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Plant-based diets to manage the risks and complications of chronic kidney disease

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Abstract | Traditional dietary recommendations for patients with chronic kidney disease (CKD) focus on the quantity of nutrients consumed. Without appropriate dietary counselling, these restrictions can result in a low intake of fruits and vegetables and a lack of diversity in the diet. Plant nutrients and plant-based diets could have beneficial effects in patients with CKD: increased fibre intake shifts the gut microbiota towards reduced production of uraemic toxins; plant fats, particularly olive oil, have anti-atherogenic effects; plant anions might mitigate metabolic acidosis and slow CKD progression; and as plant phosphorus has a lower bioavailability than animal phosphorus, plant-based diets might enable better control of hyperphosphataemia. Current evidence suggests that promoting the adoption of plant-based diets has few risks but potential benefits for the primary prevention of CKD, as well as for delaying progression in patients with CKD G3–5. These diets might also help to manage and prevent some of the symptoms and metabolic complications of CKD. We suggest that restriction of plant foods as a strategy to prevent hyperkalaemia or undernutrition should be individualized to avoid depriving patients with CKD of these potential beneficial effects of plant-based diets. However, research is needed to address knowledge gaps, particularly regarding the relevance and extent of diet-induced hyperkalaemia in patients undergoing dialysis.

The kidneys have a key role in nutritional homeostasis. In healthy individuals, sodium, potassium and phosphate body content and serum levels are tightly regulated by processes involving the kidneys[1,2]. The kidneys also regulate the amino acid pool via the synthesis, degradation, filtration and reabsorption of dietary amino acids; they are the sole means of excretion of nitrogenous waste[3,4]; they metabolize glucose and release glucose via gluconeogenesis[4,5]; and together with the lungs, they regulate acid–base status[6]. In addition, the kidneys clear low-molecular-weight proteins, which constitute a small fraction of total proteins, but have important roles in physiology, nutrient homeostasis and muscle growth. For example, immunoglobulin light chains and peptide hormones, including insulin, growth hormone and leptin, are cleared by the kidneys[7,8]. The kidneys also activate vitamin D3 by hydroxylation of calcidiol to calcitriol[9].

As loss of kidney function leads to disruption of nutrient homeostasis, patients with chronic kidney disease (CKD) are often advised to change their diet. Dietitians and nephrologists recommend that these patients restrict their intake of phosphorus, potassium, sodium and fluid, either pre-emptively or in response to clinical or laboratory findings. In addition, they emphasize the importance of tailoring protein intake according to CKD stage and type of kidney replacement therapy (KRT), while still ensuring sufficient energy intake[10–12]. Adherence to these recommendations seems prudent and may be necessary. However, without appropriate dietary counselling, such restrictions can result in frustration and lack of autonomy. In combination with societal secular trends (that is, high consumption of meat, processed foods and fast food), dietary restrictions for patients with CKD may result in a diet that lacks variety and has a low intake of fruits and vegetables[13–17].

Emerging evidence suggests that a focus on the quality and diversity of the diet, particularly with liberal consumption of plant foods, may be relevant for the prevention and management of CKD. Here, we evaluate the strength and consistency of this evidence and discuss

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Key points

- The idea that animal protein has 'high biological value' is not relevant in the context of a mixed diet and is not an a priori reason to consider plant protein inferior to animal protein for people with or without chronic kidney disease (CKD).
- Plants are the only dietary source of fibre, which shifts the gut microbiota profile towards increased production of anti-inflammatory compounds and reduced production of uraemic toxins.
- Plant fats, particularly olive oil, are anti-inflammatory and anti-atherogenic.
- Plant-based diets have low net endogenous acid load, which could mitigate metabolic acidosis in patients with CKD and potentially slow the progression of kidney disease.
- Plant phosphorus is bound to phytate and is less bioavailable than animal phosphorus; consequently, many plant-based foods have a favourable protein to phosphorus ratio.
- Restriction of plant foods as a strategy to prevent hyperkalaemia deprives patients with CKD of the potential beneficial effects of these foods; plants with low potassium content provide choice for those who need to restrict their potassium intake.

Vegan diet
A diet that excludes meat, fish, seafood, eggs and dairy.

Vegetarian diets
Diets that exclude meat, fish and seafood, but not eggs or dairy.

Dietary Approaches to Stop Hypertension
(DASH). A diet that was designed to help treat or prevent hypertension. This diet encourages reduced sodium consumption and increased intake of potassium, calcium and magnesium through the high consumption of fruit, vegetables, legumes and nuts and low consumption of meat, fish, seafood, eggs and dairy.

the possible benefits and risks of plant-based diets in patients with CKD, as well as implementation strategies and knowledge gaps. Whenever possible, we differentiate evidence regarding the use of plant-based diets in primary CKD prevention (public health initiatives) from evidence in patients with CKD who are not on dialysis and in patients on dialysis. Evidence for potential risks and benefits of plant-based diets in patients with functioning kidney transplants is indirect; for the most part, we suggest applying information from studies in patients with CKD who do not require dialysis. We consider animal welfare issues and the environmental impact of plant-based diets to be beyond the scope of this review.

Definition of a plant-based diet

In this Review, we define plant-based diets as those that emphasize the consumption of plant foods (fruit, vegetables, nuts, seeds, oils, whole grains, legumes and beans) and may or may not include small or moderate amounts of meat, fish, seafood, eggs and dairy. A vegan diet is plant-based, as are many vegetarian diets. Other examples of dietary patterns that align with the concept of plant-based diets are the Dietary Approaches to Stop Hypertension (DASH) diet, the Mediterranean diet, the Okinawan diet and the healthy-eating diet. We do not discuss weight-control diets, crash diets, detox diets or belief-based diets, although some of these diets may contain predominantly plant-based foods. As no definition of a plant-based diet is widely accepted[18], it is not currently possible to accurately define how much plant and how little meat a diet must contain in order to be plant-based. This lack of a standard definition limits the practical implementation of plant-based diets (discussed further below).

As animal foods have no fibre, high-fibre diets must contain plant foods, but some plants are higher in fibre than others. It is therefore possible to achieve a high-fibre diet that does not meet our criteria of a plant-based diet, and some plant-based diets might not be high-fibre, particularly if they are rich in highly processed foods. In the nephrology literature, a low-protein diet is widely understood to supply a protein intake of 0.6–0.8 g/kg per day, which is achievable in the context of any of the diets mentioned above.

We consider a good- or high-quality diet to be varied, relatively low in processed foods and rich in fruit and vegetables. These criteria are also achievable in the context of all of the diets discussed above, including omnivorous diets. However, not all plant-based diets are of good or high quality; a higher intake of less healthy plant foods, such as potatoes and added sugars, has been associated with a higher risk of cardiometabolic disease[19,20]. The concept of a high-quality diet must be distinguished from the concept of protein quality, which is discussed further below.

Plant proteins

Some guideline recommendations for patients with CKD suggest that at least half of their daily protein intake should come from animal sources given their 'high biological value'[10–12]. The aim of these statements may be to ensure that essential amino acids are not limiting if dietary protein levels are reduced. However, the biological value of a protein source is an outdated parameter that quantifies the proportion of the nitrogen that, after digestion, is absorbed and retained in the body[21]. Biological value is typically measured in rats on a single-food diet, sometimes after starvation[21]; however, essential amino acids are species-specific and differ between humans and rats. In humans, the biological value of a protein source has been shown to correlate with the completeness of essential amino acids in the protein source[22], leading to conflation of the two concepts. The term 'protein quality' appears to be variably applied to both biological value and completeness of essential amino acids. The idea of scoring a protein source on either its ability to be integrated into other proteins, or its amino acid composition, is irrelevant to most human diets in which mixtures of foods are eaten, usually at each meal. The requirement for essential amino acids decreases with increasing overall nitrogen intake[23], which further diminishes the usefulness of the concept of the 'completeness' of the essential amino acid profile of a particular dietary source. Different foods are better or worse sources of individual essential amino acids, but because of complementarity, few natural diets provide insufficient amounts of essential amino acids,

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Mediterranean diet
A traditional diet from countries surrounding the Mediterranean sea that emphasizes large numbers of servings of fruit, vegetables, legumes, nuts, olive oil and fish, and low numbers of servings of meat, seafood, eggs, dairy and processed food (including bread and pastries).

Okinawan diet
A traditional diet from the island of Okinawa in Japan, which has a population with exceptional longevity. This diet is low in calories and fat and high in carbohydrates. It emphasizes vegetables and soy products alongside occasional, and small, amounts of noodles, rice, pork and fish.

Healthy eating diet
A diet that exemplifies the US recommended dietary targets 2015–2020. This diet emphasizes fruits, vegetables, whole grains and fat-free or low-fat milk and milk products. It includes lean meats, poultry, fish, beans, eggs and nuts. It is low in saturated fats, trans fats, cholesterol, salt (sodium) and added sugars, and stays within daily calorie needs.

