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Review article

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Optimal patient care in advanced chronic kidney disease progressing to kidney failure

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Abstract

The transition from advanced chronic kidney disease (CKD) to kidney failure requires comprehensive management to optimize patient outcomes. This crucial period, in practical terms defined by CKD stages G4 and G5, involves complex decision-making regarding kidney replacement therapy, pre-emptive kidney transplantation and conservative kidney management. Patient preferences, quality of life, and comorbidities, especially cardiovascular disease, are essential considerations when making treatment decisions. Importantly, nephroprotective therapies should be continued even at advanced stages of CKD to stabilize kidney function and prevent cardiovascular events. Pre-emptive kidney transplantation, when feasible, offers the best outcomes and should be prioritized. Dialysis initiation should be based on clinical symptoms and shared decision-making with the patient, rather than laboratory values alone. For some, particularly older, patients with substantial comorbidities, conservative kidney management, emphasizing symptom management without kidney replacement therapy, might be preferred. Considerable disparities in access to care exist globally, especially in low- and middle-income countries, highlighting the need for tailored strategies. Registry and cohort studies have provided most of the scientific understanding in this area, but more randomized clinical trials are needed to guide advanced CKD management.

Sections

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Key points

- Transition from advanced chronic kidney disease (CKD) to kidney failure is a complex process that must be carefully managed, taking into account patient, access to care, ethical, health care organization and economic factors.
- Given that patients with advanced CKD have often been excluded from randomized controlled trials, most scientific knowledge in the field of transition to kidney failure has been obtained from epidemiological studies, which have informed current guidelines.
- Nephroprotective treatments and other therapies should be continued in CKD stages G4 and G5, as they might delay or prevent the development of uraemic syndrome and its consequences, including cardiovascular diseases; these treatments might also benefit patients requiring kidney transplantation or dialysis. Uraemic symptoms might also be mitigated through nutritional care, including low-protein diets.
- Pre-emptive transplantation should be a priority: compared with transplantation performed after any time spent on dialysis, pre-emptive transplantation is associated with better quality of life, better kidney graft function, improved patient survival and lower costs.
- Dialysis initiation must be planned in advance through a shared-decision process with patients; the decision to start dialysis is based on clinical parameters, and uraemic symptoms prevail over biological parameters. Home dialysis techniques (peritoneal dialysis and haemodialysis) should be encouraged because of their benefits for quality of life, morbidity and mortality, and lower costs compared with in-centre haemodialysis.
- The benefits and harms of dialysis initiation versus conservative care should be discussed with patients and their caregivers, particularly for older individuals and those with substantial comorbidities, with a focus on quality of life as a priority.

Introduction

In 2012, the Kidney Disease: Improving Global Outcomes (KDIGO) organization issued guidelines for classifying chronic kidney disease (CKD) based on levels of estimated glomerular filtration rate (eGFR) and albuminuria. These guidelines were strongly confirmed in a 2024 revision[1–3] and have been widely adopted for CKD diagnosis and risk stratification globally. eGFR is also used to distinguish between different levels of excretory kidney function, ranging from normal function (G1) to kidney failure (G5). The progression of CKD to stage G5 (refs. 1,3) (that is, eGFR < 15 ml/min/1.73 m^2) or rapid CKD progression from stage G4, prompts patients and nephrology teams to consider several potential outcomes and clinical decisions (Fig. 1). The transition to kidney failure marks a pivotal step for people with CKD and it is essential to manage this transition phase proactively through a collaborative decision-making process that includes the nephrologist and other health care professionals, along with the patient, and their family members and caregivers[1]. This approach should holistically consider every aspect of the patient's context, encompassing medical, psychological and social factors, as well as the overarching circumstances of the transition. Recognizing the impact of health care system dynamics and economic factors during this transition phase is also crucial. For example, not all treatment modalities discussed above are available in every part of the world, particularly in low-income and low- to middle-income countries (LICs and LMICs, respectively). Consequently, the management of advanced CKD and the transition to potential kidney failure treatment options varies widely between regions. Additionally, randomized controlled trials (RCTs) focusing on therapeutic strategies in the advanced stages of CKD and the transition to kidney failure are notably scarce. Most of the scientific insights in this area (and discussed here) are derived from registry and cohort studies[4–9].

In this Review, we explore the transition from advanced CKD to kidney failure, focusing on key management strategies such as nephroprotective therapies, pre-emptive kidney transplantation and conservative kidney management. We also highlight global disparities in access to care and emphasize the need for tailored approaches, supported by insights from cohort studies and with a call for more RCT data.

Advanced chronic kidney disease: global perspective

International comparisons

In 2017, the prevalence of all-stage CKD was estimated to be 9.1% (8.5–9.8%) in the global population[10]. Advanced CKD constitutes only 2% of this global prevalence – 0.16% for stage G4 and 0.07% for stage G5, excluding those on kidney replacement therapy (KRT)[10] – with few variations in age-standardized prevalence between world regions.

By contrast, the prevalence of kidney failure treated with KRT varies internationally more than 800-fold, from 4 per million population (pmp) in Rwanda to more than 3392 pmp in Taiwan, which is a much wider variation than that observed for CKD prevalence. This variation reflects the huge disparities in dialysis and transplantation capacity between regions[11,12].

Economic factors, including low country income level and underfunded health financing system, are the top barriers to accessing dialysis and transplantation in LICs and LMICs, and explain most, but not all, of the worldwide variation in KRT incidence[13]. The international CKD Outcomes and Practice Pattern study (CKDopps) conducted in Brazil, France, Japan, Germany and the USA showed that differences in risk factors for CKD progression explained most intercountry variations in the incidence of kidney failure (defined by sustained eGFR < 15 ml/min/1.73 m^2) but not the differences in KRT, highlighting differences in practices related to KRT initiation or access[14].

Inequities in kidney care between world regions are not limited to KRT access as they also affect the earlier stages of CKD[15]. In many regions, basic essential tests for identifying and managing CKD (for example, serum creatinine and albuminuria levels) are not available in primary care services, and medications for kidney care are funded publicly in only a minority[16].

Collectively, economic factors, inadequate health financing systems, poor recognition of CKD as a health priority despite its major impact on global health, and low adherence to CKD guidelines contribute to poor prevention of disease progression and limited access to adequate kidney care in advanced CKD.

Competing risks between cardiovascular events, death and kidney failure

CKD is associated with an increase in all-cause mortality, which includes both cardiovascular (CV) and non-CV mortality[17]. Compared with the general population, people with CKD are at a higher risk of death, with a proportionally greater risk in younger patients[18]. The incidence of CV and non-CV events increases with the progression of CKD to kidney failure[19]; eGFR and albuminuria are both associated with mortality, and CV and kidney outcomes[19]. The risk of reaching kidney failure seems to be mainly restricted to CKD stages G4 and G5, whereas an enhanced CV mortality risk is frequently already present at CKD stage 3 and then gradually increases through CKD stages G4 and G5 (refs. 17,20,21). One potential reason for this difference is related to the high mortality after CV events in people with CKD compared with those without CKD[22].

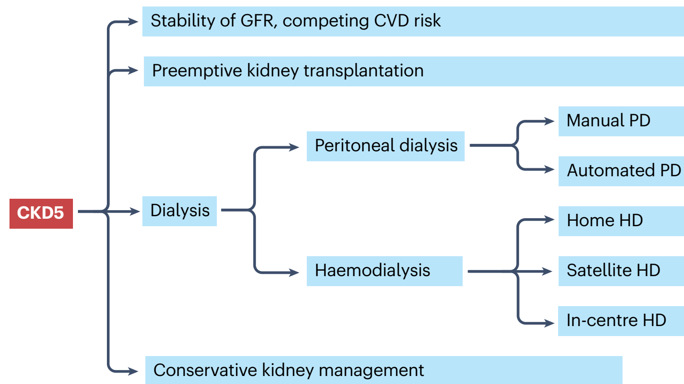

Fig. 1 | Outcomes and therapeutic choices for people with chronic kidney disease stage G5. In people with chronic kidney disease stage G5 (CKD5), the glomerular filtration rate might be stable over time, minimizing the risk of imminent kidney failure but with competitive cardiovascular disease (CVD) morbidity and mortality risks. In people with disease progressing towards kidney failure, pre-emptive kidney transplantation should be prioritized as the preferred method of kidney replacement therapy, when feasible, and preferentially through living organ donation. For patients planning to receive dialysis, the therapy modality should be chosen in advance, informed by repeated discussions between the patients and the nephrology team. Conservative kidney management should also be discussed with patients and their caregivers as a potential option in the case of kidney failure. PD, peritoneal dialysis.

Risk prediction

Progression to kidney failure

The KDIGO heatmap visually stratifies CKD risk based on eGFR and albuminuria to guide monitoring and treatment intensity[1,3], whereas the four-variable Kidney Failure Risk Equation (KFRE[23]) provides a personalized assessment of kidney failure risk over 2 or 5 years based on age, sex, eGFR and albuminuria levels. With a high predictive value (c-index on average 0.85), observed in many cohorts worldwide[23], the four-variable KFRE has been considered a tool to inform prognosis discussions and treatment planning, including the need for the creation of vascular access[24]. Using a KFRE formula based on six routine laboratory tests improved KFRE predictions slightly, as demonstrated in the German CKD cohort[25], whereas the addition of a urinary peptide signature to KFRE variables in people with CKD stages G3–G5 in the French CKD-REIN cohort did not further improve formula performance[26]. These findings are not surprising given the highly predictive value of the KFRE formula[23]. Integration of other variables in the latest version of the equation did not improve its predictive power[27]. One limitation of using the KFRE for a single patient is that it does not consider the underlying cause of CKD. For instance, conflicting results have been reported on the predictive value of the KFRE in people with polycystic kidney disease[28,29]. In people with eGFR < 15 ml/min/1.73 m^2, both KFRE risk and eGFR showed similar relationships with time to kidney failure[30].

Beyond risk prediction, evaluation of the impact of therapeutic interventions on the evolution of CKD is of substantial importance: the slope of eGFR over time might be used as a primary end point for clinical trials of CKD progression[31], or to assess the effect of therapies and to predict kidney failure at an individual level. Of note, eGFR trajectories over time and approaches to kidney failure management can vary greatly (Fig. 2).

Cardiovascular risk prediction in people with chronic kidney disease

Despite being widely used in the general population, the Framingham score seems to have limited accuracy in predicting 5- and 10-year risk of incident myocardial infarction and fatal coronary disease in people with CKD[32]. Discrepant findings were initially reported in different studies[33] but a subsequent large meta-analysis showed that eGFR and albuminuria improved cardiovascular disease (CVD) risk prediction beyond traditional CVD risk factors, particularly for CVD mortality and heart failure[34]. SCORE2, which uses eGFR and albuminuria, improved atheromatous CVD risk prediction beyond traditional CVD risk factors[35]. Incorporating additional novel risk factors such as inflammatory and procoagulant parameters did not improve risk prediction[36]. The Chronic Renal Insufficiency Cohort study investigators developed new models for 10-year risk prediction of CVD among people with CKD, including a model composed of readily clinically available variables and a biomarker-enriched model[37]. These models must be externally validated and refined in multiple diverse CKD cohorts before being clinically implemented[37]. In 2024, the American Heart Association proposed the term 'cardiovascular–kidney–metabolic syndrome' and subsequently developed new risk-prediction equations, named Predicting Risk of CVD Events equations, which included eGFR and albuminuria as variables, in addition to traditional CV and metabolic factors (reviewed by Massy and Drueke[38]).

The simultaneous assessment of composite CV outcomes in several previous studies, combining atheromatous and non-atheromatous disease events, might explain some of the reported discrepancies, given that traditional risk factors might not be the best predictors of non-atheromatous CVD events[39]. Reported discrepancies might also be related to the use of traditional creatinine-based formulae to estimate eGFR, considering that the eGFR cystatin C equation has the best associations with CVD and mortality[40,41].

Overall risk prediction

One team of researchers[27] developed an equation that uses additional covariates rather than the KFRE alone to produce a more refined outcome estimate for people with eGFR ≤ 30 ml/min/1.73 m^2, including those receiving KRT. This equation considers all potential outcomes, in a competing-risk approach. One of the drawbacks of the formula is that it cannot be universal, given the differences in health care organization across countries, which inevitably have an impact on access to KRT.

