. CKD-related cognitive impairment can range from mild cognitive deficits to severe dementia. The exact mechanisms underlying cognitive dysfunction in CKD are not fully understood, but factors such as vascular damage, inflammation, oxidative stress and accumulation of uraemic toxins may have a role. Cognitive impairment can substantially reduce QoL and the ability of patients to manage their health care. Early detection and management of cognitive dysfunction in CKD are crucial to optimize patient outcomes and improve overall well-being[191].

Depression and anxiety also substantially reduce patient well-being, especially among the older CKD population[192]. The severity of depression often increases as CKD progresses owing to the chronic burden of managing a progressive condition as well as pain, fatigue and sleep disturbances[193]. The psychological burden is worsened by complex medical regimens and associated financial issues. Social networks may shrink as physical limitations and demanding treatment regimens impose barriers to social interaction, perpetuating a cycle of isolation and cognitive decline that can amplify feelings of despair. Concerns about disease progression and the potential need for dialysis or transplantation can contribute to anxiety. Frequent medical appointments may also exacerbate anxiety by serving as reminders of patient vulnerability and dependence on health-care systems. The management of depression and anxiety in older patients with CKD requires a multidisciplinary approach, involving nephrologists, primary care physicians, mental health specialists and social workers, to address the interplay between physical and psychological well-being. Regular mental health screening is crucial to identify and manage depression and anxiety in patients with CKD. Pharmacological interventions for mental health conditions should be considered in the light of altered pharmacokinetics and pharmacodynamics in these patients[194]. Psychotherapeutic

interventions, such as cognitive-behavioural therapy, may provide patients with tools to manage anxiety and depression[194]. Lifestyle modifications, including dietary adjustments and physical activity, alongside the strengthening of social support networks, may also be beneficial[194].

CKD complications and symptoms in older adults pose a complex, substantial health burden. Development and implementation of integrated care models that coordinate services and facilitate a seamless transition across different levels of health care can improve outcomes for older patients with CKD[195]. The management of CKD in these patients should be multidisciplinary, involving dietitians, pharmacists, social workers, psychologists and possibly other specialists such as cardiologists and endocrinologists to address the multifaceted aspects of care. An integrated approach to managing multimorbidity, nutritional challenges, bone health, cardiovascular risks, fatigue, mental health and cognitive decline supports the need for appropriate non-pharmacological and pharmacological treatments and societal adjustments to accommodate an ageing population with CKD and other chronic health conditions. Interventions that maintain or improve the QoL of older patients with CKD, including pain management and palliative care services when appropriate, should be made available. In addition, health practitioners require enhanced education and training focused on geriatric nephrology to manage the complex needs of older adults with CKD. Finally, the importance of tailored education for patients and their families about managing CKD and its complications to empower them in self-care and disease management cannot be overemphasized.

The financial burden of CKD

The treatment of CKD and kidney failure imposes a substantial financial burden on global health systems. The projected rise in CKD prevalence, driven by an ageing population and risk factors such as diabetes, hypertension and CVD, will drive further cost increases, necessitating preparedness within the health-care system. The costs of dialysis and kidney transplantation currently account for a disproportionately high 1–3% of total health-care expenditure in HICs, whereas patients with kidney failure comprise only 0.01–0.03% of the population of these countries, representing a 100-fold difference in health-care resource allocation compared with the general population[196–200]. Non-health-care-related costs of CKD should also not be underestimated, including costs related to loss of productivity, costs related to informal caregivers and out-of-pocket costs related to medication and travel[201–204]. In the Netherlands the annual estimated non-health-care-related costs of kidney failure were estimated to be €8,284 for transplant recipients and €23,488 for patients on dialysis[205]. In HICs, a substantial portion of overall health-care costs is driven by a relatively small number of older adults. In the USA for example, the top 5% of health-care spenders, 40% of whom were aged ≥65 years, accounted for more than half of all health-care expenditure but only 18% of the total population[206]. Health expenditure for kidney failure is no different, with the oldest patients incurring the highest costs. Among Medicare beneficiaries with kidney failure, the overall costs were 26% higher for those aged >75 years than for those aged 45–64 years[13].