Essential amino acids
Amino acids that cannot be synthesized by an organism from other nitrogen sources.

except in infants and pre-school children[23]. Although plant and animal proteins differ in their amino acid profiles, digestibility and availability[24], these differences do not seem to be clinically relevant for the general population in the context of a varied and sufficient diet[25–28]. We were unable to identify any outcome-based studies in patients with CKD to support recommendations for the inclusion of 'high biological value' foods in the diet.

Various observational studies have evaluated sources of dietary protein and the risk of developing CKD. A higher intake of vegetable protein was associated with a lower prevalence of CKD in patients with type 2 diabetes mellitus[29] and a lower risk of developing CKD in the general population[30]. In the latter study, the risk associations with protein intake differed according to food group; those who consumed more protein from red and processed meats were at an increased risk of developing CKD, whereas CKD risk was lower among those who had a higher consumption of nuts and legumes. Substituting one serving of red meat in the diet with one serving of legumes was estimated to reduce the risk of incident CKD by 31% (HR 0.69; 95% CI 0.57–0.83)[30]. Furthermore, among National Health and Nutrition Examination Survey participants with CKD who were not on dialysis, diets with a higher proportion of protein from plant sources were associated with lower mortality[31]. It is plausible that plant protein offers advantages over animal protein in patients with CKD[32], but this hypothesis has not been extensively investigated. Studies in obese rats showed that consumption of soya protein can reduce the expression of renin–angiotensin-system- and angiogenesis-related genes, resulting in lower levels of angiotensin I and II in adipose tissue[33]. Whether similar effects are observed in the kidney is not known. However, animal studies have found that higher consumption of plant protein retards the development and progression of CKD[34]. Early mechanistic studies suggested that differences in amino acid intake, particularly of glycine and alanine, which are both abundant in plant proteins, have different effects on kidney haemodynamics[35–38], suggesting a potential mechanism for these beneficial effects. In a seminal study in which ten healthy volunteers consumed equivalent amounts of animal or plant protein for 3 weeks, consumption of plant protein resulted in reduced renal plasma flow, increased renal vascular resistance and lower fractional clearance of albumin or IgG[37].

Plant carbohydrates

Plant-based diets are rich in carbohydrates, both monosaccharides (glucose, fructose) and polysaccharides (starch and fibre)[39]. Starch is an important source of energy in modern diets, whereas dietary fibre is composed of non-digestible and non-absorbable carbohydrate polymers that influence the diversity of the gut microbiota and the synthesis of metabolites[40]. In the general population, increased fibre consumption has been consistently associated with lower levels of blood lipids, particularly total cholesterol, and body weight reduction[41,42] (TABLE 1).

Dietary fibre increases faecal bacterial mass and nitrogen excretion in humans[43]. A meta-analysis of 14 trials of controlled feeding found that fibre supplementation consistently reduced serum urea and creatinine levels[44]. In observational studies of the general population, higher consumption of fibre was associated with higher estimated glomerular filtration rate (eGFR) and a lower risk of developing CKD[45–48].

In patients with CKD, high fibre intake has been associated with a lower risk of inflammation and mortality, with an effect size that may be greater than that in people without CKD[46,49]. In patients undergoing dialysis, low fibre intake was associated with higher concentrations of inflammatory biomarkers[50–52], myocardial hypertrophy and arterial stiffness[51,52], and a higher risk of cardiovascular events and death[52,53]. Among kidney transplant recipients, those with the highest tertile of fibre intake had the lowest incidence of metabolic syndrome in the first year after kidney transplantation[54].

A number of interventional studies have explored the potential benefits of fibre consumption in people with CKD. In a small randomized controlled trial (RCT) in patients on haemodialysis, increased dietary fibre intake for 6 weeks resulted in a significant reduction in the plasma level of the uraemic toxin indoxyl sulfate and a non-significant reduction in the level of another uraemic toxin, *p*-cresol sulfate[55]. Another study in patients on haemodialysis showed that compared with placebo, 6 weeks of dietary fermentable fibre supplementation improved lipid profile and oxidative status and decreased systemic inflammation[56]. Fibre supplementation studies in patients with CKD G3–5 (REF.[57]) have reported similar reductions in plasma *p*-cresol concentration, as well as improved stool frequency[57,58].

The gut microbiota may mediate some of the salutary effects of a diet rich in fibre (FIG. 1). As some microbial species are only able to utilize specific substrates derived from either dietary protein or fibre to expand their populations, the ratio of protein to fibre intake modulates the fermentation processes mediated by the gut microbiota. Saccharolytic bacteria (also called symbiotic bacteria) ferment dietary fibre, which releases short-chain fatty acids (e.g. acetate, butyrate or propionate) that enhance gut barrier integrity and have anti-inflammatory and immunomodulatory effects[46,49]. By contrast, proteolytic bacteria ferment dietary protein, which leads to the production of several uraemic toxins (e.g. indoxyl sulfate, indole-3 acetic acid, *p*-cresyl sulfate and trimethylamine *N*-oxide) that are absorbed into the bloodstream and removed by the kidneys in people with normal glomerular filtration rate (GFR)[59–61], but accumulate in people with low GFR and have been shown to exert toxic effects in experimental systems[62]. A large number of putative uraemic toxins exist, but how their known specific toxicities translate into the fatigue, anorexia, nausea, itching, myopathy, neuropathy, serositis and encephalopathy that are collectively recognized clinically as the uremic syndrome is not well understood. Furthermore, some uraemic toxins may cause more rapid progression of CKD. For example, indoxyl sulfate increases the expression of fibrogenic genes, such as transforming growth factor beta, that increase fibrogenesis, a key pathway in the progressive loss of GFR[63].

Table 1 | **Potential beneficial effects of plant nutrients in patients with CKD**

Plant nutrients	Characteristics	Potential benefits	Refs
Proteins	Plant proteins have lower bioavailability than animal proteins Plant-based diets can be low in protein Plant proteins are rich in glycine and alanine	Favourable effects on glomerular haemodynamics and proteinuria	35–38
Carbohydrates	Plant-based diets are rich in fibre (non-absorbable carbohydrate polymers) and can be low in refined carbohydrates Plant-based diets supply absorbable complex carbohydrates, such as starch, that are an important energy source	Increased stool viscosity, which promotes stool motility and delays the absorption of potassium, glucose and free-fatty acids and so results in lower insulin release and higher fat oxidation, improving blood lipid levels and potentially enabling long-term weight loss	41
		Increased faecal bacterial mass and nitrogen excretion	43
		Favourable shift in gut bacteria from a proteolytic profile to a saccharolytic profile resulting in increased production of short-chain fatty acids and reduced production of uraemic toxins, bacterial translocation and inflammation	56–58
Fats	Plant-based diets are rich in essential monounsaturated and polyunsaturated fatty acids and low in saturated fatty acids	Improved blood lipid profile	66
		Reduction in body weight mainly due to reduced intake of saturated fat	211
		Anti-inflammatory, antioxidant and vasculoprotective properties	70,71
Anions and cations	Plant-based diets have a lower non-volatile acid load than animal-based diets	Improved control of metabolic acidosis	78,79
Phosphorus	Absorption of phosphate from plant sources is less efficient than from animal sources	Improved control of CKD-mineral bone disorders	103,104
Potassium	Potassium intake from plants contributes to promotion of alkalinity through the exchange of hydrogen ions in the distal part of the nephron	Improved control of metabolic acidosis	143
Sodium	Plant-based diets are generally low in sodium	Improved blood pressure control	173

CKD, chronic kidney disease.

In patients with CKD who are not on dialysis, a direct relationship exists between the dietary protein to fibre ratio and the levels of *p*-cresyl sulfate and indoxyl sulfates[64]. In an observational study of elderly men (aged 70–71 years) with CKD, a diet with a lower protein to fibre ratio was associated with a lower incidence of cardiovascular events[65]. The researchers attributed this finding to the effect of this pattern of diet on intermediate risk factors for cardiovascular disease (CVD), such as lowering of blood pressure, waist circumference, body weight, fasting blood glucose and high-density lipoprotein cholesterol. Short-term trials of supplementary fibre prebiotics in patients with CKD have generally shown a reduction in the production of uraemic toxins, decreases in systemic inflammation and serum urea levels, and increases in stool and urinary nitrogen excretion (Supplementary Table 1). The long-term effects of fibre prebiotics in patients with CKD warrant investigation.

Despite the evidence for beneficial effects of fibre consumption, studies suggest that the majority of patients with CKD G3–5 or on dialysis consume amounts of dietary fibre that are well below the recommendations for the general population[14–17]. Moreover, none of the current nutritional guidelines for patients with CKD discuss fibre.