Optimal management of people transitioning from advanced chronic kidney disease to kidney failure

The burden of advanced chronic kidney disease

The many consequences of CKD include inflammation, malnutrition, dysautonomia, cardiac, vascular, pulmonary and bone disease, and myriad patient-reported symptoms that have a detrimental effect on quality of life[42,43]. CKD progression worsens all of these adverse effects,

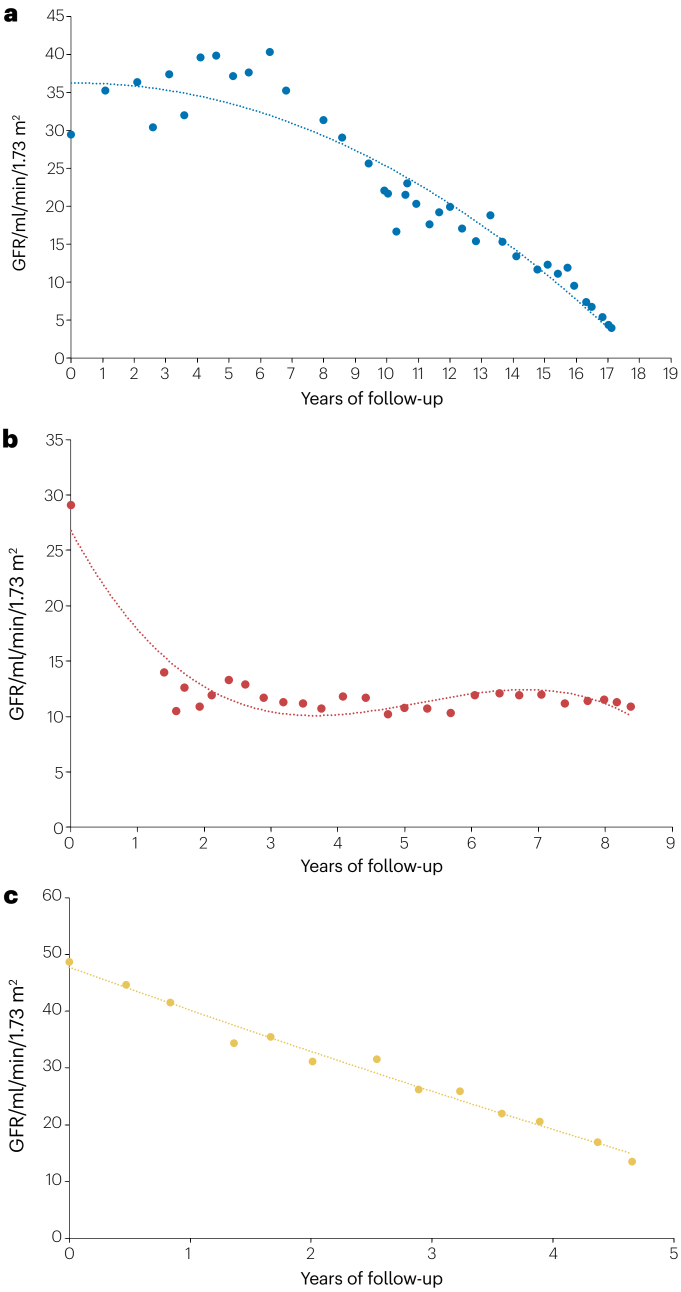

Fig. 2 | Illustrative examples of disease trajectories in people with advanced chronic kidney disease. These graphs illustrate different disease trajectories of patients with chronic kidney disease followed in a nephrology clinic. **a**, A 48-year-old patient with long-lasting hypertension and obesity had a left nephrectomy for localized clear-cell carcinoma. His glomerular filtration rate (GFR) remained stable over 7 years and he was lost to follow-up for 3 years. GFR deteriorated over the next 7 years, despite optimal treatment, at which point he chose to be treated with home haemodialysis before receiving a kidney transplant 3 years later. **b**, A 74-year-old patient with recurrent urothelial cancer had a partial right nephrectomy 7 years after a total left nephrectomy, which led to a GFR of <15 ml/min/1.73 m^2. GFR remained stable over 8 years of follow-up under conservative kidney management. Following recurrence of the urothelial cancer that would have necessitated aggressive treatment, the patient chose palliative care and died at home a few months later. **c**, A 52-year-old patient with autosomal polycystic kidney disease experienced a rapid GFR decline, with an annual loss of 7 ml/min/1.73 m^2. He received a living donor kidney transplant when his GFR reached 6 ml/min/1.73 m^2.

culminating in the development of uraemic syndrome and ultimately leading to a high symptom burden and the need for KRT. Rather than a detailed description of the different consequences of CKD, below we discuss the therapeutic management of people with advanced CKD (Table 1), aimed at stabilizing CKD and optimizing transition to further stages, managed with KRT or conservative kidney management (Box 1).

Physical activity and lifestyle interventions

People with CKD frequently have a low level of physical activity, which might lead to loss of appetite, muscle loss and frailty[44]. Several studies in people with CKD showed that exercise might have beneficial effects on quality of life and oxygen consumption, and potentially on GFR deterioration and blood pressure[44]. However, people with CKD often experience barriers to lifestyle modifications – fatigue might limit the ability to engage in physical activity or the risk of malnutrition might complicate dietary changes and restrictions. Clinical trials have tested the potential use of eHealth technologies to overcome these barriers. A 2024 review found no evidence of positive effects[45], but the UK Kidney BEAM RCT, which involved people with various stages of CKD (43% at stages G4 and G5) showed that a physical activity digital health intervention had beneficial effects on mental health-related quality of life and related secondary outcomes such as physical function, symptom burden, social interaction, anxiety or depression[46]. Of note, this digital health intervention was also cost-effective[47].

Physical exercise can also be beneficial to people with sarcopenic obesity who might be denied access to kidney transplantation programmes and should be recommended as early as possible in the course of CKD[48]. Given that physical exercise is also beneficial to transplant recipients[49] and people receiving dialysis[49,50], exercise training should be amongst the recommendations for people in a transition phase from advanced CKD.

Glycaemic management in advanced chronic kidney disease

Managing blood glucose in advanced CKD (stages G4 and G5) is complex owing to altered glucose metabolism, reduced insulin clearance and increased risks of both hyperglycaemia and hypoglycaemia[51,52]. Kidney dysfunction impairs insulin metabolism, leading to prolonged insulin action, drug accumulation and higher risk of hypoglycaemia. Traditional glycaemic markers such as glycated haemoglobin (HbA_{1c}) also become less reliable as CKD progresses owing to anaemia and altered red blood cell lifespan.

Key approaches to glycaemia management in advanced CKD currently include the use of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) and insulin. GLP1-RAs are recommended for improvement of glycaemic control and CV protection in people with type 2 diabetes, particularly those with CKD[1,53]; their effects on kidney-related endpoints are discussed below. Insulin remains an essential therapy, with careful dose titration to minimize hypoglycaemia; basal insulin analogues are preferred. Insulin usually leads to weight gain, which might affect transplant wait-listing. Of note, the use of metformin and sulfonylureas are generally not recommended in advanced CKD owing to the risks of lactic acidosis and hypoglycaemia, respectively, whereas dipeptidyl peptidase-4 (DPP-4) inhibitors can be used with dose adjustments[54].

Glycaemic targets should balance hyperglycaemia avoidance while minimizing hypoglycaemia risk, with a key role for individualized HbA_{1c} goals and frequent blood glucose monitoring, including continuous glucose monitoring. Collaborative care with a focus on both glycaemic and kidney health is also essential[55,56].

Nutritional management

General considerations. When CKD progresses, patients spontaneously lower their caloric and protein intake[57], mostly owing to loss of appetite and nausea[42,58] as well as reduced physical activity[44]. Malnutrition is common in people with CKD but a meta-analysis of six cohort studies from the USA, Japan and Sweden[59] showed that plant-based diets and Mediterranean-type diets are associated with lower mortality (3983 events; adjusted relative risk 0.73 (95% CI 0.63–0.83). The study found no statistically significant association between healthy dietary patterns and the risk of kidney failure.

Salt intake. Salt intake should be moderately restricted to 4–6 g per day to improve control of hypertension through intrinsic effects and maximize the pharmacological effects of renin–angiotensin–aldosterone system (RAAS) inhibitors and other drugs, including hydrochlorothiazide and diltiazem[60,61]. The effects of salt intake reduction on CKD progression are debatable[60,61], but salt intake should be similarly restricted in patients receiving dialysis to avoid excessive weight gain between dialysis sessions[62]. The blood-pressure-lowering effects of moderate salt intake restriction are maintained after transplantation[63].

Optimal protein intake and uraemic toxins. High dietary protein intake is common among adults consuming Western diets (average of 1.3 g protein/kg of body weight/day, in contrast to the 0.6 g protein/kg/day recommended by metabolic studies and current CKD international guidelines[64]). Reducing protein intake should be encouraged to limit the accumulation of protein metabolism products with potential toxic effects. The observations that reducing protein intake by 40% instantly lowers blood urea nitrogen[65] should be an incentive for patients and health care providers to develop an adequate dietary plan. However, it can be difficult for patients to change their diet and to reduce protein intake as kidney excretory function declines, especially if these changes counter the dietary patterns prevalent in their culture and immediate environment. Approximately one third of patients do not change their diet, 50% reduce intake to 0.6 g protein/kg/day after 2–3 dietary consultations, and 15–20% try a very-low protein intake 0.3–0.4 g protein/kg/day supplemented with amino acid and ketoacid preparations[66] (of note, such supplements are not available in all countries). An optimal diet should also provide sufficient energy (at least 25–30 kcal/kg/day) to prevent unwanted weight loss[64]. Transitioning towards a vegetarian-like diet, such as a plant-dominant low-protein (PLADO) diet or a Mediterranean diet, is recommended in CKD[67–69]. Of note, dietary fibre regulates phosphate absorption and can improve control of phosphoraemia, hyperparathyroidism and acid stress[70]. A vegetarian diet can also improve constipation, which is common in CKD and is often associated with hyperkalaemia and mortality[71].

The risk of muscle wasting should also be considered, especially in patients without access to dietitians and in frail populations (for example, patients > 80 years of age or those with multiple comorbidities)[72]. Of note, pharmacological approaches alone (such as the use of angiotensin blockers and SGLT2 inhibitors) might delay the need for dialysis but will not prevent the CKD-associated dysmetabolism that can only be controlled by optimal nutrient intake[67,72]. Barriers to wider implementation of dietary interventions in advanced CKD include physicians' negative perception and motivation, limited access to a dietitian, adequate dietary advice and dietetic supplements[73], as well as a lack of support to help patients to modify their diets. A precision medicine approach might help to address some of these barriers[66] — patient demographics, social, psychological, education, and compliance factors, all of which might influence therapeutic needs, as

Table 1 | Therapeutic interventions in advanced chronic kidney disease and transition to kidney failure

Lifestyle and therapeutic interventions	Advanced CKD (stages G4 to G5)	Transplantation[a]	Dialysis
Aerobic exercise	Recommended	Recommended	Recommended
Nutritional evaluation and counselling (yearly)	Recommended	Recommended	Recommended
Salt intake	4–5 g per day	4–5 g per day	4–5 g per day or lower
Caloric intake	25–35 kcal/kg BW/day[b]	≤35 kcal/kg BW/day	30-35 kcal/kg BW/day
Protein intake	0.55–0.6 g/kg BW/day 0.6-0.8 g/kg BW/day[c] 0.3–0.4 g/kg BW/day with KA	No restriction	≥1.2 g/kg BW/day
Calcium intake	1 g/day calcium element	1 g/day calcium element	1 g/day calcium element
Phosphate intake	800 mg/day	<1,500 mg/day	<1,200 mg/day
Iron supplementation	As needed; IV therapy has better tolerance and efficacy	As needed; IV therapy has better tolerance and efficacy	PD: IV therapy has better tolerance and efficacy; HD: IV during session
Correction of anaemia	Therapy initiation if Hb < 9.5 dl, or clinical signs of anaemia are present (Hb target = 10–12 g/dl)	Might be used but usually discontinued after transplantation	Initiation if Hb < 10 dl, or clinical signs of anaemia are present (Hb target = 10–12 g/dl)
Blood pressure targets	130/80 mmHg or 120/80 according to recommendations	130/80 mmHg	130/80 mmHg or higher, according to dialysis tolerance

BW, body weight; CKD, chronic kidney disease; GFR, glomerular filtration rate; Hb, haemoglobin; HD, haemodialysis; IV, intravenous; KA, ketoacid–amino acid supplementation; PD, peritoneal dialysis. [a]For GFR > 30 ml/min/1.73 m^2; when GFR < 30 ml/min/1.73 m^2 see CKD stages 4 to 5. [b]kg BW/day: kg of ideal body weight per day. [c]In individuals with diabetes.

well as the responses to the nutritional therapy prescribed, should be considered in nutrition management[66].

Potassium restriction. Potassium intake is often a focus of patient dietary consideration but, increasingly, data suggest that dietary potassium does not have a large impact on serum potassium levels. In fact, dietary potassium absorption can be reduced with vegetarian diets, which typically include potassium-rich foods, and dietary fibre, and clinically relevant increases in serum potassium generally result from other factors such as constipation, acidosis, insulinopaenia, infection or catabolism[74]. Therefore, dietary potassium control before the start of maintenance dialysis might not be a priority for most patients, apart from those with a history of hyperkalaemic episodes, who should be educated on foods that are rich in potassium, such as ultraprocessed foods[1]. Novel potassium binders are well tolerated and effective at treating hyperkalaemic episodes[75,76], but whether they provide protection against chronic hyperkalaemia in people with CKD[77], as demonstrated in people with heart failure treated with finerenone, remains unclear[78]. Finally, treating constipation is an effective way of reducing hyperkalaemic episodes and mortality in people with advanced CKD[79].