Spending on kidney failure is rapidly increasing. In the USA, total kidney failure-related costs increased from US$37 billion in 2011 to $52 billion in 2021 (ref. 13). In the UK, renal health services project a doubling of costs between 2023 and 2033 and the need for a 400% increase in dialysis capacity to meet future demand[204]. Globally, the increase in demand for dialysis treatment will probably further outpace dialysis capacity, leaving many patients without access, particularly in regions that are already struggling to provide basic renal care. In LICs and lower-middle-income countries, more than 90% of people with kidney failure currently do not receive KRT owing to economic factors[25]. The GKHA identified substantial gaps in the public funding of kidney health services, which force a large proportion of patients to pay for treatment entirely themselves. Consequently, patients experience catastrophic out-of-pocket expenses, high rates of treatment discontinuation and subsequent mortality[207,208]. A systematic review of studies reporting outcomes related to dialysis in Sub-Saharan Africa published between 1990 and 2015 reported that even among the few people who were able to access health services to receive a diagnosis of kidney failure, mortality was >95% owing to a lack of access to dialysis[209]. Among the small number who did receive dialysis, treatment duration was mostly short-lived and often discontinued within 2 weeks owing to an inability to pay[209–211].

Although per-patient costs are lower for CKD than for kidney failure (but still double that of patients without CKD), the total expenditure for CKD is far larger because this group constitutes the vast majority of patients. Among US Medicare beneficiaries aged >65 years in 2021, the prevalence of CKD was 13.5%, but this group (which did not include patients with kidney failure) accounted for a quarter of total Medicare spending ($76.8 billion)[13]. Alarmingly, CKD-related costs in the USA rose by 40% between 2011 and 2021, driven primarily by increases in the costs of prescription drugs (138%), outpatient services (108%) and hospice services (52%) as well as physician and supplier costs (43%)[13]. Globally, similar cost increases are expected. In Chile, the prevalence of CKD stage 3–5 is projected to double and the direct costs related to the treatment of CKD are projected to triple between 2021 and 2041 (ref. 212). In China, the total economic burden of CKD is expected to increase from $179 billion in 2019 to $198 billion in 2025 in accordance with the projected rise in CKD prevalence[213].

CKD frequently co-occurs with other non-communicable diseases, particularly in older individuals. Patients with multimorbidities require additional specialized care, leading to substantially higher costs[214,215]. In the USA in 2021, patients with concomitant CKD, heart failure and diabetes had an annual per-patient cost of $50,000, which was 2.5 times higher than that of patients with CKD alone ($20,000)[13]. In the Netherlands in 2016, around 80% of total hospital costs for patients with CKD category G4 or G5 were not related to renal treatment, with older patients in particular requiring ischaemia-related cardiology care and diabetes-related care[214]. In Australia, the number of hospitalizations due to CKD or kidney failure doubled between 2000 and 2020; the main non-dialysis-related reasons for hospitalization in these patients were heart failure, diabetes and sepsis[216]. Notably, 70% of all CKD-related hospitalizations occurred in patients aged >65 years, and the rate of hospitalization was four times higher in those aged >85 years than in those aged 65–74 years. Ageing of the population is therefore likely to lead to a substantial increase in the number of CKD-related hospitalizations and associated costs.

Although the per-patient cost of CKD depends mostly on the presence of comorbidities and consequent hospitalizations, it also varies by CKD category and patient age. In the USA, costs tend to increase with age among patients with CKD categories G1–G3. By contrast, in those with advanced CKD (categories G4 and G5) treatment costs per patient seem to decrease with age, especially for the oldest patients[13]. A similar pattern was seen in the Netherlands, where costs for patients with CKD category G4 or G5 were lower for those aged >75 years than for those aged 65–74 years[214]. This finding suggests that in some countries,

older individuals with advanced CKD and their physicians may often opt for non-dialytic treatment options, such as CCM, which are considerably less costly than KRT[217]. Observational studies have shown that the odds of receiving CCM increase exponentially with age[26,27]. This increase is understandable given the high mortality of older patients with kidney failure in the first year after initiation of dialysis[218]. However, age should not be the only criterion that is considered when deciding on CCM versus KRT. Although dialysis provides a survival advantage over CCM, this benefit may be substantially reduced in older individuals with multimorbidities[217,219–222]. An ongoing randomized controlled trial is comparing the survival and person-centred outcomes of patients aged >65 years receiving dialysis versus conservative care, with the aim of providing robust evidence on the optimal treatment approach for older individuals[223].