Plant fats

The dietary fat profile of plant foods is rich in essential monounsaturated and polyunsaturated fatty acids (PUFAs). As plant foods replace sources of saturated fat, plant-based diets tend to lower both cholesterol levels and body weight in the general population[66,67]. Unsaturation of the fatty acid backbone results in increased 3D volume. As fatty acids are constituents of phospholipid membranes, a diet rich in polyunsaturated fat leads to more voluminous, fluid and spacious cell membranes, favouring exchanges between the intracellular and extracellular compartments and reducing the risk of atherosclerosis[68]. Furthermore, the inflammatory cascade starts with the synthesis of eicosanoids, which are pro-inflammatory signalling molecules derived from PUFAs. Eicosanoids that are derived from fish and plant fatty acids (omega 3 (n-3) PUFAs) are less pro-inflammatory than those derived from meat fatty acids (n-6 PUFAs, for example, arachidonic acid); thus, the relative amounts of these fatty acids in the diet affect the balance of the inflammatory cascade[69].

The main sources of plant fat are vegetable oils, margarines and nuts; these foods contain bioactive PUFAs that have beneficial effects on health (Supplementary Table 2). For example, olive oil — an important component of

Mediterranean diets — contains oleic acid, which is rich in polyphenols and vitamin E and has anti-inflammatory, antioxidant and vasculoprotective properties. The consumption of olive oil in the general population is associated with a lower risk of death, CVD morbidity and stroke[70,71]. Notably, no studies have evaluated the potential benefits of increased olive oil consumption in patients with CKD.

The relationship between dietary plant-fat quality and CKD has been assessed in observational studies. In a cross-sectional analysis of patients with diabetes, a lower intake of PUFAs from plants (that is, linolenic and linoleic acids, which are present in vegetable oils and margarines) was associated with CKD[72]. A serum fatty acid pattern reflecting low linoleic acid intake and high saturated fat intake was associated with metabolic syndrome, insulin resistance and inflammation in two independent surveys of elderly individuals (70 years) with CKD G3–4 who were not on dialysis[73]. Among patients on haemodialysis, the linoleic acid level as a proportion of total plasma fatty acids was inversely associated with markers of inflammation and risk of death[74]. As nutrients are not consumed in isolation, this observational evidence cannot adequately disentangle whether the benefits observed reflect the result of increased plant-fat intake, reduced meat-fat intake or both. Nonetheless, multiple studies suggest that excess intake of saturated fat and animal fat might increase the risk of CKD[75–77]. To our knowledge, no interventional studies have investigated the potential benefits of increased plant-fat intake or substitution of meat fats for plant fats in patients with CKD.

Plant anions and cations

As mentioned above, acid–base homeostasis is a vital function of living organisms that is regulated by the kidney. Many biochemical reactions of metabolism either produce or consume acids and bases, and under normal physiological conditions, the net endogenous acid production (NEAP) is modulated primarily by the diet. A diet with more acid increases NEAP and acid load, contributing to increased expression of aldosterone, angiotensin II and endothelin. In animal studies, activation of these pathways has been shown to accelerate

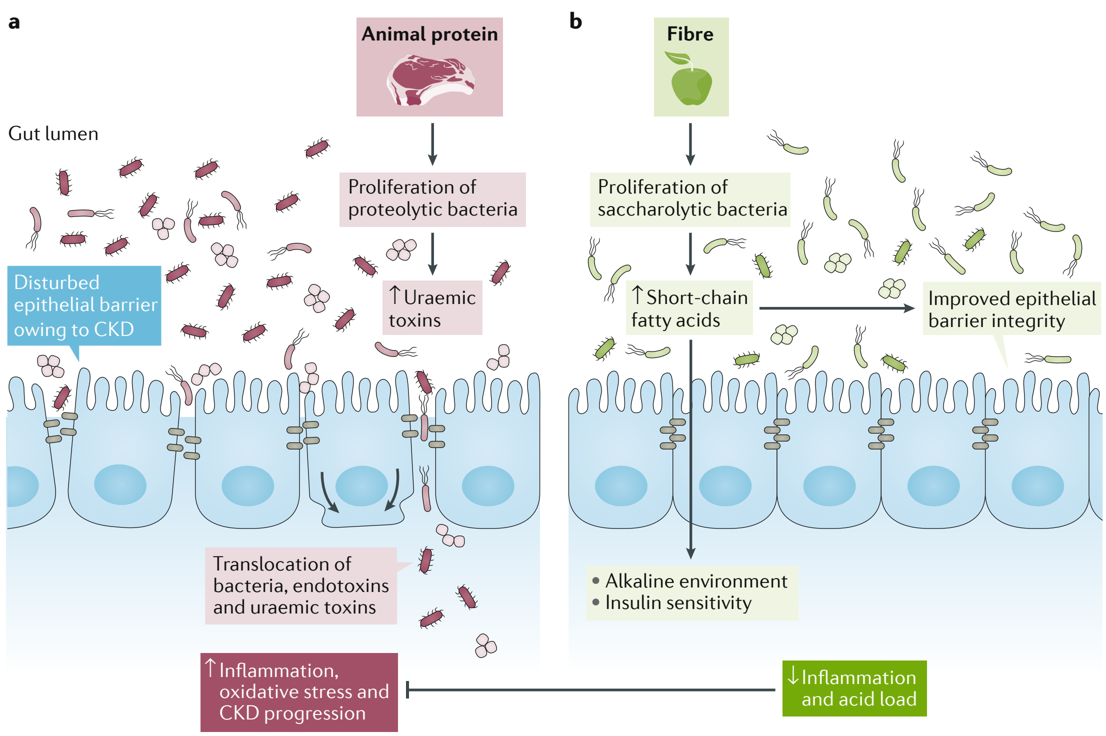

Fig. 1 | **The effects of animal proteins and fibre on the gut microbiota and uraemic milieu in chronic kidney disease.** **a** | A diet that is rich in animal proteins leads to the expansion of populations of proteolytic bacteria that ferment dietary protein and generate uraemic toxins such as indoxyl sulfate, indole-3 acetic acid, *p*-cresyl sulfate and trimethylamine *N*-oxide. These toxins are normally cleared by the kidneys but accumulate in the blood of patients with chronic kidney disease (CKD). The uraemic milieu of patients with advanced CKD leads to changes in the colonic environment that result in microbial dysbiosis and disturbances in the intestinal barrier. Intestinal excretion of nitrogen compounds (such as urea or uric acid) increases as glomerular filtration rate and tubular elimination declines. Furthermore, CKD-induced oedema of the intestinal mucosa alters its permeability, enabling translocation of bacteria and endotoxins through the intestinal barrier, which in turn stimulates monocytes and leads to increased synthesis of inflammatory cytokines. The nitrogen-rich environment further promotes the growth of proteolytic bacteria, which outcompete symbiotic saccharolytic bacteria. **b** | Consumption of fibre promotes the growth of saccharolytic bacteria, which compete with proteolytic bacteria and therefore mitigate the harmful effects of animal protein intake. In addition, fibre metabolism increases the generation of short-chain fatty acids in the gut, which promote gut-barrier integrity. Short-chain fatty acids can translocate into the blood and have been associated with improved insulin sensitivity and a more alkaline environment[59–61,232].

kidney damage and eGFR decline, whereas provision of dietary alkali reverses these processes[78–80]. Plant-based diets, compared with animal-based diets, have a lower non-volatile acid load, as they are richer in organic anions than cations. The effects of increased fibre intake on the gut microbiota (that is, increased generation of short-chain fatty acids (alkali) and reduced generation of uraemic toxins) also contribute to an alkaline environment[81–85] (FIG. 2). In epidemiological studies, NEAP is usually estimated from equations developed in healthy individuals who utilize both dietary constituents and excretion of acids into urine.

In the general population, a higher dietary acid load or NEAP has been consistently associated with the presence of albuminuria and CKD in cross-sectional studies[86,87] and a higher risk of developing CKD[88–90]. As GFR decreases, the ability of the kidney to excrete and neutralize acid is significantly and progressively reduced; therefore, metabolic acidosis is a hallmark of patients with advanced CKD and those on dialysis. In line with the role of metabolic acidosis in accelerating kidney function decline, observational studies in patients with CKD who are not on dialysis have generally shown that both a high dietary acid load and high NEAP are associated with a faster decline in eGFR and increased risk of KRT[91–94]. A higher acid load was also found to be accompanied by increased serum phosphorus concentration and increased phosphorus excretion in patients with CKD, perhaps representing an adaptation to help maintain acid–base balance[95].

Quantifying the organic acid content of fruits and vegetables is challenging as it varies within species and with growing conditions, ripeness and storage. The main anions in plant-based diets are citrate and malate, which are metabolized to bicarbonate and contribute to alkalization. As a general rule, the alkalinizing potential of fruits and vegetables is proportional to their potassium content, as anions are bound by potassium, forming potassium salts. However, some anions in plants, such as oxalate, which is usually present in the form of potassium oxalate and is found at high levels in rhubarb and spinach, cannot be metabolized by humans, so do not provide any alkali. Oxalic acid present in the food releases H^+ and thus increases acidity[96]. Consumption of oxalate-rich plants is generally discouraged in patients with CKD and in people who are at risk of kidney stones because of the risk of oxalate crystals depositing in the kidney in settings of low urine volume[97].