Phosphorus and mineral metabolism. Compared with potassium, phosphorus intake should be more tightly controlled. Serum phosphorus regulation is impaired as early as stage G3 CKD[80,81] and its levels increase progressively, accompanied by alterations in bone health as CKD advances. High dietary phosphorus intake increases serum fibroblast growth factor 23 (FGF23), a well-identified cardiotoxin, and parathyroid hormone (PTH), which induces osteodystrophy[82]. Serum FGF-23 levels are not routinely measured in clinical practice and high serum phosphorus is therefore generally a late finding, typically detected at stage 5 or during the transition to dialysis. Reducing phosphorus intake to 800 mg/day is recommended as early as stages G3b–G4[57], and implies a substantial reduction in protein intake as phosphorus is mainly contained in proteins. Given that 1 g protein contains 13 mg phosphorus, an intake of 0.6–0.8 g protein/kg body weight/day is optimal for control of hyperphosphataemia.

Box 1 | Important outcomes and clinical decisions in the transition from advanced chronic kidney disease to kidney failure

I. Estimated glomerular filtration rate can remain stable for extended periods, even at stage G5, with optimal management. In such cases, cardiovascular diseases and other mortality factors are competing risks.
II. Renin–angiotensin–aldosterone system inhibitors, sodium–glucose co-transporter 2 inhibitors, glucagon-like peptide-1 receptor agonists and non-steroidal mineralocorticoid receptor antagonists are guideline-directed medical therapies for people with chronic kidney disease, as they stabilize kidney function and offer global cardioprotective benefits.
III. Pre-emptive kidney transplantation should be considered a priority when feasible, as it offers the best outcomes in terms of patient survival, quality of life and cost-effectiveness compared with other forms of kidney replacement therapy.
IV. Dialysis technique selection should be planned through therapeutic education programmes prior to the onset of kidney failure, with patients taking a prominent role in choosing between pre-emptive kidney transplantation, peritoneal dialysis and haemodialysis.
V. Informed patients might opt for conservative kidney management, whereby they do not undergo kidney replacement therapy but receive outpatient optimized clinical care primarily from their nephrology team, and often from a geriatric team, ensuring compassionate support through the end of life.

Heart- and kidney-protective drugs used in advanced chronic kidney disease and at dialysis initiation

In addition to moderate reduction of salt intake, different types of therapeutic classes can or should be used in advanced CKD for heart and kidney protection (Fig. 3 and Table 2). In most, if not all patients, a combination of different anti-hypertensive drugs is also necessary to achieve satisfactory blood-pressure control[83,84].

Renin–angiotensin–aldosterone system inhibitors. Current guidelines support the prescription of a RAAS inhibitor for people with CKD, particularly those with proteinuria, diabetes or heart failure[3,85–88]. However, the eGFR thresholds for which these recommendations might not be indicated are not clearly defined[85,86]. This uncertainty might explain important differences in RAAS inhibitor prescription across countries. In 5870 patients from the CKDopps cohort, RAAS inhibitor prescription patterns varied by country and were especially underused in the USA, where only half of eligible patients were prescribed this class of drug. These prescriptions were less frequent at advanced CKD stages[89]. In 34,602 participants with moderate and advanced CKD from 17 cohort studies from the iNET-CKD network, inadequate blood-pressure control was reported, with heterogeneous prescription patterns across world regions. RAAS inhibitors were commonly prescribed as first-line treatment for hypertension in all countries[84].

The balance of risks and benefits of RAAS inhibitor use is not clearly established in advanced CKD, and stopping treatment might lead to a small increase in eGFR and avoid drug-related hyperkalaemia and other adverse events associated with these drugs[85,86]. In the STOP-ACEi trial, people with progressing CKD stages G4 and G5 already receiving RAAS inhibitor therapy were randomly assigned to discontinue or continue their treatment[86,90]. The study found no significant difference in GFR at 3 years between the two groups, nor in the initiation of KRT or incidence of adverse events[86,90]. However, the number of CV events was higher in the discontinuation group than in the continuation group[86,90]. Considering the very high rate of CV events in people with CKD, this is an important finding. Of note, the STOP-ACEi trial has limitations, including a high selection bias, given that the rate of inclusion in the study was <10%, and the study cohort was predominantly white European[86,90]. A nationwide study in Sweden found that stopping RAAS inhibitor treatment was associated with higher absolute risks of mortality and major adverse cardiovascular events (MACEs), and with a lower absolute risk of initiating KRT[91]. Given that RAAS inhibition might be beneficial at the start of haemodialysis, particularly owing to its cardioprotective effects[92], these drugs should not be discontinued at advanced CKD stages unless adverse effects such as hyperkalaemia occur. On this matter, the benefit of potassium-lowering drugs for clinically significant outcomes is far from being proven[93].

Sodium–glucose co-transporter 2 inhibitors. Large RCTs and meta-analyses of SGLT2 inhibitor studies show significant heart- and kidney-protective effects of these drugs in people with CKD (with or without diabetes) at high CV or kidney risk[94–102]. Despite a high level of evidence[95], and their inclusion in current treatment recommendations[1,103], SGLT2 inhibitors are still underused[104,105]. Evidence of benefit in people transitioning to kidney failure is more limited, as people with very low GFR were excluded from key RCTs (the DAPA-CKD trial[99] excluded patients with eGFR < 25 ml/min/1.73 m² and those with eGFR < 20 ml/min/1.73 m² were excluded from the EMPA-KIDNEY trial[100,101]). Whether SGLT2 inhibition should be maintained in people with CKD G5 remains uncertain[106]. Of note, the heart- and kidney-protective effects of empagliflozin continued for up to 1 year after treatment discontinuation, a further argument for its use in the context of transition to kidney failure[100,105]. In a 2024 report of a target trial emulation study in people with type 2 diabetes, initiation of an SGLT2 inhibitor in stage G5 was associated with a lower risk of long-term dialysis than no SGLT2 inhibitor use[107]. In summary, SGLT2 inhibitors should not be stopped below GFR < 20 ml/min/1.73 m² until the start of dialysis or kidney transplantation[1,108].

Glucagon-like 1 peptide receptor agonists. The beneficial effects of GLP-1 RAs on kidney-related outcomes in people with obesity, with or without diabetes, have been extensively demonstrated[54], but people with low GFR (<25–30 ml/min/1.73 m²) have been excluded from most trials[1,109]. However, the GLP-1 RA semaglutide was renoprotective in people with an eGFR > 25 ml/min/1.73 m² and type 2 diabetes[110], or obesity without diabetes[111]. Although the additive benefits of combination therapies with SGLT2 inhibitors are incompletely understood[105], GLP-1 RAs might have effects that are independent of and possibly additive to those of SGLT2 inhibitors[111].

Cohort studies in kidney transplant recipients with diabetes report beneficial effects of GLP-1 RAs[112–114], although whether treatment was initiated immediately after kidney transplantation is unknown. For patients with diabetes treated with dialysis, preliminary reports from cohort studies are favourable[115–117] but need to be confirmed in RCTs. Overall, in people with diabetes, we suggest maintaining GLP-1 RA treatment when dialysis is initiated or until patients receive a kidney transplant.

Diuretics and mineralocorticoid receptor antagonists. After RAAS inhibitors, diuretics are amongst the most important drugs that should be used in CKD[1]. Loop diuretics and thiazides should not be discontinued in advanced CKD[118–121] given that their mechanism of action goes beyond volume depletion; thiazide diuretics are important to consider in people with advanced CKD and hypertension[118,121]. A registry study from Sweden suggests that in people with advanced CKD, antihypertensive therapy with diuretics might be associated with further kidney benefits and similar cardioprotection compared with calcium channel blockers[122]. Of note, at the initiation of haemodialysis (HD), the prescription and higher doses of loop diuretics was not associated with improved outcomes during the first year of treatment[123].

Potassium-sparing diuretics (for example, amiloride and triamterene) and steroidal mineralocorticoid receptor antagonists (MRAs) such as spironolactone or eplerenone, should be avoided in advanced CKD owing to the enhanced risk of hyperkalaemia[1,121]. MRA initiation is not recommended[1] at eGFR < 25 ml/min/1.73 m². Of note, the non-steroidal MRA (nsMRA) finerenone protected against CV outcomes, but not kidney-related outcomes, in people with CKD G4 (7% of 13,023 RCT participants)[124].

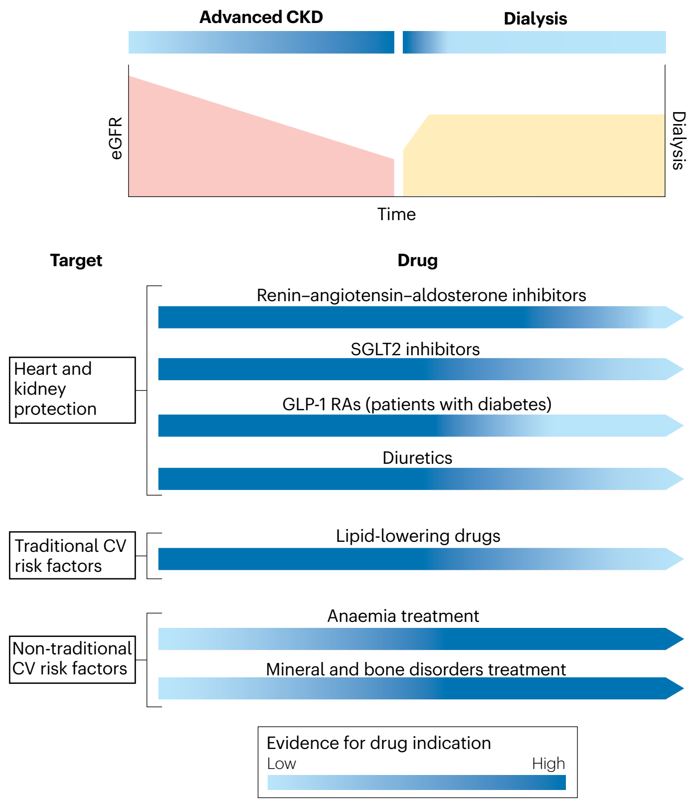

Fig. 3 | Use of heart- and kidney-protective drugs from advanced chronic kidney disease to dialysis. In progressive chronic kidney disease (CKD), estimated glomerular filtration rate (eGFR) continues to decline and kidney replacement therapy (KRT) is eventually required to address kidney failure. Throughout this transition, different drugs might be used to mitigate the decline in kidney function and the associated increased risk of cardiovascular (CV) disease. The figure illustrates how drug therapy indication might change for patients choosing dialysis as KRT, based on current evidence. GLP-1 RAs, glucagon-like peptide 1 receptor agonists; SGLT2, sodium–glucose co-transporter 2.

Lipid-lowering therapies. Declining kidney function is associated with an increased risk of CVD, which is the leading cause of death in people with CKD. People with stage G3 and G4 disease, respectively, are at a twofold and threefold higher risk of CV death than those with normal kidney function, and are therefore at a high and very high CV risk[19,125,126]. Guidelines from the KDIGO Lipid Work Group in 2013 (ref. 127) recommended treatment with a statin, or statin plus ezetimibe, for adults aged ≥ 50 years with CKD and eGFR < 60 ml/min/1.73 m² who are not being treated with dialysis or kidney transplantation, or statin alone in those with eGFR ≥ 60 ml/min/1.73 m². However, clinical epidemiological data reported in 2022 suggested that the limited treatment efficacy of statins in patients receiving dialysis might be due, at least partly, to a higher intracellular cholesterol production linked to hyperphosphataemia[128]; such findings might open up the possibility of statin therapy initiation in people receiving dialysis, provided that phosphate levels are controlled.

The SHARP clinical trial provided evidence of the efficacy and safety of lowering LDL cholesterol with a combination of ezetimibe and simvastatin compared with placebo among people with a wide range of CKD stages, including CKD G5 with dialysis[129]. In the CKD-REIN study,

Table 2 | Medications used in advanced chronic kidney disease and transition to kidney failure

Medication	Advanced CKD (stages G4 to G5)	Transplantation	Dialysis
RAAS inhibitors	Target: maximal dose according to blood pressure and proteinuria	Target: maximal dose according to blood pressure and proteinuria, if present	Target: maximal tolerated dose
Lipid-lowering therapy	Target: LDL-C ≤ 0.55 g/l with statin	Target: LDL-C ≤ 0.55 g/l with statin	Target: LDL-C ≤ 0.55 g/l with statin
SGLT2 inhibitors	Recommended for GFR 80–20 ml/min/1.73 m^2. Should not be started for eGFR < 20 ml/min/1.73 m^2 but can be maintained	Might be used in stable patients	No sufficient data to recommended SGLT2 inhibitor use
nsMRA	Finerenone might be used in CKD G4	Insufficient data available	Insufficient data available
GLP-1 RAs	Semaglutide might be initiated if eGFR > 25 ml/min/1.73 m^2 and type 2 diabetes or obesity without diabetes are present	Preliminary reports from cohort studies are favourable for individuals with type 2 diabetes	Cohort studies are positive in stable patients with type 2 diabetes
Diuretics	Loop-diuretics and thiazides can be used with equivalent efficacy	Loop-diuretics and thiazides can be used	Loop-diuretics might preserve residual diuresis
Phosphate binders	Can be used in patients with overt hyperphosphataemia	Not recommended	Might be used in patients with overt hyperphosphataemia

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1 RAs, glucagon-like 1 peptide receptor agonists; LDL-C, low-density lipoprotein cholesterol; nsMRA, non-steroidal mineralocorticoid receptor antagonists; RAAS, renin–angiotensin–aldosterone system; SGLT2, sodium–glucose co-transporter 2.