Ethical aspects of the management of kidney failure in older patients are complex and depend on the availability of resources and the clinical situation of patients. In low-resource countries, individuals who are very old may compete with younger individuals for a limited supply of donor kidneys or access to dialysis. In HICs, recommending CCM solely to lower health-care costs would be unethical. However, CCM should be offered as a viable treatment option during the shared decision-making process to collaboratively determine a treatment approach that respects the values and wishes of the patient. Shared decision-making may be compromised by difficulty in accurately informing individual patients about the pros and cons of CCM versus KRT given the low quality of the available data on CCM and very different individual situations. CCM is often argued to potentially be associated with better QoL than KRT, but this conclusion is based on small, low-quality studies. A Dutch observational study that included 366 patients aged >70 years, reported that those who received CCM had lower median survival (2.4 versus 4.3 years) but similar physical and mental QoL to those who received dialysis[217]. However, QoL data were obtained from only 23% of participants on dialysis and 18% of those on CCM, suggesting potential for bias. Moreover, patients on dialysis had significantly higher scores for vitality, mental health and social interactions than those on CCM[217]. Among 456 European patients who started dialysis at mean age 76 years, symptom burden worsened considerably before starting KRT and stabilized after initiation of dialysis[224]. These data are consistent with a positive effect of KRT on QoL by stopping the progressive deterioration of QoL that is associated with increasing severity of kidney failure.

Conclusions and recommendations

The rapidly ageing population will greatly increase the global burden of CKD and many of its risk factors, posing major challenges to health-care systems and economies. Pharmacological advances and public health interventions have made progress in reducing the prevalence of CKD risk factors, but the effect of the demographic shift of ageing seems to be outpacing these efforts.

As the fastest rates of population ageing are in LMICs, these regions will probably be disproportionately affected by the increasing burden of CKD. As life expectancy increases, the risk of accumulation of traditional CKD risk factors and the duration of exposure to CKD risk factors also rises. The number of older patients with diabetes, hypertension, obesity and CVD is increasing, particularly in LICs, and this trend is expected to continue. The health systems of these countries currently lack the capacity and financing to provide treatment for CKD and kidney failure to all those who need it and this disparity is likely to worsen as the number of older individuals with CKD increases.

To prevent worsening of the CKD epidemic as life expectancy increases, efforts must be scaled up to address modifiable risk factors and initiate primary prevention strategies in high-risk individuals at a sufficiently early age to prevent CKD in later life. Public awareness campaigns should focus on educating individuals about the link between ageing, risk factors and CKD, and should encourage regular health check-ups, (self) screening for early signs of kidney damage to enable early intervention and adherence to lifestyle interventions such as dietary advice, smoking cessation and physical activity. Beyond primary prevention, early intervention and management strategies to slow CKD progression are vital. Efforts to improve access to early detection and diagnosis of not only CKD, but also modifiable risk factors such as hypertension and diabetes, through cost-effective screening programmes for high-risk individuals would help to delay disease progression. For CKD screening, UACR testing is widely available and offers clinically actionable results at a low cost. Novel families of kidney-protective drugs can delay CKD progression and will probably further improve the cost-effectiveness of CKD screening in high-risk populations. The effect of population ageing on CKD prevalence could be substantially mitigated if these novel drugs were made widely available and affordable. For patients living in low-resource settings, enhanced global collaboration and innovative financing models are required to ensure sustainable access to novel drugs and established treatments such as RAS inhibitors.

Delaying progression to kidney failure is essential to reduce the health and financial burden of KRT. The proportion of patients with kidney failure who receive CCM will probably increase in parallel with the ageing population, as older patients are more likely to choose this treatment option. An ongoing clinical trial is investigating the optimal treatment approach in this population[223]. In the meantime, increased access to CCM is needed so that patients can choose this option through a process of shared decision-making if it aligns with their values and preferences. Interventions that maintain or improve the QoL of older patients, including pain management and palliative care services, should also be made available.

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Author contributions

All authors contributed equally to this article.

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Additional information

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