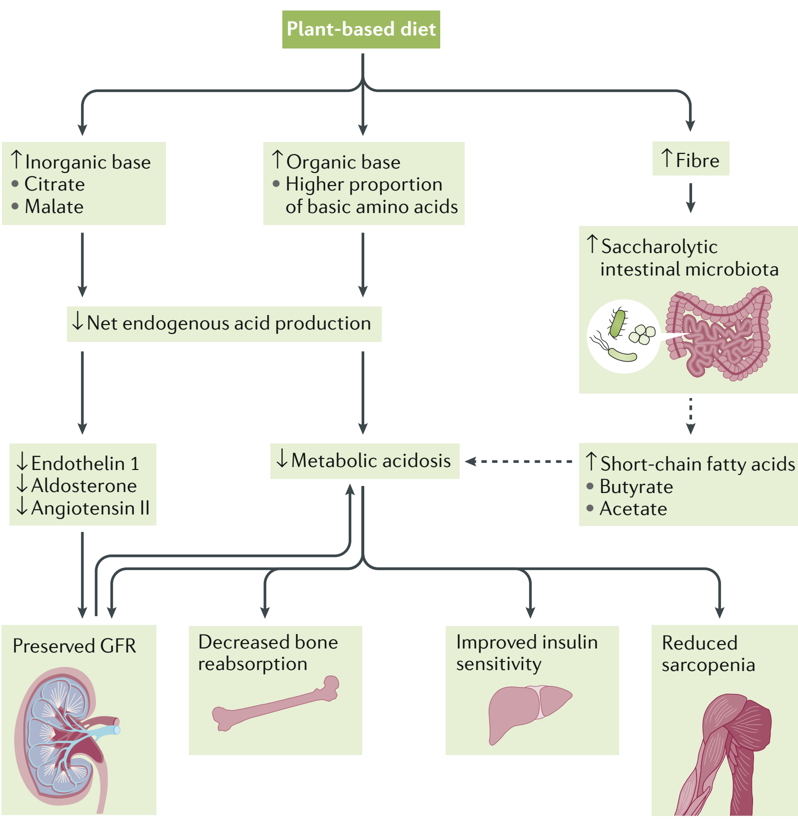

Fig. 2 | **Plant food intake and acid-base homeostasis in people with low glomerular filtration rate.** In people with normal kidney function, high net endogenous acid production and low short-chain amino acid production will not result in metabolic acidosis because the kidney has excess capacity to excrete acid. When glomerular filtration rate (GFR) is low, however, there is a tendency towards metabolic acidosis, which is worsened by high net endogenous acid production and low short-chain fatty acid production. A plant-based diet might mitigate this effect by reducing net endogenous acid production (as a result of increased alkali intake) and enabling increased metabolism of fibre by the microbiota, which results in increased translocation of short-chain fatty acids into the circulation. Improved control of metabolic acidosis has subsequent positive effects on end organ metabolism, including preservation of kidney function and muscle mass[78,79,84]. Dashed arrows represent proposed mechanisms for which limited evidence is available[82–85].

Plant phosphorus

Phosphorus is an essential nutrient that is naturally present as organic phosphate in most foods and is added during industrial processing as the approved food additive inorganic phosphorus. Although 40–60% of phosphate bound to animal protein is absorbed in the gut, the absorption of phosphate bound to plant protein is lower at 20–50%[98]. In plants, organic phosphate is grouped in phytates, which are difficult for humans to digest. Concurrent fibre intake in plant-based diets also slows phosphate absorption. By contrast, inorganic phosphorus added during industrial processing is almost 100% absorbed in a passive paracellular route driven by the luminal concentration gradient[99].

As patients with advanced CKD and on dialysis have difficulty in eliminating excess dietary phosphorus, current guidelines recommend restriction of phosphorus intake to reduce the risk of hyperphosphataemia and associated bone and mineral metabolism disorders[11,100–102]. A few studies have compared the effects of different phosphate sources on serum phosphorus levels and other mineral and bone disorders in people with CKD. Collectively, they demonstrate that consumption of plant foods results in lower phosphorus intake and better control of phosphataemia than consumption of animal foods. In a crossover trial that included nine patients with CKD G3, consumption of plant protein was compared with consumption of animal protein with the same phosphorus content (800 mg per day). Plasma phosphorus was higher after 1 week of the meat diet (mean 3.5 mg/dl before versus 3.7 mg/dl after) compared with 1 week of the plant diet (mean 3.5 mg/dl before versus 3.2 mg/dl after; P for interaction 0.02). The plant diet also resulted in improved circadian phosphataemia control and lower urinary phosphate excretion and serum FGF-23 levels[103]. Similarly, an uncontrolled 4-week study of a plant-based diet in people with mild to advanced CKD was found to be efficacious in lowering urine phosphorus[104]. An observational analysis in a large cohort of patients with CKD G3–5 found that those in the lowest quintile of proportion of protein intake from plant sources had higher urinary phosphate excretion than those in the highest quintile of plant protein intake[105].

Plant potassium

Fruits and vegetables are naturally rich in potassium. The potassium in foods[106,107] and in inorganic salts[108–110] seems to be completely absorbed by the proximal intestinal tract. Net absorption, however, depends on intestinal secretion and faecal volume. Potassium absorption may be influenced by the alkaline load of plant foods, which facilitates intracellular potassium deposition[111,112] and kidney excretion[113]; and by concomitant fibre intake, which increases faecal potassium excretion by increasing stool volume and decreasing transit time[114]. Feeding trials in healthy people suggest that the 24 h urine potassium recovery from animal-based diets is about 80% and that from plant-based diets is about 50–60%[115,116]; however, these studies were limited by the use of single 24 h urine collections[117]. The lower bioavailability of plant potassium might be a disadvantage of plant-based diets if absorption of the potassium ion and its biological activity in the body underlie the potential protective effects of high-potassium diets discussed below. However, many patients with CKD are at risk of hyperkalaemia, and potassium-restricted diets are often prescribed for these patients. In this case, the lower bioavailability of plant potassium might be advantageous in enabling patients to benefit from the other salutary effects of plant-based diets without precipitating hyperkalaemia.

Few studies have evaluated the effect of dietary potassium on kidney outcomes, but the available data tend to suggest beneficial effects of increased dietary potassium intake. We note, however, that these studies measure the overall potassium intake and do not distinguish between potassium from plants and that from animal foods. Prospective observational studies in the general population and in people with CKD G1–2 have shown consistent associations between higher potassium intake (estimated by dietary recall or 24 h urinary potassium excretion) and a lower risk of developing CKD (Supplementary Table 3). Similarly, observational studies have found that high potassium intake or high urinary potassium excretion was associated with a lower risk of all-cause mortality (Supplementary Table 4). As these studies are observational, whether the associations are explained by potassium intake, by other nutrients in high-potassium foods or in a high-potassium dietary pattern, or are confounded by other aspects of socio-economic status, poverty and lifestyle is unknown. A trial of dietary potassium supplementation to control blood pressure and reduce progression of CKD[118] in patients with CKD G3–4 is currently underway.

In patients with CKD G3–5, the associations between dietary potassium and clinical outcomes are less consistent than those in the general population or in patients with less severe kidney disease. Among 3,939 patients with a mean GFR of 45 ml/min/1.73 m^2, higher urinary excretion of potassium was associated with an increased risk of CKD progression[119]. In another cohort study that included 1,821 patients, higher urinary potassium excretion was associated with CKD progression[120]. Finally, a post hoc analysis of the Modification of Diet in Renal Disease study in 812 patients found no association between urinary potassium excretion and risk of KRT after a follow-up of 6 years[121]. A potential limitation of these and other studies of CKD progression is the use of creatinine-based GFR because circulating creatinine levels are influenced by meat intake and muscle mass, which may be reduced in patients with CKD. To our knowledge, only one study has examined the effects of dietary potassium restriction on clinical outcomes: in patients with CKD G3–4 potassium restriction compared with habitual diet led to the stabilization of neuropathy scores and several other nerve-related or general health scores over 24 months[122].

A single study has evaluated the association between dietary potassium and clinical outcomes in patients on haemodialysis. Compared with the lowest quartile of dietary potassium intake (estimated by a food frequency questionnaire), higher quartiles of intake were associated with a progressive increase in risk of 5-year mortality (P for trend = 0.03)[123]. In kidney transplant recipients, high urinary potassium excretion was associated with a lower risk of graft failure[124]. The more scarce and inconsistent outcome associations attributed to dietary potassium in patients with CKD G3–5 and those on dialysis call for caution and warrant further investigation, preferably in the form of intervention trials that differentiate between animal-based and plant-based sources of dietary potassium.