63% of the patients were receiving lipid-lowering therapy at inclusion, most commonly statin monotherapy, with the percentage on treatment increasing with advancing CKD stage[125]. At least half of the patients in the CKD-REIN cohort had LDL cholesterol (LDL-C) values that exceeded the recommended target.

A greater use of evidence-based lipid-lowering therapy would likely increase the number of patients meeting LDL-C treatment targets and reduce the risk of CVD morbidity and mortality in people with advanced CKD.

Other medications

Anaemia treatment. Even if more prevalent in people receiving dialysis, anaemia is a frequent complication in non-dialysis-dependent CKD[81,130] and is associated with increased morbidity and mortality, and with decreased quality of life[81,130]. Guidelines recommend target haemoglobin values of 10–12 g/dl in most people with CKD, which might require the use of iron supplementation and erythropoiesis-stimulating agents (ESAs)[131–134]. Spontaneously higher haemoglobin values should be respected. The CKDopps observational cohort of patients under nephrology care revealed that many patients with haemoglobin <10 g/dl were not treated at all for anaemia. Oral iron therapy was the medication most often prescribed but discontinuation of anaemia treatment was very common[135]. In another report from a CKDopps cohort of 5,145 patients, iron deficiency, as captured by transferrin saturation coefficient, was associated with a higher risk of all-cause mortality and MACEs in people with advanced CKD, with or without anaemia[136]. In an analysis of trajectories of haemoglobin levels over time in patients from the CKD-REIN cohort, two-thirds of patients had a stable haemoglobin trajectory and low risk of adverse events. The other third had a non-linear trajectory declining at different rates, with increased risks of events. Better attention should be paid to dynamic changes of haemoglobin in CKD[137].

Novel anti-anaemic agents such as oral inhibitors of hypoxia-inducible factor prolyl hydroxylase have been authorized for clinical use in the USA, Europe and Asia (reviewed by Locatelli and Vecchio[138]). Given that these agents can be used before and after dialysis initiation, they might offer a benefit in the context of transition to kidney failure, but more extensive real-world data are needed, particularly on hard safety endpoints compared with established ESA therapies[138]. In summary, although guidelines recommend treating iron deficiency and correcting anaemia in CKD, real-world studies demonstrate undertreatment of these conditions.

Pharmacological treatment of mineral bone disorders. CKD is commonly associated with mineral bone disorders (MBDs), including abnormal metabolism of phosphorus, calcium, vitamin D and PTH. As kidney function declines, mineral homeostasis progressively deteriorates[80,82]. Indeed, 2017 KDOQI guidelines[139] recommend beginning to monitor the metabolic abnormalities that accompany CKD–MBD at stage G3, with treatment decisions based on serial measurements of serum concentrations of calcium, phosphate, bicarbonate and PTH. In CKDopps, we found that prescription of medications to treat or prevent CKD–MBD abnormalities (including phosphate binders and nutritional and active vitamin D) was generally low and varied across countries. Indeed, only 15–39% of people with phosphorus >5.5 mg/l were prescribed phosphate binders[140]. This finding may be understandable, given the low level of evidence in the field of CKD–MBD, particularly in patients with CKD G3a–G5 not receiving dialysis, where the optimal PTH level is not known and normalization of serum phosphate level is recommended with the lowest 2 C degree of evidence[139]. Although opportunities to improve treatment of MBD in advanced CKD exist, the effects of currently available interventions require additional evaluation.

Chronic kidney disease medications after kidney transplantation

In the early phases of kidney transplantation, treatment regimens are dominated by the use of drugs for immunosuppression and against infection. Antihypertensive medications, ESAs and statins might be used even at early stages after transplantation, but an in-depth discussion is beyond the scope of this review. Data on the use of SGLT2 inhibitors in kidney transplantation are limited to small case series[141] and so these drugs cannot be recommended based on our current knowledge.

Chronic kidney disease medications at the initiation of dialysis

Medications used in advanced CKD might be useful when patients are receiving HD. In an international cohort of patients receiving haemodialysis (DOPPS)[92], patients prescribed a RAAS inhibitor at dialysis initiation (reflecting drug prescription in advanced CKD stages) had lower mortality than those not prescribed an RAAS inhibitor.

Estimating the effects of clinical interventions among people with advanced CKD is challenging given that most RCTs have excluded patients with eGFRs < 30 ml/min/1.73 m^2. Observational evidence and biological plausibility support the concept that inadequate control of certain CKD-associated risk factors drives worse outcomes in the early dialysis period. In fact, although RCTs of new interventions that reduce the risk of adverse clinical outcomes among CKD patients, such as SGLT2 inhibitors, GLP-1 RAs and nsMRAs recruited patients with eGFR > 20 ml/min/1.73m^2, participants continued to use the medications until they reached kidney failure in the studies. Such results, therefore, reflect the use of cardioprotective medications even in people with advanced CKD at the transition period to kidney failure. New RCTs are underway to specifically assess the impact of these new interventions on people with advanced CKD and those receiving dialysis[142]. In a DOPPS analysis of people with incident kidney failure, the modifiable risk factors most strongly associated with early mortality were catheter use, poor nutrition, lack of pre-kidney failure nephrology care and absence of residual kidney function[143]. Several of these factors are the end goals of nephrology care, and the extent to which pharmacological intervention improves any of the above is debatable. Among people with CKD G5 with dialysis and residual kidney function, RAAS inhibition seems to preserve residual urine volume for longer according to a meta-analysis of RCTs[144].

As discussed earlier, people with very advanced CKD were excluded from RCTs with SGLT2 inhibitors. These drugs might be used in people treated by dialysis in the future; one study showed that dapagliflozin was well tolerated, slightly dialysable and did not accumulate in patients receiving dialysis[145]. By contrast, nsMRA initiation is not recommended in people with low GFR and two RCTs reported in 2025 showed that spironolactone did not reduce the incidence of MACEs and CV mortality in patients treated by HD[146,147].

Another well-known risk factor for worse outcomes in the early dialysis period is haemoglobin variation. Excessive haemoglobin levels might be a key driver of worse outcomes among patients using high ESA doses and regulatory agencies worldwide define absolute variations of haemoglobin as a safety measure in clinical trials[144]. Clinically, people with incident kidney failure often have acute inflammation and frequently reach advanced stages of kidney failure undertreated for anaemia with haemoglobin, transferrin saturation and ferritin levels below the recommended targets[144]. During acute events, such as dialysis initiation, these patients will often require high ESA and iron doses, all of which are linked to worse outcomes, either through excessive haemoglobin levels or other associated adverse consequences. To what degree new interventions for anaemia, such as hypoxia-inducible factor-prolyl hydroxylases, can reduce adverse events related to anaemia management in the early dialysis period remains unclear[138].

Kidney transplantation should be a priority

Pre-emptive kidney transplantation

Pre-emptive kidney transplantation (Fig. 2c) should be considered in people with declining GFR[3], with the pre-transplantation work-up of both donors and recipients carried out weeks or months before the planned transplantation, according to centre practices[148], for any patient with GFR < 15 ml/min/1.73 m^2. Transplant surgery should be performed when dialysis would have been initiated[148], that is, when the GFR is 7–10 ml/min/1.73 m^2. Several cohort studies, either published several decades ago[149,150] or more recently[151–153], from the USA[149,150], Europe[151,153] and Japan[152], clearly show that outcomes after pre-emptive transplantation are significantly better in terms of graft survival, patient quality of life and costs, compared with transplantation after dialysis.

Access to pre-emptive kidney transplantation is obviously easier when patients can benefit from a living-donor kidney, compared with waiting for a deceased-donor kidney. Pre-emptive kidney transplantation from a living donor was also associated with better graft survival than kidney transplantation from a deceased-donor kidney in an analysis of more than 20,000 kidney transplants from the French registry[151]. However, many disincentives to kidney donation exist in high-income countries (HICs)[154]; some propose that these barriers could be partly overcome by donor compensation[155], but this is a controversial proposition. Much improvement is needed to develop pre-emptive kidney transplantation in most countries. For instance, in France, pre-emptive kidney transplantation accounted for only 3.5% of patients receiving KRT in 2021 (ref. 156). In LMICs, pre-emptive transplantation should be encouraged; barriers might include lack of transplant infrastructure, cultural and socioeconomic factors[157,158]. As a note of caution, a 2020 study reported that kidney transplant recipients were at a 2.7-fold greater risk of global mortality than eGFR-matched people with CKD, mainly owing to infections[159].

Post-maintenance dialysis kidney transplantation

The survival advantage of kidney transplantation compared with dialysis was demonstrated many years ago[160], at a time when survival of patients treated by HD was much lower than current rates. Nonetheless, more recent cohort studies performed in HICs confirm these results with evidence of a cumulative deleterious effect of dialysis duration before kidney transplantation, even for as few as 6 months[151].

Access to kidney transplantation must be improved for patients already receiving dialysis. For instance, in the French registry[156], only 52% of patients younger than 60 years were on the waiting list after 1 year on dialysis. Patients can sometimes wait several years for transplantation (Fig. 2a) despite registration for pre-emptive transplantation. In the USA, access to kidney transplantation is also quite variable depending on the type of ownership of dialysis facilities[161] — patients treated at for-profit facilities had a lower likelihood of accessing kidney transplantation than those treated at non-profit facilities.

Dialysis technique choice and start

Urgent-start dialysis

Urgent-start dialysis should be avoided because it is associated with high morbidity and mortality[162]. One of the drawbacks of urgent-start dialysis is the underuse of peritoneal dialysis (PD) and home HD compared with in-centre HD[162,163], in addition to the delay in access to kidney transplantation. In many cases, urgent-start dialysis is linked to late referral for specialized nephrology care[162], but it might be necessary even in patients followed in a nephrology clinic[164]. In the CKD-REIN cohort, the risk of urgent-start dialysis was higher in patients living alone, with low health literacy, with heart failure or hyperpolypharmacy (that is, with prescription of >10 drugs) but was not associated with age or lower eGFR at initiation. The risk was lower in patients with a planned dialysis modality and more nephrologist visits in the 12 months preceding dialysis initiation[164].

Dialysis initiation is a high-risk period for patients

The initiation of dialysis in people with CKD represents a period of substantial risk, marked by increased vulnerability to various health

Box 2 | Recommendations for developing a dialysis modality choice strategy

1. *Develop standardized protocols*: implement standardized yet flexible protocols that include patient assessment tools, educational resources and regular follow-up mechanisms to monitor patient satisfaction and outcomes.
2. *Enhance patient education programmes*: offer robust education programmes that clearly articulate the risks and benefits of each modality, supplemented by real-life patient experiences and interactive decision aids.
3. *Facilitate patient-centred discussions*: encourage open discussions in clinic settings that allow patients to express their fears, expectations and preferences regarding their treatment options.
4. *Use technology*: incorporate telehealth and online platforms to provide ongoing support and education, creating flexibility in how patients access information and communicate with health care providers.

complications. These risks include CV events, infections and hospitalizations, all of which increase in the first few months of dialysis initiation[165]. In a seminal DOPPS report, mortality in the period up to 120 days from dialysis initiation was approximately 27/100 patient-years, consistently higher than in later periods for all participating countries[165]. DOPPS data also showed that better pre-kidney failure care in a nephrology clinic is associated with decreased mortality in the first year of HD[143]. International variations in these risks are also noteworthy. For instance, Japan has lower mortality and longer survival among people receiving dialysis than the USA and several European countries, which can be attributed to different practice patterns and health care systems[165].

Practice patterns, particularly in vascular access, also have a crucial role in patient outcomes. The use of arteriovenous fistulas, which are recommended as the preferred form of vascular access[166], varies considerably by country[167–169]. The DOPPS reported a higher prevalence of arteriovenous fistula use in Japan and several European countries, in contrast to a higher reliance on central venous catheters in the USA, which are associated with higher complication rates and worse outcomes[167,168].

The influence of global differences in practice patterns during the transition to kidney failure on early dialysis outcomes is not yet fully understood. Current international research efforts are focused on examining disparities among countries in establishing functional vascular access, enhancing patient self-care education and mitigating adverse variations in outcome-related biomarkers such as haemoglobin and iron parameters. These studies are aimed at shedding light on the diverse factors present during the dialysis initiation period and their potential impact on patient outcomes.

Choice of dialysis technique

Choosing the appropriate dialysis modality is a critical decision for patients approaching kidney failure. This decision involves multiple factors including evidence-based medical considerations[170–172], patient preferences, lifestyle factors and logistical considerations. To optimize patient outcomes and satisfaction, a structured, patient-centred approach should be employed in the decision-making process (Box 2).

Medical considerations. The choice between HD and PD often depends on the physical condition of the patient. Factors such as CV stability, residual kidney function and peritoneal membrane characteristics are key. For example, PD might be preferable for people with residual kidney function and those seeking to avoid the haemodynamic instability associated with HD.

Patient preferences and lifestyle. Understanding the lifestyle, employment circumstances and personal preferences of the patient is vital. Home PD and HD might be more suitable for patients who prefer a flexible schedule or who wish to maintain employment. Conversely, HD might be more suitable for those who prefer the structure of a dialysis centre or who require more medical supervision. In some countries, satellite HD units offer an alternative between home and centre HD, favouring self-care HD by patients, with assistance from nurses.