Other plant nutrients

Plant-based diets are generally low in sodium (unless this is added during food preparation) and rich in a variety of phytochemicals, vitamins, antioxidants and minerals (TABLE 2). Consumption of plant foods may therefore be important in preventing micronutrient deficiency (e.g. of magnesium, zinc, vitamin K and vitamin C) in patients with CKD. Supplementation with *N*-acetyl cysteine, a thiol-containing antioxidant that is present in high amounts in some plants including soy, has been shown to improve endothelial function and reduce plasma homocysteine concentration, pulse pressure and risk of cardiovascular events in patients on haemodialysis[125,126].

Plants are rich sources of vitamins with the exception of vitamins B_{12} and D. Studies in patients with CKD (mostly conducted in those on dialysis) have shown that their mean intake of many vitamins is lower than the recommended dietary allowance and that their serum concentrations of some vitamins are lower than in the general population[127,128]. In particular, most patients on dialysis are deficient in vitamin K, and this deficiency has been associated with vascular calcification, bleeding risk and increased risk of cardiovascular disease[129,130]. As the principal dietary source of vitamin K, vitamin K1

Table 2 | **Potential beneficial effects of plant micronutrients in patients with CKD**

Nutrient	Main plant sources	Potential benefits[a]	Refs
Phytochemicals and antioxidants			
N-acetyl cysteine	Soy	Improved endothelial function, lower cardiovascular event risk	125
Flavonoids	Berries, apples, onions, citrus fruits, grapes	Antioxidant, antihypertensive, antidiabetic and anti-inflammatory	212,213
Carotenoids	Peppers, carrots, grape leaves, sweet potatoes, pumpkin, tomatoes	Antioxidant, preservation of kidney function	214
Vitamins			
Vitamin C	Peppers, cherries, chives, guavas, orange juice	Anti-inflammatory, lower cardiovascular morbidity and mortality risk	215
Vitamin K	Spinach raw, kale, Brussels sprouts, broccoli	Reduced vessel calcification, lower cardiovascular risk	129,130
B_{12}	Bread, muesli, pickled cucumber, sauerkraut, seaweed, spinach, mushrooms, kiwi fruit	Lower cardiovascular risk, less rapid CKD progression	216,217
Folate	Leeks, arrowroot, edamame, radishes, peppers, spinach	Lower cardiovascular risk	218
Minerals			
Iron	Beans, spinach, seaweed, parsley, chives, mushrooms, peppers, tomatoes, raisins, cashews, oatmeal	Prevention and treatment of iron-deficiency anaemia, reduction in inflammation	219
Magnesium	Seaweed, chives, parsley, tomatoes, peppers, radishes, leeks	Reduced vessel calcification, lower cardiovascular disease risk and bone-mineral disorders, blood pressure control	220,221
Zinc	Wholegrain breads, cereals, oats, brown rice, nuts, seeds, legumes, tofu, soy, fortified cereals	Antioxidant, less rapid CKD progression, lower erythropoietin resistance	222

CKD, chronic kidney disease. [a]Most of the available evidence is from observational studies.

(phylloquinone, PK) is mainly present in green vegetables, dietary restrictions that result in reduced consumption of plant foods are likely to contribute to this deficiency.

Potential benefits of plant-based diets

The potential role of a healthy diet in improving health or managing disease is far more complex than delivering a combination of nutrients, and dietary recommendations for CVD and diabetes are shifting from a focus on single nutrients to a focus on whole foods and dietary patterns. The latter approach might more easily translate into recommendations that patients can follow, but precision is lost because of the broad variety of food sources. Here, we evaluate whether plant foods or plant-based diets might affect the incidence and progression of CKD; however, a number of caveats apply. First, most of the available studies are observational analyses in which causality cannot be inferred and confounding by socio-economic and lifestyle factors is probable. Second, analysis of dietary patterns is generally population-based, that is, low and high adherence to a dietary pattern are compared within a specific cohort. The actual food content of a diet is unlikely to be comparable between populations in different countries or regions; for example, high adherence to a Mediterranean diet in the USA might result in an average consumption of olive oil that is similar to low adherence to a Mediterranean diet in southern Europe. Third, as the available studies evaluate dietary patterns rather than prescribed diets, serving sizes and food choices vary, making it difficult to estimate average energy and single-nutrient intakes.

A 2019 systematic review and meta-analysis that included data from 55 large cohort studies with a total of >4 million participants, reported that the magnitude of association between red and processed meat consumption and all-cause mortality, cardiovascular disease or type 2 diabetes mellitus was very small and the evidence was of low certainty[131]. Based on these findings, the Nutritional Recommendations Consortium[132] recommended that adults continue their current meat consumption habits owing to “low certainty” of the evidence for potential harmful effects and the difficulty in altering the habits and preferences of meat eaters. The guideline panel did not consider the environmental impacts of red meat consumption. This recommendation, which has been criticized and is controversial[133,134], highlights the limitations of evidence in this area, serving as a reminder of the importance of incorporating patients’ choices and preferences in the face of uncertainty.

Plant foods. In the general population, a higher frequency of consumption of fruits and vegetables was associated with a lower incidence of CKD and lower acid load[135] (TABLE 3). Among participants of the ONTARGET trial, increasing fruit or vegetable intake to >14 servings per week was estimated to have the potential to reduce the risk of incident CKD and CKD progression by 4.5% and 2%, respectively[136,137]. Among women with a history of gestational diabetes[138], a higher consumption of nuts was associated with lower odds of albuminuria, but not with eGFR values. However, other observational studies in the general population failed to identify associations between the consumption of fruits and vegetables or whole grains and the rate of eGFR decline[139,140]. In the absence of interventional data, it is plausible that a dietary pattern of increased plant foods and reduced animal foods rather than consumption of individual plant foods explains salutary outcomes. Alternatively, the lack of associations in some studies might be explained by the inclusion of populations with a low and narrow range of plant-food intake.

Four well-designed RCTs in patients with CKD who were not on dialysis have demonstrated that alkali-rich plant foods provide a comparable benefit to oral sodium bicarbonate by improving metabolic acidosis and reducing GFR decline[141–144]. The largest of these studies involved 108 patients with CKD G3 and macroalbuminuria who were randomly assigned to either 3 years of usual care or interventions that were designed to reduce dietary acid by 50% using either sodium bicarbonate or alkali-rich fruits (apples, apricots, oranges, peaches, pears, raisins and strawberries) and vegetables (carrots, cauliflower, eggplant, lettuce, potatoes, spinach, tomatoes and zucchini)[143]. The acid-reducing interventions resulted in similar reductions in urine excretion of angiotensinogen and greater preservation of eGFR to those obtained with usual care, and these findings were confirmed in a 5-year extension study[144]. In addition, the group of participants who were assigned to a plant-based diet had lower systolic blood pressure and better body weight control, improved lipid profile and higher serum levels of vitamin K1 than those who were assigned to bicarbonate therapy or usual care[144]. This finding raises questions about plausible causality behind these associations and illustrates the relevance of considering plant-based diets as a pattern in research and practice.

In people undergoing dialysis, two studies that evaluated the effect of soy consumption reported reductions in inflammatory markers[145] and lipoprotein (*a*) levels[146], respectively. Similarly, in kidney transplant recipients, a diet supplemented with soy reduced the low-density lipoprotein cholesterol concentration[147]. There is a paucity of studies evaluating the potential beneficial effects of other plant-based foods such as seeds, oils, whole grains, legumes and beans in patients with CKD. Such studies should be a priority for future research.

Plant-food-rich dietary patterns. A number of studies have evaluated the relationship between established dietary pattern scores or diet patterns that are rich in plant foods and risk of CKD (TABLE 4). In the general population and in cohorts of patients with CKD G3–5, studies have shown that adherence to a Mediterranean diet (reviewed in Chaveau et al.[148]), a DASH diet or patterns of diet that are consistent with vegetarian, plant-based or healthy plant-based diets show consistent associations with a lower CKD prevalence, a lower risk of incident CKD and slower progression to kidney failure[149,150]. However, few interventional studies of these diets have been conducted. A small 90-day RCT of a Mediterranean diet in 40 patients with CKD G2 (REF.[151]) reported improvements in lipid profile and inflammation; and short-term pilot trials in patients with CKD G3–4 found that DASH pattern diets were feasible and well tolerated[152].