Logistical considerations. Accessibility to dialysis centres, availability of family or community support and the ability of the patient to manage dialysis at home influence modality choice. Geographic and socio-economic factors can also have a substantial role in determining which treatment options are feasible for a patient.

Patient education and informed decision making. Providing patients with comprehensive education about the benefits and limitations of each modality is crucial. Decision aids, informational sessions with health care providers who specialize in different dialysis modalities and discussions with patients currently receiving dialysis can enhance understanding and support informed choice.

Multidisciplinary approach. A team consisting of nephrologists, dialysis nurses, social workers, dietitians, psychologists and financial coordinators should collaborate to present the best options tailored to the individual needs of the patient. This team approach helps to address all aspects of care and supports the patient throughout the decision-making process and beyond.

Continuous evaluation. Post-modality selection, continuous assessment of patient satisfaction, health outcomes and quality of life is essential. Adjustments to the dialysis modality might be necessary as the medical status, preferences and lifestyle of the patient change over time.

Haemodialysis initiation: current recommendations

Initiating HD in patients with kidney failure requires careful consideration of both clinical and timing aspects. The current guidelines suggest starting HD based on a combination of clinical symptoms, fluid overload, uraemic complications and specific laboratory markers, rather than GFR alone. According to KDIGO guidelines, starting dialysis should be considered when eGFR drops below 10 ml/min/1.73 m^2 in people who are symptomatic. In asymptomatic patients[1,2], close monitoring is advised until symptoms develop or other uraemic complications arise.

The decision to initiate HD should be tailored to each patient, considering their quality of life, nutritional status, volume status and overall health. Early referral to a nephrology specialist is crucial for optimal preparation and education before starting dialysis. This process involves planning for vascular access well in advance of the first dialysis session to minimize the use of temporary catheters, which are associated with higher complication rates.

Incremental HD, whereby treatment frequency is adapted to residual kidney function, offers a method of preserving kidney function, reducing side effects and improving quality of life. This approach is suitable for patients with substantial residual function but requires close monitoring and a personalized care plan. Moreover, by aligning treatment intensity with individual patient needs, incremental HD is aimed at optimizing outcomes and patient satisfaction, offering a nuanced way to manage kidney failure. However, the clinical benefits of incremental HD are far from being proven and need to be evaluated[173–175].

The presence of a functional, previously chosen access for dialysis initiation is the very definition of a planned dialysis start and recognized as standard of care[162]. Timely, tailored, and repeated discussions about vascular access strengthen patient participation in vascular access decision-making and broaden vascular access options[176]. However, even among patients referred early to predialysis care, up to 60% of patients initiate dialysis with a central venous catheter[177]. In people with advanced CKD (eGFR < 20 ml/min/1.73 m^2) and under nephrology care, a recent CKDopps analysis showed that only 39% of men and 34% of women had already undergone dialysis access creation (either vascular or peritoneal)[178].

The ideal timing for referral for vascular access remains an unsolved question. The 2019 update of the Kidney Disease Outcomes Quality Initiative clinical practice guideline for vascular access considers it reasonable to refer most patients with progressive kidney function decline to vascular access creation when eGFR declines to 15–20 ml/min/1.73 m^2 (ref. 166). However, timely referral is likely to vary with patient factors, such as the rate of progression of CKD, characteristics influencing arteriovenous access maturation[179] and behaviour towards decision making (avoidance, wait and see, active intention)[180], as well as health care-related factors, such as pre-dialysis care coordination[181] and waiting time for surgeon evaluation[182].

In a recent analysis from the CKD-REIN study, we found that eGFR decline was steeper before vascular access creation than after, with a mean difference of 2.0 (1.4–2.5) ml/min/1.73 m^2 per year ($P < 0.001$)[183]. An explanation of this positive finding might be that physicians and patients become more aware of the importance of implementing and adhering to preventive measures as CKD progresses[183].

Peritoneal dialysis initiation: current recommendations

The initiation of PD involves timely and patient-centred decision making, particularly when considering the modalities of incremental PD and acute-start PD in urgent scenarios[184]. Incremental PD, whereby PD is initiated with fewer exchanges or lower dialysate volumes than in standard protocols, is recommended for patients with residual kidney function. This approach aligns with the philosophy of preserving residual kidney function while minimizing the burden of treatment, thereby potentially enhancing the quality of life and prolonging technique survival. The International Society for Peritoneal Dialysis guidelines support the use of incremental PD as a viable initial strategy, advocating its use to match the dialysis dose to the needs of the patient, thereby providing a more personalized treatment approach[184].

By contrast, acute-start PD is used in urgent situations in which HD is not feasible or is contraindicated, and no pre-dialysis planning has occurred. Acute-start PD can be a lifesaving option for patients presenting with acute kidney injury or sudden-onset kidney failure. Current recommendations suggest that, with appropriate infrastructure and expertise, PD can be initiated safely without a break-in period, using special catheters that permit immediate use. This method is advantageous in reducing the need for temporary vascular access and its associated complications, thus providing an effective alternative to HD in emergency settings.

The International Society for Peritoneal Dialysis guidelines emphasize careful patient selection and preparation as key factors for success in both incremental and acute start PD[184]. Adequate training of the medical team, proper catheter placement technique and rigorous infection control measures are crucial to minimize complications and improve patient outcomes. Moreover, ongoing assessment of patient status and residual kidney function is essential, to adjust the dialysis regimen appropriately over time.

In conclusion, both incremental PD and acute-start PD offer valuable dialysis strategies that can be tailored to meet individual patient needs and clinical circumstances. These approaches necessitate thoughtful implementation and continuous evaluation to optimize outcomes and enhance patient quality of life.

Conservative care management

Conservative kidney management, also known as conservative non-dialytic management, offers a patient-centred approach for individuals with advanced CKD and is especially relevant for older patients with significant comorbidities in whom dialysis might not provide a survival benefit or improved quality of life[185,186]. For example, a target trial emulation study from the US Department of Veterans reported in 2024 showed that older adults starting dialysis when their eGFR fell below 12 ml/min/1.73 m^2 had modest gains in life expectancy and less time at home[172]. Conservative kidney management involves the kidney care team, as well as the palliative and geriatric medicine clinical teams in a chronic process that must be planned with the patient and their relatives. This management approach focuses on the comprehensive management of symptoms and the preservation of kidney function without recourse to dialysis or transplant[186].

Conservative kidney management involves meticulous control of blood pressure and diabetes, dietary modifications, careful fluid management and the use of medications to manage anaemia and MBD associated with CKD. Palliative care is integral to conservative care and addresses not only physical symptoms such as pain, nausea, itching or fatigue but also provides psychological, social and spiritual support[186]. The goal is to slow the progression of kidney disease and manage the complications that arise from diminished kidney function. Education and support for patients and their families are crucial components, ensuring that they understand the nature of the disease, the expected outcomes and the focus on maintaining comfort and quality of life[185]. Such a multidisciplinary approach helps patients to navigate their conditions with dignity and aligns medical interventions with their personal values and goals. Regularly scheduled discussions about goals of care and advance care planning are essential, enabling patients to make informed decisions about their treatment options.

Ultimately, conservative kidney management underscores the importance of individualized care and highlights the necessity of aligning treatment with the overall health status of the patient and their personal preferences. By focusing on symptom management and quality of life, conservative care provides a viable alternative to dialysis for many patients, supporting them through the advanced stages of CKD with respect and compassion.

Barriers for nephrologists and the kidney care team

Nephrologists historically viewed dialysis as the only therapeutic solution for people with advancing CKD. Nevertheless, considering the lack of benefit of early-start dialysis and the comorbidity burden in the oldest patients, the question of whether dialysis is advantageous to such patients emerged in the past decades. In 2015, KDIGO described conservative kidney management as planned holistic patient-centred care that does not include dialysis[185]. Nowadays, even if conservative care is available worldwide, its application remains heterogeneous across different regions, influenced by social and cultural diversity, as well as local health care policies[11].

The transition from CKD G4–G5 to conservative kidney management is a chronic process that can be planned in advance[187]. As the disease progresses, the extent of symptoms and biological disturbances increases and physicians should carefully help patients to manage this period with adjustment of diet and drugs. Weighing geriatric health issues (frailty, nutritional status and geriatric syndrome) and patient preferences, the kidney care team should be able to distinguish those who will benefit from dialysis and those for whom conservative care will be the therapeutic option of choice, in a shared decision-making process. The advantages and burden of dialysis must be fully and clearly discussed, including the associations between dialysis in older individuals and high early mortality, significant cognitive decline, loss of independence and reduced quality of life[188]. The kidney care team must check that the patient understands the two options: dialysis leading to more days of life with possibly exacerbated mental and physical deterioration, versus conservative care with a possibly shorter life but without the burden of dialysis and potentially better health-related quality of life. Importantly, clinicians should be mindful of their interactions with the patient and their family members. For instance, a paternalistic attitude might hinder prioritization of patient autonomy.

The best way to deliver high-quality conservative kidney management is probably to develop an institutional programme, offering explicit treatment recommendations, based on practice culture, financial incentives and patient preferences[189]. Of note, given the duty to provide care, the nephrologist might associate conservative management with lack of care and increasing risk of death, leading to moral distress. Medical education should include training on how to initiate a discussion about supportive care, communication skills and palliative care[190].

Patient views

Although a shared decision-making process and advance care planning represent the cornerstones of the conservative kidney management approach, communication between the kidney care team and patients remains a key concern. Although conservative care is mentioned by nephrologists as being widely available in their facilities, few patients report having heard of it[191].

The nephrologist–patient interaction is influenced by cultural aspects: experience, concepts of health, spirituality, beliefs and values[185]. To be receptive of the views of the patients, the kidney care team must become aware of their own views. Moreover, nomenclature for kidney function and disease should be used cautiously and the nephrologist should not hide behind words. The clinician must consider what the patient hears and use language that is accessible and clear.

Patients and caregivers consistently prioritize symptoms and lifestyle-based outcomes, whereas health care professionals are more traditionally focused on clinical endpoints, such as mortality and hospitalization. People choosing conservative care often emphasize the ability to remain at home as a motivator. Older patients, especially women, seem to prioritize their comfort and quality of life rather than extending their life expectancy at all costs[191].

Finally, conservative kidney management is characterized by considerable uncertainty. The kidney care team proceeds in a grey zone, possibly far from their comfort zone. Evidently, treatment options include a temporal dimension and should accommodate the option for patients to change their mind at any time. It is thus necessary to accept that a decision or a statement can evolve over time, and particularly in the face of death. However, <10% of patients managed conservatively switched to dialysis over a 3-year follow-up[192] and older patients changed their choice from dialysis to conservative care more often than the opposite[188].

Organization of health care

Health care organization might have an impact on the transition from advanced CKD to kidney failure and conservative kidney management. In many parts of the world, treatment choice depends on availability. As mentioned earlier, dialysis access is poor in many regions, with PD often being the least common modality. In LMICs, where dialysis access is severely limited, conservative care becomes the only choice, even in cases where KRT access would have significantly extended patient survival.

High-income countries

In two HICs, the USA and France, a shift from fee-for-service to value-based models is underway, with a transformation of nephrology care from a dialysis-centred approach to a patient-centred approach favouring better care at advanced CKD stages.

In the USA, the Kidney Care Choices[193] and the End-Stage Renal Disease Treatment Choices[194] models are two salient examples of value-based models within the realms of CKD care. Supported by Medicare, these models promote early CKD diagnosis, coordinated care and patient engagement, thus fostering a patient-centred approach[195], which seems appropriate, but is quite complex in practice.

Despite these advances, the landscape of CKD care in the USA is not without its challenges. Disparities in care due to socio-economic factors, limited patient education and lack of early disease detection persist. The supply of donor kidneys still falls short of demand, and the transition to home dialysis faces substantial barriers. Moving forward, these issues must be addressed through policy changes, educational initiatives, technology-assisted early detection methods, as well as strategies to increase kidney donations and facilitate home dialysis. With sustained Medicare backing and the potential for ongoing innovation, the future of CKD care in the USA looks promising, with an emphasis on more effective and equitable care.

In France, the fee-for-service that prevailed until September 2019 favoured in-centre HD economically over pre-emptive transplantation, home dialysis (including PD) or conservative care[196,197]. A new bundling system has been promoted for patients with CKD stages G4 and G5 (ref. 198) whereby patients should be seen by a nephrologist, a dietician, a clinical nurse and possibly other professional members of a kidney care team, at least once a year. Centres that do not comply with these requirements receive lower amounts of the bundle: this strong incentive has been transforming the care of patients with advanced CKD, as patients and professionals realize that CKD care requires a holistic approach, including optimized lifestyle and dietary habits, counselling and therapeutic education.

Low-income countries and low- to middle-income countries

The transition from CKD to dialysis in LICs and LMICs can be particularly challenging owing to limited resources, lack of infrastructure and financial constraints. Although dialysis facilities might exist, accessibility remains highly inequitable in these regions. Funding of non-dialysis

CKD care solely through private and out-of-pocket means is present in only 20% of LICs and 9% of LMICs), reflecting the immense financial burden of KRT provision[199]. High out-of-pocket payments make dialysis unsustainable and plunge many families into poverty. Only 13% and 19% of patients in LICs and LMICs, respectively, can afford the direct cost of dialysis[200]. A framework for health care strengthening was developed by the WHO and supports the assessment of various challenges that health systems in LICs and LMICs face when providing kidney care to their population (reviewed by Okpechi et al.[201]). Up to 98% of patients with kidney failure in LICs do not receive KRT and, for those who initiate therapy, it is often ceased early owing to cost constraints.

Conclusions

In summary, the transition from advanced CKD to kidney failure represents a critical and complex phase of the progressive CKD journey and requires a holistic and patient-centred approach. This transition requires careful management of nephroprotective therapies, such as RAAS inhibitors, SGLT2 inhibitors and GLP-1 RAs, to stabilize kidney function and slow disease progression, and to prevent CV events, even in advanced stages of CKD. Pre-emptive kidney transplantation is emphasized as the optimal treatment option when feasible, offering the best outcomes in terms of survival, quality of life and cost-effectiveness. However, for older patients or those with substantial comorbidities, conservative kidney management might be the preferred option, focusing on symptom relief without initiating dialysis. Disparities in access to care, particularly in LICs and LMICs, highlight the need for tailored strategies to ensure equitable management of CKD globally. Registry and cohort studies have contributed significantly to our understanding of CKD management, reinforced now by target trial emulation studies, but more randomized clinical trials are necessary to refine treatment approaches during this critical transition phase.

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References

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* **105**, S117–S314 (2024).
2. Levin, A. et al. Executive summary of the KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: known knowns and known unknowns. *Kidney Int.* **105**, 684–701 (2024).
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int. Suppl.* **3**, 1–150 (2013).
4. Feldman, H. I. et al. The chronic renal insufficiency cohort (CRIC) study: design and methods. *J. Am. Soc. Nephrol.* **14**, S148–S153 (2003).
5. Stengel, B. et al. The French Chronic Kidney Disease-Renal Epidemiology and Information Network (CKD-REIN) cohort study. *Nephrol. Dial. Transpl.* **29**, 1500–1507 (2014).
6. Eckardt, K.-U. et al. The German Chronic Kidney Disease (GCKD) study: design and methods. *Nephrol. Dial. Transplant.* **27**, 1454–1460 (2012).
7. Hoshino, J. et al. A nationwide prospective cohort study of patients with advanced chronic kidney disease in Japan: the reach-J CKD cohort study. *Clin. Exp. Nephrol.* **22**, 309–317 (2018).
8. Dienemann, T. et al. International network of chronic kidney disease cohort studies (iNET-CKD): a global network of chronic kidney disease cohorts. *BMC Nephrol.* **17**, 121 (2016).
9. Jager, K. J. et al. The EQUAL study: a European study in chronic kidney disease stage 4 patients. *Nephrol. Dial. Transpl.* **27**, iii27–31 (2012).
10. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet* **395**, 709–733 (2020).
11. Bello, A. K. et al. Status of care for end stage kidney disease in countries and regions worldwide: international cross sectional survey. *BMJ* **367**, l5873 (2019).
12. van Rijn, M. H. C., de Pinho, N. A., Wetzels, J. F., van den Brand, J. A. J. G. & Stengel, B. Worldwide disparity in the relation between CKD prevalence and kidney failure risk. *Kidney Int. Rep.* **5**, 2284–2291 (2020).
13. Yeung, E. et al. Current status of health systems financing and oversight for end-stage kidney disease care: a cross-sectional global survey. *BMJ Open.* **11**, e047245 (2021).
14. Pinho et al. Understanding international variations in kidney failure incidence and initiation of replacement therapy. *Kidney Int. Rep.* **7**, 2364–2375 (2022).
15. Neuen, B. L. et al. National health policies and strategies for addressing chronic kidney disease: data from the International Society of Nephrology Global Kidney Health Atlas. *PLoS Glob. Public Health* **3**, e0001467 (2023).
16. Htay, H. et al. Global access of patients with kidney disease to health technologies and medications: findings from the global kidney health atlas project. *Kidney Int. Suppl.* **8**, 64–73 (2018).
17. Writing Group for the CKD Prognosis Consortium et al. Estimated glomerular filtration rate, albuminuria, and adverse outcomes. *JAMA* **330**, 1266–1277 (2023).
18. Kula, A. J., Prince, D. K., Katz, R. & Bansal, N. Mortality burden and life-years lost across the age spectrum for adults living with CKD. *Kidney360* **4**, 615–621 (2023).
19. Levey, A. S. et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. *Kidney Int.* **80**, 17–28 (2011).
20. Hallan, S. I. et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. *BMJ* **333**, 1047 (2006).
21. Grams, M. E. et al. Predicting timing of clinical outcomes in patients with chronic kidney disease and severely decreased glomerular filtration rate. *Kidney Int.* **93**, 1442–1451 (2018).
22. Tonelli, M. et al. Risk of coronary events in people with chronic kidney disease compared with those with diabetes: a population-level cohort study. *Lancet* **380**, 807–14 (2012).
23. Tangri, N. et al. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. *JAMA* **315**, 164–11 (2016).
24. Bhandari, S., Mehta, S., Ives, N. & Cockwell, P. Utility of 2-year kidney failure risk equation for advanced chronic kidney disease: analysis from the STOP-ACEi trial. *Nephrol. Dial. Transplant.* **39**, 884–887 (2023).
25. Zacharias, H. U. et al. A predictive model for progression of CKD to kidney failure based on routine laboratory tests. *Am. J. Kidney Dis.* **79**, 217–230.e1 (2021).
26. Massy, Z. A. et al. Machine learning-based urine peptidome analysis to predict and understand mechanisms of progression to kidney failure. *Kidney Int. Rep.* **8**, 544–555 (2023).
27. Grams, M. E. et al. The kidney failure risk equation: evaluation of novel input variables including EGFR estimated using the CKD-EPI 2021 equation in 59 cohorts. *J. Am. Soc. Nephrol.* **34**, 482–494 (2023).
28. Ali, I., Donne, R. L. & Kalra, P. A. A validation study of the kidney failure risk equation in advanced chronic kidney disease according to disease aetiology with evaluation of discrimination, calibration and clinical utility. *BMC Nephrol.* **22**, 194 (2021).
29. Hundemer, G. L. et al. Performance of the kidney failure risk equation by disease etiology in advanced CKD. *Clin. J. Am. Soc. Nephrol.* **15**, 1424–1432 (2020).
30. Chu, C. D. et al. Utility of the kidney failure risk equation and estimated GFR for estimating time to kidney failure in advanced CKD. *Am. J. Kidney Dis.* **82**, 386–394.e1 (2023).
31. Inker, L. A. et al. A meta-analysis of GFR slope as a surrogate endpoint for kidney failure. *Nat. Med.* **29**, 1867–1876 (2023).
32. Weiner, D. E. et al. The Framingham predictive instrument in chronic kidney disease. *J. Am. Coll. Cardiol.* **50**, 217–224 (2007).
33. Matsushita, K., Ballew, S. H. & Coresh, J. Cardiovascular risk prediction in people with chronic kidney disease. *Curr. Opin. Nephrol. Hypertens.* **25**, 518–523 (2016).
34. Matsushita, K. et al. Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. *Lancet Diabetes Endocrinol.* **3**, 514–525 (2015).
35. Matsushita, K. et al. Incorporating kidney disease measures into cardiovascular risk prediction: development and validation in 9 million adults from 72 datasets. *Eclinicalmedicine* **27**, 100552 (2020).
36. Shlipak, M. G. et al. Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. *JAMA* **293**, 1737–1745 (2005).
37. Bundy, J. D. et al. Risk prediction models for atherosclerotic cardiovascular disease in patients with chronic kidney disease: the CRIC study. *J. Am. Soc. Nephrol.* **33**, 601–611 (2022).
38. Massy, Z. A. & Drueke, T. B. Combination of cardiovascular, kidney, and metabolic diseases in a syndrome named cardiovascular-kidney-metabolic, with new risk prediction equations. *Kidney Int. Rep.* **9**, 2608–2618 (2024).
39. Drüeke, T. B. & Massy, Z. A. Atherosclerosis in CKD: differences from the general population. *Nat. Rev. Nephrol.* **6**, 723–735 (2010).
40. Lees, J. S. et al. Glomerular filtration rate by differing measures, albuminuria and prediction of cardiovascular disease, mortality and end-stage kidney disease. *Nat. Med.* **25**, 1753–1760 (2019).
41. Lees, J. S. et al. Assessment of cystatin C level for risk stratification in adults with chronic kidney disease. *JAMA Netw. Open* **5**, e2238300 (2022).
42. Kalantar-Zadeh, K. et al. Patient-centred approaches for the management of unpleasant symptoms in kidney disease. *Nat. Rev. Nephrol.* **18**, 185–198 (2022).
43. Speyer, E. et al. Symptom burden and its impact on quality of life in patients with moderate to severe CKD: the international chronic kidney disease outcomes and practice patterns study (CKDopps). *Am. J. Kidney Dis.* **84**, 696–707.e1 (2024).
44. Mallamaci, F., Pisano, A. & Tripepi, G. Physical activity in chronic kidney disease and the EXerCise introduction to enhance trial. *Nephrol. Dial. Transplant.* **35**, ii18–ii22 (2020).
45. Curtis, F. et al. Lifestyle interventions delivered by eHealth in chronic kidney disease: a scoping review. *PLoS ONE* **19**, e0297107 (2024).