As vegetarian and vegan diets generally offer protein quantities that are consistent with low-protein diets (that is, 0.6–0.8 g/kg/day) and very-low-protein diets (that is, 0.3 g/kg/day), respectively, they have been evaluated as low-protein dietary interventions to reduce progression to kidney failure in clinical trials[153–157]. In patients

Table 3 | **Studies investigating the association between plant foods and CKD outcomes**

Plant foods (assessment)	Population (n)[a]	Follow-up (years)	Outcomes	Results	Ref.
Non-fermented and fermented fruit and vegetable diet (FFQ)	General (9,229)	8.2 (mean)	Incident CKD; incident proteinuria; NEAP	Lower risk of CKD and proteinuria with higher consumption of non-fermented fruits and vegetables Lower risk of proteinuria but not CKD, with higher consumption of fermented fruits and vegetables Higher NEAP among participants with the lowest fruit and vegetable consumption	135
Whole grain, vegetable and fruit intake (FFQ)	General (3,787)	15 (median)	Annual change in eGFR decline and ACR	No association between intake of whole grains, fruit and/or vegetables and decline in eGFR	139
Nut consumption (FFQ)	Women with a history of gestational DM (607)	NA (cross-sectional study)	eGFR, UACR, microalbuminuria	Higher nut consumption associated with lower UACR and microalbuminuria No association of nut consumption with eGFR	138
Fruit and vegetable intake (FFQ)	Haemodialysis (8,078)	2.7 (median)	Death and causes of death	Higher tertile of fruit and vegetable consumption was associated with lower incidence of all-cause and non-cardiovascular death	162

ACR, albumin to creatinine ratio, CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FFQ, food frequency questionnaire; NEAP, net endogenous acid production; UACR, urinary albumin to creatinine ratio. [a]All studies were in adult populations.

Table 4 | **Studies investigating the association between plant-based dietary patterns and CKD outcomes**

Dietary pattern (assessment)	Population (*n*)	Follow-up (years)	Outcomes	Results	Ref.
General population					
Vegan, ovo-lacto-vegetarian and omnivore diets (FFQ)	5,113	NA (cross-sectional study)	Prevalence of CKD	People who adhered to vegetarian, vegan and ovo-lacto-vegetarian diets were less likely to have CKD	223
DASH dietary pattern (FFQ)	1,410	6.1 (median)	Incident CKD	Higher adherence to a DASH diet was associated with lower risk of incident CKD	224
Lacto-vegetarian dietary patterns (FFQ)	1,630	6.1 (median)	Incident CKD	Higher adherence to a lacto-vegetarian diet was associated with lower risk of incident CKD	225
Four plant-based dietary patterns: overall, healthy, pro-vegetarian and less healthy (FFQ)	14,686	24.0 (median)	Incident CKD; kidney function decline	Higher adherence to the healthy and pro-vegetarian diets were associated with lower CKD risk Adherence to the less healthy diet was associated with high CKD risk Adherence to the overall and healthy diets were associated with slower eGFR decline	226
Adapted healthy eating index (FFQ)	12,155	24.0 (median)	Incident CKD	Higher adherence to healthy dietary patterns was associated with lower risk of incident CKD	227
Patients with CKD G3–5					
Plant-based generated dietary pattern (FFQ)	3,972	6.0 (median)	All-cause mortality and kidney failure	Higher adherence to a plant-based diet was associated with lower risk of mortality No association between diet and risk of kidney failure	228
DASH pattern (24-h dietary recall)	1,110	7.8 (median)	Incident kidney failure	Lower adherence to a DASH diet was associated with a greater risk of kidney failure; this association was stronger in patients with diabetes and in non-Hispanic black patients	229
Patients on haemodialysis					
Mediterranean and DASH dietary patterns (FFQ)	8,110	2.7 (median)	All-cause and cardiovascular mortality	No association between dietary patterns and mortality	163
Plant-based generated dietary pattern (FFQ)	8,110	2.7 (median)	All-cause and cardiovascular mortality	No association between plant-based diets and mortality	164
Kidney transplant recipients					
Mediterranean, fats and sugar and whole-grain dietary patterns (FFQ)	160	1 (exact duration)	Metabolic syndrome	Mediterranean pattern was associated with a lower risk of metabolic syndrome components Fats and sugar pattern was associated with higher risk of metabolic syndrome No association between whole-grain dietary patterns and metabolic syndrome	160
DASH diet (FFQ)	632	5.3 (median)	Renal function decline and all-cause mortality	DASH diet was associated with a lower risk of renal function decline and all-cause mortality	161

The table does not include studies of Mediterranean dietary patterns that are reviewed elsewhere[148]. CKD, chronic kidney disease; DASH, Dietary Approaches to Stop Hypertension; eGFR, estimated glomerular filtration rate; FFQ, Food Frequency Questionnaire.

with CKD G3–5, low-protein and very-low-protein plant-based diets shifted the gut microbiota to a more favourable profile and lowered serum concentrations of indoxyl sulfate and *p*-cresyl sulfate[158,159]. A short-term (8-week) randomized crossover trial reported that patients with CKD who followed a vegetarian low-protein diet exhibited similar levels of albumin, protein catabolic rate, lipids and calcium to those who followed an animal-based low-protein diet[157].

Two observational studies have evaluated the effects of dietary pattern in stable kidney transplant recipients. The first study, which included 160 adult kidney transplant recipients, reported that adherence to a Mediterranean diet (the highest versus the lowest tertile of Mediterranean dietary pattern score) was associated with a lower incidence of metabolic syndrome in the first year after transplantation (OR 0.52; 95% CI 0.21–1.24)[160]. A subsequent study that included 632 kidney transplant recipients reported that those in the highest tertile of adherence to a DASH dietary pattern had a 57% lower risk of kidney function decline (HR 0.57; 95% CI 0.33–0.96) and a 52% lower risk of death (HR 0.52; 95% CI 0.32–0.83) than those in the lowest tertile of adherence during a median follow-up of 5.3 years[161].

Using food frequency questionnaires, the DIET-HD study showed that just 4% of 8,000 mostly European patients on prevalent haemodialysis consumed four or more daily servings of fruit and vegetables, which is the recommended intake for the general population[162]. Compared with the lowest tertile of servings per week (a median of 2), higher fruit and vegetable consumption was associated with a lower risk of death[162]. However, in the same cohort, no associations were found between adherence to a Mediterranean diet, DASH diet[163] or dietary patterns suggestive of a plant-based or Western diet[164] and risk of death. Taken together, these findings might suggest that it is the consumption of fruits and vegetables rather than the overall dietary pattern that is beneficial. Moreover, the effect of dietary patterns might differ between patients who do and do not require dialysis because of differences in age, comorbidity or frailty, or because factors that have enabled these patients to survive long term with CKD might explain the effects of dietary patterns. An excellent study design and data analysis notwithstanding, using the same predetermined questions on food consumption or cooking methods in countries as culturally diverse as Sweden, Greece and Argentina might have introduced error. In any case, the observations need to be confirmed or refuted in an independent cohort.

Potential risks of plant-based diets

Traditionally, the main reasons for discouraging the adoption of plant-based diets by patients on maintenance dialysis are concerns regarding the risks of undernutrition and hyperkalaemia. Here, we review the evidence relating to these concerns.

Undernutrition. General population studies that compared different plant-based and animal-based diets have convincingly shown that the risk of nutritional deficiencies is low if plant sources are diverse. Even strict vegetarians and vegans exceeded their minimum requirements for protein and had serum amino acid levels that exceeded the lower limit of reference ranges[165–167]. The achieved plasma amino acid profile of plant-based diets and animal-based diets is essentially the same, with the exception of a lower lysine to arginine ratio, of no known harm, with a plant-based diet[166]. Likewise, the dietary mean energy and protein intake is not fundamentally different in people with different levels of plant intake, including vegans[168]. Among elderly people (≥65 years) in Taiwan, vegetarians had significantly lower daily total energy and cholesterol intake, but consumed a higher percentage of polyunsaturated fat, calcium and fibre compared with omnivores. In this study, the likelihood of having hypertension or the metabolic syndrome did not differ significantly between vegetarians and omnivores[169].

Patients with CKD who are not on dialysis and adhere to low-protein, plant-based diets do not generally need ketone or amino acid supplementation if they consume at least 0.6 g/kg per day of protein[154,155] and have an average protein intake of 0.7–0.9 g/kg per day[153]. Classical interventional studies of low-protein diets in patients with CKD G3–4 reported no increased risk of undernutrition[156,157], better compliance with protein restrictions and higher caloric intake with plant-based diets than with animal-based diets[157]. These benefits might be explained by lower levels of appetite-suppressing uraemic toxins with plant-based diets[170]. Patients on dialysis who adhere to plant-based diets have also been reported to attain adequate protein intake (1.1–1.25 g/kg/day) without signs of undernutrition[171,172].

Hyperkalaemia. Plant-based diets are associated with a reduction in blood pressure[173], and a lower ratio of sodium to potassium intake resulting from these diets has been associated with a lower risk of hypertension and improved blood pressure control in the general population[174–176]. Furthermore, multiple trials, mostly in people with hypertension, have shown that use of potassium supplements (typically in the form of potassium chloride) reduces blood pressure and lowers the risk of stroke[177]. These findings have motivated public health policies to increase potassium intake and reduce sodium consumption.

By contrast, various guidelines based on expert opinion suggest that in general, patients with CKD G3–5, including those on dialysis, should restrict their dietary potassium intake to prevent hyperkalaemia[114,178,179]. Dietary guidance for these patients sometimes presumes or prescribes intake of animal protein and focuses on vegetables as discretionary sources of potassium, leading to the popular belief that vegetables are the highest sources of potassium. Recognizing that animal-based foods are also high in potassium[180] and that their consumption is discretionary is a necessary paradigm shift in thinking about dietary advice for patients with CKD.