46. Greenwood, S. A. et al. Evaluating the effect of a digital health intervention to enhance physical activity in people with chronic kidney disease (Kidney BEAM): a multicentre, randomised controlled trial in the UK. *Lancet Digit. Health* **6**, e23–e32 (2024).
47. Greenwood, S. A. et al. Kidney beam — a cost-effective digital intervention to improve mental health. *Kidney Int. Rep.* **9**, 3204–3217 (2024).
48. Tantisattamo, E. et al. Novel approaches to sarcopenic obesity and weight management before and after kidney transplantation. *Curr. Opin. Nephrol. Hypertens.* **30**, 14–26 (2021).
49. Martins, P. et al. Association between physical activity and mortality in end-stage kidney disease: a systematic review of observational studies. *BMC Nephrol.* **22**, 227 (2021).
50. Zoccali, C., Manfredini, F., Kanbay, M. & Mallamaci, F. Intradialysis exercise in hemodialysis patients: effective but complex and costly. *Nephrol. Dial. Transplant.* **39**, 7–9 (2023).
51. American Diabetes Association Professional Practice Committee for Diabetes. 9. Pharmacologic approaches to glycemic treatment: standards of care in diabetes — 2026. *Diabetes Care* **49**, S183–S215 (2025).
52. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* **98**, S1–S115 (2020).
53. Herrington, W. G. & Haynes, R. Diabetic kidney disease — semaglutide flows into the mainstream. *N. Engl. J. Med.* **391**, 178–179 (2024).
54. de Boer, I. H. et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* **102**, 974–989 (2022).
55. ElSayed, N. A. et al. Summary of revisions: standards of care in diabetes — 2023. *Diabetes Care* **46**, S5–S9 (2022).
56. Bakris, G. L. & Molitch, M. Microalbuminuria as a risk predictor in diabetes: the continuing saga. *Diabetes Care* **37**, 867–875 (2014).
57. Kalantar-Zadeh, K. & Fouque, D. Nutritional management of chronic kidney disease. *N. Engl. J. Med.* **377**, 1765–1776 (2017).
58. Faye, M. et al. Five-year symptom trajectories in nondialysis-dependent CKD patients. Clin. J. Am. Soc. Nephrol. **17**, 1588–1597 (2022).
59. Kelly, J. T. et al. Healthy dietary patterns and risk of mortality and ESRD in CKD: a meta-analysis of cohort studies. *Clin. J. Am. Soc. Nephrol.* **12**, 272–279 (2017).
60. Burnier, M. Sodium intake and progression of chronic kidney disease — has the time finally come to do the impossible: a prospective randomized controlled trial? *Nephrol. Dial. Transplant.* **36**, 381–384 (2020).
61. Borrelli, S. et al. Sodium intake and chronic kidney disease. *Int. J. Mol. Sci.* **21**, 4744 (2020).
62. Tomson, C. R. V. Advising dialysis patients to restrict fluid intake without restricting sodium intake is not based on evidence and is a waste of time. *Nephrol. Dial. Transplant.* **16**, 1538–1542 (2001).
63. Afsar, B., Afsar, R. E., Caliskan, Y. & Lentine, K. L. A holistic review of sodium intake in kidney transplant patients: more questions than answers. *Transplant. Rev.* **38**, 100859 (2024).
64. Ikizler, T. A. et al. KDOQI clinical practice guideline for nutrition in CKD: 2020 update. *Am. J. Kidney Dis.* **76**, S1–S107 (2020).
65. Fouque, D. et al. Insulin-like growth factor-1 and its binding proteins during a low-protein diet in chronic renal failure. *J. Am. Soc. Nephrol.* **6**, 1427–1433 (1995).
66. Wang, A. Y.-M. et al. Precision medicine for nutritional management in end-stage kidney disease and transition to dialysis. *Semin. Nephrol.* **38**, 383–396 (2018).
67. Carrero, J. J. et al. Plant-based diets to manage the risks and complications of chronic kidney disease. *Nat. Rev. Nephrol.* **16**, 1–18 (2020).
68. Bakis, H., Chauveau, P., Combe, C. & Pfirmann, P. Mediterranean diet for cardiovascular risk reduction in chronic kidney disease. *Adv. Kidney Dis. Health* **30**, 496–501 (2023).
69. Joshi, S., McMacken, M. & Kalantar-Zadeh, K. Plant-based diets for kidney disease: a guide for clinicians. *Am. J. Kidney Dis.* **77**, 287–296 (2021).
70. Goraya, N. & Wesson, D. E. Plant-based diets across the spectrum of kidney disease. *Clin. J. Am. Soc. Nephrol.* **20**, 1142–1149 (2025).
71. Sumida, K. et al. Constipation and Incident CKD. *J. Am. Soc. Nephrol.* **28**, 1248–1258 (2017).
72. Fouque, D., Mafra, D. & Bellizzi, V. Dietary protein intake in CKD: quantity and quality. *Clin. J. Am. Soc. Nephrol.* https://doi.org/10.2215/CJN.0000000777 (2025).
73. Wang, A. Y.-M. et al. Assessing global kidney nutrition care. *Clin. J. Am. Soc. Nephrol.* **17**, 38–52 (2022).
74. St-Jules, D. E. & Fouque, D. Etiology-based dietary approach for managing hyperkalemia in people with chronic kidney disease. *Nutr. Rev.* **80**, 2198–2205 (2022).
75. Weir, M. R. et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N. Engl. J. Med.* **372**, 211–221 (2014).
76. Agarwal, R. et al. Patiromer versus placebo to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER): a phase 2, randomised, double-blind, placebo-controlled trial. *Lancet* **394**, 1540–1550 (2019).
77. St-Jules, D. E., Clegg, D. J., Palmer, B. F. & Carrero, J.-J. Can novel potassium binders liberate people with chronic kidney disease from the low-potassium diet? *Clin. J. Am. Soc. Nephrol.* **17**, 467–472 (2022).
78. Packer, M. Potassium binders for patients with heart failure? The real enlightenment of the DIAMOND trial. *Eur. Heart J.* **43**, 4374–4377 (2022).
79. Sumida, K. et al. Laxative use and risk of dyskalemia in patients with advanced CKD transitioning to dialysis. *J. Am. Soc. Nephrol.* **32**, 950–959 (2021).
80. Levin, A. et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. *Kidney Int.* **71**, 31–38 (2007).
81. Moranne, O. et al. Timing of onset of CKD-related metabolic complications. *J. Am. Soc. Nephrol.* **20**, 164–171 (2009).
82. Zoccali, C. et al. The systemic nature of CKD. *Nat. Rev. Nephrol.* **13**, 1–15 (2017).
83. Costes-Albrespic, M. et al. Antihypertensive treatment patterns in CKD stages 3 and 4: the CKD-REIN Cohort Study. *Kidney Med.* **6**, 100912 (2024).
84. Pinho et al. Considerable international variation exists in blood pressure control and antihypertensive prescription patterns in chronic kidney disease. *Kidney Int.* **96**, 983–994 (2019).
85. Weir, M. R. et al. Use of renin-angiotensin system blockade in advanced CKD: an NKF-KDOQI controversies report. *Am. J. Kidney Dis.* **72**, 873–884 (2018).
86. Ingelfinger, J. R. Discontinuation of RAS inhibitors in advanced CKD — has equipoise occurred? *N. Engl. J. Med.* **387**, 2083–2084 (2022).
87. Cheung, A. K. et al. Executive summary of the KDIGO 2021 clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int.* **99**, 559–569 (2021).
88. Pugh, D., Gallacher, P. J. & Dhaun, N. Management of hypertension in chronic kidney disease. *Drugs* **79**, 365–379 (2019).
89. Pecoits-Filho, R. et al. Prescription of renin-angiotensin-aldosterone system inhibitors (RAASi) and its determinants in patients with advanced CKD under nephrologist care. *J. Clin. Hypertens.* **21**, 337–11 (2019).
90. Bhandari, S. et al. Renin–angiotensin system inhibition in advanced chronic kidney disease. *N. Engl. J. Med.* **387**, 2021–2032 (2022).
91. Fu, E. L. et al. Stopping renin-angiotensin system inhibitors in patients with advanced CKD and risk of adverse outcomes: a nationwide study. *J. Am. Soc. Nephrol.* **32**, 424–435 (2021).
92. Karaboyas, A. et al. DOPPS data suggest a possible survival benefit of renin angiotensin-aldosterone system inhibitors and other antihypertensive medications for hemodialysis patients. *Kidney Int.* **94**, 589–598 (2018).
93. Bushinsky, D. A. et al. Patiromer treatment in patients with CKD, hyperkalemia, and hyperphosphatemia: a post hoc analysis of 3 clinical trials. *Am. J. Kidney Dis.* **82**, 97–104 (2023).
94. Shi, Q. et al. Benefits and harms of drug treatment for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ.* **381**, e074068 (2023).
95. Rangaswami, J. & Mathew, R. O. Reducing kidney disease burden in type 2 diabetes with SGLT2 inhibitors: shifting the goalposts upstream. *Clin. J. Am. Soc. Nephrol.* **18**, 1119–1121 (2023).
96. Braunwald, E. Gliflozins in the management of cardiovascular disease. *N. Engl. J. Med.* **386**, 2024–2034 (2022).
97. Zannad, F. et al. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. *Lancet* **396**, 819–829 (2020).
98. Wheeler, D. C. et al. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. *Lancet Diabetes Endocrinol.* **9**, 22–31 (2021).
99. Heerspink, H. J. L. et al. Dapagliflozin in patients with chronic kidney disease. *N. Engl. J. Med.* **383**, 1436–1446 (2020).
100. EMPA-KIDNEY Collaborative Group. et al. Long-term effects of empagliflozin in patients with chronic kidney disease. *N. Engl. J. Med.* **392**, 777–787 (2025).
101. The EMPA-KIDNEY Collaborative Group. et al. Empagliflozin in patients with chronic kidney disease. *N. Engl. J. Med.* **388**, 117–127 (2022).
102. Wheeler, D. C. et al. A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. *Kidney Int.* **100**, 215–224 (2021).
103. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* **102**, S1–S127 (2022).
104. Singh, T., Li, T., Mandebrot, D., Astor, B. C. & Mehr, A. P. Prescribing patterns for sodium-glucose Co-transporter 2 Inhibitors (SGLT2i): a survey of nephrologists. *Kidney Int. Rep.* **8**, 1669–1671 (2023).
105. Leaf, D. E. & Bansal, N. Another win for SGLT2 inhibitors in chronic kidney disease. *N. Engl. J. Med.* **392**, 822–823 (2025).
106. Heerspink, H. J. L., Berger, S., Gansevoort, R. T. on behalf of the Renal Life Cycle Trial Investigators. Will SGLT2 inhibitors be effective and safe in patients with severe CKD, dialysis, or kidney transplantation. *Clin. J. Am. Soc. Nephrol.* **18**, 1500–1502 (2023).
107. Yen, F.-S. et al. Sodium-glucose cotransporter-2 inhibitors and the risk for dialysis and cardiovascular disease in patients with stage 5 chronic kidney disease. *Ann. Intern. Med.* **177**, 693–700 (2024).
108. Cohen, T. D. et al. Safety of sodium-glucose cotransporter 2 inhibitors in kidney transplant recipients with diabetes mellitus. *Diabetes Metab.* **51**, 101627 (2025).
109. Holliday, M. W., Frost, L. & Navaneethan, S. D. Emerging evidence for glucagon-like peptide-1 agonists in slowing chronic kidney disease progression. *Curr. Opin. Nephrol. Hypertens.* **33**, 331–336 (2024).
110. Perkovic, V. et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N. Engl. J. Med.* **391**, 109–121 (2024).

111. Apperloo, E. M. et al. Semaglutide in patients with overweight or obesity and chronic kidney disease without diabetes: a randomized double-blind placebo-controlled clinical trial. *Nat. Med.* **31**, 278–285 (2024).
112. Zelada, H. et al. Efficacy, tolerability, and safety of glucagon-like peptide 1 receptor agonists (GLP1-RA) in kidney transplant recipients with diabetes. *Clin. Transplant.* **39**, e70144 (2025).
113. Cohen, T. D. et al. Glucagon-like peptide 1 receptor agonists and renal outcomes in kidney transplant recipients with diabetes mellitus. *Diabetes Metab.* **51**, 101624 (2025).
114. Bellos, I., Lagiou, P., Benetou, V. & Marinaki, S. Safety and efficacy of sodium-glucose transport protein 2 inhibitors and glucagon-like peptide-1 receptor agonists in diabetic kidney transplant recipients: synthesis of evidence. *J. Clin. Med.* **13**, 6181 (2024).
115. Lai, H.-W., See, C. Y., Chen, J.-Y. & Wu, V.-C. Mortality and cardiovascular events in diabetes mellitus patients at dialysis initiation treated with glucagon-like peptide-1 receptor agonists. *Cardiovasc. Diabetol.* **23**, 277 (2024).
116. Thomas, A. M., Lamb, K. & Howard, O. Glucagon-like peptide-1 receptor agonists use for type 2 diabetes mellitus in end-stage renal disease. *J. Am. Pharm. Assoc.* **63**, 1612–1616 (2023).
117. Orandi, B. J. et al. GLP-1 receptor agonist outcomes, safety, and body mass index change in a national cohort of patients on dialysis. *Clin. J. Am. Soc. Nephrol.* **20**, 1100–1110 (2025).
118. Agarwal, R. et al. Chlorthalidone for hypertension in advanced chronic kidney disease. *N. Engl. J. Med.* **385**, 2507–2519 (2021).
119. Agarwal, R., Sinha, A. D. & Tu, W. Mechanisms of antihypertensive effect of chlorthalidone in advanced chronic kidney disease. *Clin. J. Am. Soc. Nephrol.* **19**, 1025–1032 (2024).
120. Jafar, T. H. & Feng, L. Understanding the BP-lowering mechanism of chlorthalidone in advanced kidney disease. *Clin. J. Am. Soc. Nephrol.* **19**, 949–951 (2024).
121. Agarwal, R., Verma, A. & Georgianos, P. I. Diuretics in patients with chronic kidney disease. *Nat. Rev. Nephrol.* **21**, 264–278 (2025).
122. Faucon, A.-L. et al. A nationwide cohort study comparing the effectiveness of diuretics and calcium channel blockers on top of renin-angiotensin system inhibitors on chronic kidney disease progression and mortality. *Kidney Int.* **104**, 542–551 (2023).
123. Tabibzadeh, N. et al. Diuretic prescriptions in the first year of haemodialysis: international practice patterns and associations with outcomes. *Clin. Kidney J.* **17**, sfae141 (2024).
124. Sarafidis, P. et al. Outcomes with finerenone in participants with stage 4 CKD and type 2 diabetes. *Clin. J. Am. Soc. Nephrol.* **18**, 602–612 (2023).
125. Massy, Z. A. et al. Achievement of low-density lipoprotein cholesterol targets in CKD. *Kidney Int. Rep.* **4**, 1546–1554 (2019).
126. Massy, Z. A. et al. Is a treat-to-target approach to lipid-lowering therapy appropriate in patients with chronic kidney disease? A prospective French cohort study. *J. Nephrol* **34**, 1467–1477 (2021).
127. KDIGO clinical practice guideline for lipid management in chronic kidney disease. *Kidney Int. Suppl.* **3**, 1–56 (2013).
128. Massy, Z. A. et al. Association of serum phosphate with efficacy of statin therapy in hemodialysis patients. *Clin. J. Am. Soc. Nephrol.* **17**, 546–554 (2022).
129. Baigent, C. et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. *Lancet* **377**, 2181–2192 (2011).
130. Canney, M. et al. Regional variation in hemoglobin distribution among individuals with CKD: the ISN International Network of CKD Cohorts. *Kidney Int. Rep.* **8**, 2056–2067 (2023).
131. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int. Suppl.* **2**, 179 (2012).
132. Kliger, A. S. et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for anemia in CKD. *Am. J. Kidney Dis.* **62**, 849–859 (2013).
133. Locatelli, F. et al. Kidney disease: improving global outcomes guidelines on anaemia management in chronic kidney disease: a European renal best practice position statement. *Nephrol. Dial. Transplant.* **28**, 1346–1359 (2013).
134. Bhandari, S. et al. UK Kidney Association clinical practice guideline: update of anaemia of chronic kidney disease. *BMC Nephrol.* **26**, 193 (2025).
135. Lopes, M. B. et al. A real-world longitudinal study of anemia management in non-dialysis-dependent chronic kidney disease patients: a multinational analysis of CKDopps. *Sci. Rep.* **11**, 1784 (2021).
136. Guedes, M. et al. Serum biomarkers of iron stores are associated with increased risk of all-cause mortality and cardiovascular events in nondialysis CKD patients, with or without anemia. *J. Am. Soc. Nephrol.* **32**, 2020–2030 (2021).
137. Gall, L. L. et al. Haemoglobin trajectories in chronic kidney disease and risk of major adverse cardiovascular events. *Nephrol. Dial. Transplant.* **39**, 669–682 (2023).
138. Locatelli, F. & Vecchio, L. D. Hypoxia-inducible factor–prolyl hydroxyl domain inhibitors: from theoretical superiority to clinical noninferiority compared with current ESAs? *J. Am. Soc. Nephrol.* **33**, 1966–1979 (2022).
139. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD-MBD). *Kidney Int. Suppl.* **7**, 1–59 (2017).
140. Liabeuf, S. et al. International variation in the management of mineral bone disorder in patients with chronic kidney disease: results from CKDopps. *Bone* **129**, 115058 (2019).
141. Sweiss, H. et al. Safety and efficacy of sodium-glucose cotransporter-2 inhibitors in solid organ transplant recipients. *Prog. Transpl.* **33**, 261–265 (2023).
142. US National Library of Medicine. *ClinicalTrials.gov* https://www.clinicaltrials.gov/study/NCT05374291 (2025).
143. Karaboyas, A. et al. Estimating the fraction of first-year hemodialysis deaths attributable to potentially modifiable risk factors: results from the DOPPS. *Clin. Epidemiol.* **12**, 51–60 (2020).
144. Liu, Y., Ma, X., Zheng, J., Jia, J. & Yan, T. Effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on cardiovascular events and residual renal function in dialysis patients: a meta-analysis of randomised controlled trials. *BMC Nephrol.* **18**, 206 (2017).
145. Barreto, J. et al. Pharmacokinetic properties of dapagliflozin in hemodialysis and peritoneal dialysis patients. *Clin. J. Am. Soc. Nephrol.* **18**, 1051–1058 (2023).
146. Walsh, M. et al. Spironolactone versus placebo in patients undergoing maintenance dialysis (ACHIEVE): an international, parallel-group, randomised controlled trial. *Lancet* **406**, 695–704 (2025).
147. Rossignol, P. et al. Spironolactone in patients on chronic haemodialysis at high risk of adverse cardiovascular outcomes (ALCHEMIST): a multicentre, double-blind, randomised, placebo-controlled trial and updated meta-analysis. *Lancet* **406**, 705–718 (2025).
148. Abramowicz, D. et al. Does pre-emptive transplantation versus post start of dialysis transplantation with a kidney from a living donor improve outcomes after transplantation? A systematic literature review and position statement by the Descartes working group and ERBP. *Nephrol. Dial. Transplant.* **31**, 691–697 (2016).
149. Meier-Kriesche, H.-U. et al. Effect of waiting time on renal transplant outcome. *Kidney Int.* **58**, 1311–1317 (2000).
150. Mange, K. C., Joffe, M. M. & Feldman, H. I. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N. Engl. J. Med.* **344**, 726–731 (2001).
151. Prezelin-Reydit, M. et al. Prolonged dialysis duration is associated with graft failure and mortality after kidney transplantation: results from the French transplant database. *Nephrol. Dial. Transpl.* **34**, 538–545 (2018).
152. Goto, N. et al. Association of dialysis duration with outcomes after transplantation in a Japanese cohort. *Clin. J. Am. Soc. Nephrol.* **11**, 497–504 (2016).
153. Strohmaier, S. et al. Survival benefit of first single-organ deceased donor kidney transplantation compared with long-term dialysis across ages in transplant-eligible patients with kidney failure. *JAMA Netw. Open* **5**, e2234971 (2022).
154. McCormick, F., Held, P. J., Chertow, G. M., Peters, T. G. & Roberts, J. P. Removing disincentives to kidney donation: a quantitative analysis. *J. Am. Soc. Nephrol.* **30**, 1349–1357 (2019).
155. Held, P. J., McCormick, F., Ojo, A. & Roberts, J. P. A cost-benefit analysis of government compensation of kidney donors. *Am. J. Transpl.* **16**, 877–885 (2015).
156. REIN annual report 2021: summary. https://www.agence-biomedecine.fr/IMG/pdf/rapport_rein_2021_2023-06-26.pdf (2023).
157. Gadelkareem, R. A. et al. Preemptive living donor kidney transplantation: access, fate, and review of the status in Egypt. *World J. Nephrol.* **12**, 40–55 (2023).
158. Shah, D. S. Insights from Nepal into implementing transplantation programmes in low-resource settings. *Nat. Rev. Nephrol.* **21**, 812 (2025).
159. Cheddani, L. et al. Higher mortality risk among kidney transplant recipients than among estimated glomerular filtration rate-matched patients with CKD — preliminary results. *Nephrol. Dial. Transplant.* **36**, 176–184 (2020).
160. Wolfe, R. A. et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N. Engl. J. Med.* **341**, 1725–1730 (1999).
161. Gander, J. C. et al. Association between dialysis facility ownership and access to kidney transplantation. *JAMA* **322**, 957 (2019).
162. Chan, C. T. et al. Dialysis initiation, modality choice, access, and prescription: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int.* **96**, 37–47 (2019).
163. Cheetham, M. S. et al. Home versus in-centre haemodialysis for people with kidney failure. *Cochrane Database Syst. Rev.* **2024**, CD009535 (2024).
164. Fages, V. et al. Urgent-start dialysis in patients referred early to a nephrologist — the CKD-REIN prospective cohort study. *Nephrol. Dial. Transpl.* **36**, 1500–1510 (2021).
165. Robinson, B. M. et al. Worldwide, mortality risk is high soon after initiation of hemodialysis. *Kidney Int.* **85**, 158–165 (2014).
166. Lok, C. E. et al. KDOQI clinical practice guideline for vascular access: 2019 update. *Am. J. Kidney Dis.* **75**, S1–S164 (2020).
167. Pisoni, R. L. et al. International comparisons of native arteriovenous fistula patency and time to becoming catheter-free: findings from the dialysis outcomes and practice patterns study (DOPPS). *Am. J. Kidney Dis.* **77**, 245–254 (2021).
168. Pisoni, R. L. et al. Facility hemodialysis vascular access use and mortality in countries participating in DOPPS: an instrumental variable analysis. *Am. J. Kidney Dis.* **53**, 475–491 (2009).
169. Faye, M. et al. Vascular access in Senegalese patients starting chronic haemodialysis. *Afr. J. Nephrol.* **26**, 3–8, https://doi.org/10.21804/26-1-5381 (2023).
170. Couchoud, C. et al. Dialysis modality choice in diabetic patients with end-stage kidney disease: a systematic review of the available evidence. *Nephrol. Dial. Transpl.* **30**, 310–320 (2015).
171. Combe, C., Rigothier, C. & Chauveau, P. Evidence-based choice of dialysis technique in diabetics with end-stage kidney disease: half a loaf is better than no bread. *Nephrol. Dial. Transpl.* **30**, 160–162 (2015).
172. Montez-Rath, M. E. et al. Effect of starting dialysis versus continuing medical management on survival and home time in older adults with kidney failure: a target trial emulation study. *Ann. Intern. Med.* **177**, 1233–1243 (2024).

173. Jaques, D. A. et al. Outcomes of incident patients treated with incremental haemodialysis as compared with standard haemodialysis and peritoneal dialysis. *Nephrol. Dial. Transpl.* **37**, 2514–2521 (2022).
174. Wanner, C., Lopau, K. & Haberstroh, H. The safety and feasibility of incremental dialysis must be proven before its widespread use. *Kidney Int.* **101**, 468–471 (2022).
175. Murea, M. et al. From niche to norm: a multi-action plan to close gaps and mainstream incremental hemodialysis. *Kidney Int.* **108**, 201–213 (2025).
176. Elliott, M. J. et al. Patient and clinician perspectives on shared decision making in vascular access selection: a qualitative study. *Am. J. Kidney Dis.* **81**, 48–58.e1 (2023).
177. Pisoni, R. L., Zepel, L., Port, F. K. & Robinson, B. M. Trends in US vascular access use, patient preferences, and related practices: an update from the US DOPPS practice monitor with international comparisons. *Am. J. Kidney Dis.* **65**, 905–915 (2015).
178. Hecking, M. et al. Sex-specific differences in mortality and incident dialysis in the chronic kidney disease outcomes and practice patterns study. *Kidney Int. Rep.* **7**, 410–423 (2021).
179. de Pinho, N. A. et al. Predictors of nonfunctional arteriovenous access at hemodialysis initiation and timing of access creation: a registry-based study. *PLoS ONE* **12**, e0181254 (2017).
180. Griva, K. et al. Patient-related barriers to timely dialysis access preparation: a qualitative study of the perspectives of patients, family members, and health care providers. *Kidney Med.* **2**, 29–41 (2020).
181. Flythe, J. E. et al. Targeting patient and health system barriers to improve rates of hemodialysis initiation with an arteriovenous access. *Kidney360* **2**, 708–720 (2021).
182. Lopez-Vargas, P. A. et al. Barriers to timely arteriovenous fistula creation: a study of providers and patients. *Am. J. Kidney Dis.* **57**, 873–882 (2011).
183. Tabcheh, A.-H. et al. Arteriovenous access creation and eGFR decline in patients with CKD. *J. Am. Soc. Nephrol.* **35**, 1570–1573 (2024).
184. Brown, E. A. et al. International Society for Peritoneal Dialysis practice recommendations: prescribing high-quality goal-directed peritoneal dialysis. *Perit. Dial. Int.* **40**, 244–253 (2020).
185. Davison, S. N. et al. Executive summary of the KDIGO controversies conference on supportive care in chronic kidney disease: developing a roadmap to improving quality care. *Kidney Int.* **88**, 447–459 (2015).
186. Davison, S. N. et al. Conservative kidney management and kidney supportive care: core components of integrated care for people with kidney failure. *Kidney Int.* **105**, 35–45 (2024).
187. McMahan, R. D. & Sudore, R. L. Making advance care planning easier for adults with kidney disease and their clinicians. *Nat. Rev. Nephrol.* **20**, 564–565 (2024).
188. Hamroun, A., Glowacki, F. & Frimat, L. Comprehensive conservative care: what doctors say, what patients hear. *Nephrol. Dial. Transpl.* **38**, 2428–2443 (2023).
189. Ladin, K. et al. Characterizing approaches to dialysis decision making with older adults: a qualitative study of nephrologists. *Clin. J. Am. Soc. Nephrol.* **13**, 1188–1196 (2018).
190. Hounkpatin, H. O. et al. Patients' and kidney care team's perspectives of treatment burden and capacity in older people with chronic kidney disease: a qualitative study. *BMJ Open.* **10**, e042548 (2020).
191. Hamroun, A. et al. Barriers to conservative care from patients' and nephrologists' perspectives: the CKD-REIN study. *Nephrol. Dial. Transpl.* **37**, 2438–2448 (2022).
192. Morton, R. L. et al. Conservative management and end-of-life care in an Australian cohort with ESRD. *Clin. J. Am. Soc. Nephrol.* **11**, 2195–2203 (2016).
193. Jain, G. & Weiner, D. E. Value-based care in nephrology: the kidney care choices model and other reforms. https://innovation.cms.gov/innovation-models/kidney-care-choices-kcc-model (2021).
194. Centers for Medicare & Medicaid Services. ESRD treatment choices (ETC) model. https://innovation.cms.gov/innovation-models/esrd-treatment-choices-model (2025).
195. Lin, E., Dave, G. & Kshirsagar, A. V. The new kidney-focused companies: a privatized approach to value-based care and addressing social determinants of health. *J. Am. Soc. Nephrol.* **34**, 17–20 (2023).
196. Durand-Zaleski, I., Combe, C. & Lang, P. International study of health care organization and financing for end-stage renal disease in France. *Int. J. Health Care Finance Econ.* **7**, 171–183 (2007).
197. Vanholder, R. et al. Reimbursement of dialysis: a comparison of seven countries. *J. Am. Soc. Nephrol.* **23**, 1291–1298 (2012).
198. Arrêté du 25 septembre 2019 relatif aux forfaits alloués aux établissements de santé dans le cadre de la prise en charge de patients atteints de maladie rénale chronique en application de l'article L. 162-22-6-2 du code de la sécurité sociale. *Journal Officiel de la République Française* (2019).
199. Bello, A. et al. ISN — global kidney health atlas: a report by the International Society of Nephrology: an assessment of global kidney health care status focussing on capacity, availability, accessibility, affordability and outcomes of kidney disease. https://www.theisn.org/wp-content/uploads/media/ISN%20Atlas_2023%20Digital.pdf (2023).
200. Bello, A. K. et al. Global overview of health systems oversight and financing for kidney care. *Kidney Int. Suppl.* **8**, 41–51 (2018).
201. Okpechi, I. G. et al. Building optimal and sustainable kidney care in low resource settings: the role of healthcare systems. *Nephrology* **26**, 948–960 (2021).

Author contributions

All authors researched data for the article and wrote the manuscript. C.C., N.A.d.P., M.G., L.F., D.F., S.L., A.N., B.S., Z.A.M. and R.P.-F. made substantial contributions to discussions of the content. C.C., N.A.d.P., L.F., D.F., S.L., B.S., Z.A.M. and R.P.-F. reviewed or edited the manuscript before submission.

Competing interests

The authors declare no competing interests.

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