First, observational studies do not demonstrate a convincing association between dietary potassium and circulating potassium levels in people with CKD, including those on haemodialysis[105,118,123,181,182]. Error in the estimation of potassium in the diet could potentially account for this lack of association. Dietary recall underestimates potassium consumption by failing to account for the use of potassium additives or potassium salt substitutions, overestimates potassium consumption by underestimating the amount of potassium that is lost in cooking (soaking or boiling leads to a loss of 60–80% of the potassium content of several raw foods)[183] and introduces inaccuracy through failing to account for the differential bioavailability of potassium from different sources.

Second, rather than dietary intake, comorbidities (such as heart failure, diabetes or metabolic acidosis) and medications (such as renin–angiotensin–aldosterone system inhibitors) may determine serum potassium levels[180]. Although potassium regulation is primarily dependent on functional kidney mass[184], compensatory mechanisms maintain potassium homeostasis until the very late stages of CKD. These mechanisms include increased bowel excretion[185,186] and intracellular deposition of potassium[187,188], as well as increased insulin-mediated cellular uptake of potassium[189], particularly when potassium is consumed in combination with dietary carbohydrates and sugar[190]. Potassium balance studies in patients with CKD who did not require dialysis showed that consumption of 2–5 g of potassium chloride increased circulating potassium levels[191,192], but these increases were highly variable and did not correlate with the amount consumed or with the extent of potassium clearance. However, in eight patients undergoing maintenance haemodialysis, oral intake of 0.25 mmol/kg potassium chloride salt led to an increase in serum potassium levels of 0.8 mmol/l at 2 h, which was approximately twice the expected increase based on the volume of distribution of potassium[190]. Coadministration of glucose blunted this rise to 0.4 mmol/l, demonstrating the limitations of studies of single nutrients and highlighting the importance of studying meals and foods as a whole.

Finally, few interventional studies have explored the effect of substituting animal-based foods with plant-based foods on the risk of hyperkalaemia in patients with CKD. In a pilot trial of 11 patients with CKD G3–4, following a DASH-like diet led to an increase in mean serum potassium levels from baseline at 1 week (+0.28 ± 0.4 mmol/l; $P = 0.04$), but no significant difference was observed at 2 weeks (+0.15 ± 0.28 mmol/l; $P = 0.1$) and hyperkalaemia was not observed during this study[152]. A series of 1-year clinical trials in patients with CKD G3–4 who did not have hypertension or diabetes reported that consuming alkali-rich fruit and vegetables did not cause hyperkalaemia[142,143]; this finding was confirmed by the same researchers in a similar study with a 5-year intervention[144]. Another study in 13 patients with CKD G3–4 showed that provision of a plant-based diet (with 70% of dietary protein from plant sources) for 4 weeks resulted in two occurrences of hyperkalaemia in the same patient who was known to have type IV renal tubular acidosis; the hyperkalaemia was resolved with food substitution[104]. In 22 patients with CKD G4–5 who consumed an unrestricted vegan diet for 3 months, no meaningful changes in serum potassium were observed[156]. The controlled nature of these studies, the selection of patients and small sample sizes limit generalization of the results; however, it is plausible that diet exerts less influence on the circulating levels of potassium of patients with advanced CKD than is generally thought. To our knowledge, intervention studies of the effects of plant-based diets on risk of hyperkalaemia have not been conducted in patients on maintenance dialysis; however, we think that such studies are needed.

Implementation of plant-based diets

Much of the evidence discussed above is from mechanistic basic science studies or observational clinical studies, which tempers our inferences. We are mindful of the unintended and unstudied potential negative consequences of dietary change in routine clinical practice. For these reasons, we do not recommend or suggest that patients with CKD should be routinely prescribed or educated about plant-based diets. However, the many potential benefits summarized above are encouraging. We offer the suggestions regarding implementation below for caregivers who are interested in promoting plant-based diets and for the many patients who are interested in adopting potentially beneficial strategies in the absence of conclusive evidence.

Recommendations on dietary modifications for primary prevention of CKD are not based on CKD evidence but instead are extrapolated from evidence relating to dietary approaches to prevent hypertension or CVD. We think it is prudent that following lifestyle advice for primary CVD prevention, including consumption of plant foods, continues to be recommended to people who are at risk of developing CKD.

In patients with CKD, successful transition to a plant-based diet will require agreement between the patient and their caregiver, with the understanding that in some cases the best results will be obtained with a strategy that is flexible and patient centred[193]. Health-care workers must be mindful of the social and cultural implications of food and diet, the reality that most families prepare meals for more than one person at a time, and the costs and constraints that are faced by many people with CKD given the bidirectional relationship that exists between CKD and poverty at both micro-economic and macro-economic levels[194].

Plant-based diets have often been prescribed to people with CKD G4–5 as low-protein options to retard progression to kidney failure. Our experience in such cases is that communication is key and entails explaining the benefits and harms, describing the main changes and listening to the patient's perceptions and fears, possibly with involvement of family members or other caregivers. Patient motivation is crucial and choosing

Table 5 | **The potassium content of common plant foods per gram of fibre**

Plant food	Potassium content (milligrams of potassium per gram of fibre)		
	<75	75–150	>150
Fruit	Lemons, raspberries, pears, apples, blueberries, peanuts	Blackberries, dried plums, strawberries, peaches, oranges, grapes, grapefruit, tangerines	Kiwi, mangoes, cherries, cashew nuts, bananas, apricots, pineapples, melons, peeled tomatoes
Vegetables and herbs	Basil, red radishes, carrots, eggplants	Mushrooms, green beans, olives, peppers, broccoli, asparagus, beetroot, fennel, onions, garlic	Sweet potatoes, potatoes, lettuce, zucchini (courgettes), celery, thistle, rocket (arugula), cucumber, chard, spinach, pumpkins
Legumes	Peas, dry chickpeas, beans, dry lentils, lupins	Dry beans	Soy
Cereals	Barley, corn flakes, rye bread, wholewheat bread, white bread, wheat flour, pasta, brown rice	Buckwheat, white rice	None

Plant foods that are low in potassium per unit of fibre might be useful options for patients with chronic kidney disease who have or are at risk of hyperkalaemia. Plant foods with a high potassium content per unit of fibre may be less suitable for these patients, but might be useful in other individualized diets.

Table 6 | **Adaptation of a typical dialysis meal plan to conform with plant-based dietary patterns**

Meal	Typical meal plan	Adaptations		
		Pro-vegetarian	DASH-style	Mediterranean-style
Breakfast	2 slices of toasted white bread, ½ small pear, omelette (1 egg, 1 egg white, 1 tbsp margarine), 1 cup of tea without sugar	2 slices of toasted oat bread, ½ small pear, omelette (2 white eggs, ½ tbsp margarine), 240 ml of reduced-fat milk, 1 cup of tea without sugar	2 slices of toasted oat bread, 1 small pear, 240 ml of reduced-fat milk, 1 cup of tea without sugar	2 slices of toasted oat bread, 1 small pear, 10 almonds, 240 ml of reduced-fat milk; 1 cup of tea without sugar
Lunch	Pasta with chicken (120 g pasta, 1 tbsp unsalted butter, 86 g chicken, 150 g boiled sweet potato, 1 tbsp olive oil), 1 cup of lemonade (237 ml)	Salad with beans (160 g boiled broccoli, 2 cups of lettuce, 200 g beans, 1 cup of cucumber, 15 g nuts, 1 tbsp olive oil), 2 slices of toasted oat bread, 1 cup of pineapple	Pasta with chicken (120 g pasta, 1 tbsp unsalted butter, 57 g chicken), salad (2 cups of lettuce, 1 cup of peeled cucumber), 10 almonds, 200 g hummus	Salad with chicken (80 g boiled broccoli, 100 g boiled cauliflower, 2 cups of lettuce, 57 g chicken, 2 tbsp olive oil), 1 slice of toasted oat bread, 1 cup of berries or grapes
Dinner	150 g couscous, 2 tbsp olive oil, 150 g salmon, 130 g raw carrot, 200 ml ginger ale	150 g couscous, 100 g lentils, 150 g peppers, 1 tbsp olive oil, ½ cup of boiled carrots	150 g couscous, 1½ tbsp olive oil, 1 cup of mushrooms, 100 g salmon	150 g couscous, 2 tbsp olive oil, 1 cup of zucchini, 1 cup of mushrooms, 100 g salmon
Snacks	120 g canned grapes, 240 ml reduced-fat milk	100 g hummus, 1 slice of toasted oat bread, 240 ml of reduced-fat milk, ½ cup of berries	1 large piece of apple, 240 ml of reduced-fat milk, 15 g mixed nuts	1 large piece of apple, 1 slice of toasted oat bread, 2 slices tofu
Calories	2,150	2,170	2,150	2,150
Protein (g)	92	89	91	93
Sodium (mg)	2,140	1,448	1,713	1,200
Potassium (mg)	1,650 (42 mEq)	3,206 (82 mEq)	2,033 (52 mEq)	3,000 (77 mEq)
Phosphorus (mg)	780	916	541	1,400
Fibre (g)	21.7	58	26.6	37

Diet characteristics obtained from REF.[230]. Nutritional information obtained from REF.[231]. DASH, Dietary Approaches to Stop Hypertension; tbsp, tablespoon.

to adopt a plant-based diet rather than feeling that it is imposed can improve their adherence. Advice regarding a plant-based diet must be centred on the patient, their context and their values, and a multi-faceted intervention is most likely to be successful, including novel methods such as the use of telehealth (remote coaching or phone apps)[195–197] (Supplementary Table 5). As no standard definitions exist and the approach is necessarily patient centred, it is not possible to say what proportion of the diet should be from plant sources. In addition, research into cost-effective strategies to promote adherence is needed.

In a cross-sectional evaluation of dietary recalls from patients on haemodialysis in the USA, the top sources of dietary potassium were meat products (beef, chicken, Mexican food, hamburgers), followed by legumes in fifth place[123]. It is possible that these patients were already restricting high-potassium plant foods, but animal potassium sources receive less attention from dietitians and practitioners. Furthermore, potassium additives in processed foods can increase potassium content threefold[198–200]. More accurate information on low-potassium plant foods is required, and policy is needed to improve food labelling by detailing the added potassium (and phosphates) used in processing. Plant foods with a low potassium to fibre ratio[114] might be particularly suitable to recommend to patients with CKD (TABLE 5) because high fibre intake is associated with higher stool volume and therefore increased potassium excretion in stool, as well as with reductions in constipation, heart disease, stroke, diabetes, colorectal cancer and death[201–203]. Cooking methods such as freezing or boiling (and discarding the water) can be used to reduce potassium content in foods up to 60% if this is desired[204].

For patients who choose to adhere to vegetarian or vegan diets, we think it is prudent to follow the general recommendation[205,206] to consume vitamin B_{12} supplements or fortified foods to prevent risk of deficiencies. However, safe levels of vitamin B_{12} supplementation for patients with CKD remain to be determined and patients who take these supplements need to be closely monitored for adverse effects. In some settings, it may be important to advise combining plant foods that have complementary essential amino acids, such as rice (low in lysine) and beans (low in methionine)[207], but a varied diet with adequate nitrogen will rarely be deficient in essential amino acids in adults.

Although we recognize that in some socio-economic contexts such an approach may not be feasible, we advocate for consumption of fresh plant foods to avoid the risks connected with additives and conservation agents. People who consume vegetarian diets have been reported to have slightly increased pesticide concentrations in urine[208] and the potential harmful effects of pesticides on kidney function are not known. Given the societal shifts towards plant-based diets and the commercialization of plant-based substitutes for meat products such as hamburgers and nuggets, a need exists for research on the health implications of ultra-processed plant proteins. The techniques used for the production of products such as starch and oil may result in protein degradation[209]. Furthermore, ultra-processed plant foods may have high fat and salt contents and, similar to other types of

Interdialytic weight gain
Change in body weight between two dialysis sessions. It is routinely assessed and used together with clinical symptoms and signs and predialysis blood pressure readings to make decisions regarding the amount of fluid removal during a dialysis session. It is also used as a basis for fluid and salt intake recommendations.

ultra-processed food, a higher content of phosphorus additives and acidity regulators (such as citric acid, sodium diacetate, magnesium chloride or sodium bicarbonate) than minimally processed or unprocessed food.

Theoretically, high consumption of fruits with a high liquid content (e.g. those with >85% water such as watermelon, melon, orange, tangerine, grapefruit) or of natural fruit juices could lead to fluid overload and a higher interdialytic weight gain in anuric patients. Although direct evidence regarding this issue and even basic information on estimated liquid intake from plant-based diet regimes is lacking, this possibility brings to mind the risk of unintended consequences of dietary advice. From a practical perspective, plant foods with low fluid content could be recommended for the small proportion of people with CKD who require fluid restriction (mostly those on dialysis). Interdialytic weight gain could then be considered during follow-up and further feedback provided for the patient.

In a recent survey of kidney dietitians, about 20% of respondents felt comfortable with liberalizing the restrictions on various food groups including fruits and vegetables, beans and legumes, and whole grains. Respondents were generally more comfortable with liberalizing the phosphorus restriction than the potassium restriction[210]. Until the safety and effectiveness of plant-based diets have been adequately evaluated in patients with kidney disease, caution and strict monitoring are warranted. As one of the key factors that determines dietary intake is pleasure, potential exists to enhance dietary intake through liberalization of plant foods in the diet if patients feel that they have regained varied choices and joy from eating.

Box 1 | **Research priorities for further studies of plant-based diets**

Research recommendations for all stages of CKD
- Patient preferences regarding plant-based diets, including societal perspectives
- Risk of hyperkalaemia, sudden death and mortality
- Generation of toxic middle molecules and protein-bound toxins
- Quality of life and burden of uraemic symptoms
- Trials of fibre in people with CKD
- Trials of olive oil in people with CKD
- Trials of nuts, seeds oils, whole grains, legumes and beans and risk of CKD
- Studies of the health implications of ultra-processed plant foods

Outcomes in patients with CKD G4–5 not using KRT
- Time until need for KRT
- Quality of life and burden of uraemic symptoms during conservative management[a]

Outcomes in patients undergoing dialysis
- Metabolic complications: lipid profile, blood pressure control, inflammation, CKD-mineral and bone disorders
- Intradialytic symptoms and risk of fluid overload

Outcomes in kidney transplant recipients
- Risk of graft failure
- Incidence of post-transplant diabetes mellitus and metabolic syndrome
- Metabolic complications: lipid profile, blood pressure control, inflammation, CKD-mineral and bone disorders

CKD, chronic kidney disease; KRT, kidney replacement therapy. [a]Treatment of advanced CKD without KRT for reasons of patient choice or resource constraints.

We suggest endorsing kidney-friendly adaptations of established plant-based diets such as the DASH diet and the Mediterranean diet (TABLE 6; Supplementary Table 6) and recommend discussion with patients about the possibility of choosing such a diet, with close supervision, until adequate studies have been performed. Dietary patterns may be easier to teach and learn than specific instructions relating to individual foods or even more challenging instructions relating to individual micronutrients such as phosphate, details of which may not be included on labelling or in widely available nutritional information. Further modifications for patients who have or who are at risk of hyperkalaemia include the choice of low-potassium plants, plants with a low potassium to fibre ratio and boiling for demineralization.

Conclusions and research gaps

Based on the evidence discussed in this Review, we find little risk and potentially marked benefits in promoting the adoption of plant-based diets for primary prevention of CKD, as well as for delaying CKD progression in patients with established CKD G3–5. These diets may also have additional benefits in managing and preventing the metabolic complications of CKD and enabling increased fibre intake, which might result in reduced risk of vascular disease, cancer and death.

However, many gaps exist in knowledge regarding plant-based diets in the setting of CKD and further research is necessary to address these areas (BOX 1). Although excellent trials have investigated the benefits of plant-based diets in controlling acidosis and delaying CKD progression, additional intervention trials are required, particularly to assess the safety of dietary liberalization in terms of risk of hyperkalaemia in patients with CKD 4–5. We find no clear evidence to support limiting plant-based foods in normokalaemic patients, including those with advanced stage CKD. As plant-based diets are associated with a reduction in uraemic toxins, they could potentially alleviate symptoms associated with uraemia at any level of GFR. Given that initiation of dialysis is based on these symptoms, such an effect has the potential to delay the need for KRT and to improve quality of life in patients receiving conservative management. Studies are needed to investigate these hypotheses.

Evidence regarding the safety and efficacy of plant-based diets in patients on KRT is scarce and mixed, and further research, particularly on the risks of diet-induced hyperkalaemia, is warranted. However, we consider that the widely implemented dietary restrictions aimed at limiting potassium intake may not be fully justified and may deprive the patient of many other healthy nutrients. Clinical studies are required to better characterize the benefits and harms of these dietary regimes.

We realize that our suggestions are not aligned with traditional dietary restrictions for people with kidney disease, termed the renal diet. However, the current kidney nutrition recommendations from the Kidney Disease Outcomes Quality Initiative[10] and European Best Practices Guidelines[11] were issued in 2001 and 2007, respectively, before most of the data discussed in this Review were published. We note that the Kidney

Disease Outcomes Quality Initiative, in collaboration with the US Academy of Nutrition and Dietetics, is currently updating their guideline for nutrition in CKD, with publication scheduled for November 2020. As most of the available data are observational, it is unlikely that the new guideline will include evidence-graded recommendations for plant-based diets, but we hope that our Review awakens interest and motivates actions towards the development of interventional studies to demonstrate the risks and benefits of plant-based diets, while remaining mindful of the wishes of patients.

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