Clinical Kidney Journal

Clinical Kidney Journal, 2023, vol. 16, no. 11, 1723–1736

https://doi.org/10.1093/ckj/sfad103
Advance Access Publication Date: 4 May 2023
CKJ Review

CKJ REVIEW

Ultraprocessed foods and chronic kidney disease—double trouble

Carla Maria Avesani[1], Lilian Cuppari[2], Fabiana Baggio Nerbass[3], Bengt Lindholm[1] and Peter Stenvinkel[1]

[1]Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Technology and Intervention, Karolinska Instituted, Stockholm, Sweden, [2]Division of Nephrology and Nutrition Program, Federal University of São Paulo and São Paulo, Brazil and [3]Pró-Rim Foundation, Joinville, Santa Catarina, Brazil

Correspondence to: Carla Maria Avesani; E-mail: Carla.Avesani@ki.se

ABSTRACT

High energy intake combined with low physical activity generates positive energy balance, which, when maintained, favours obesity, a highly prevalent morbidity linked to development of non-communicable chronic diseases, including chronic kidney disease (CKD). Among many factors contributing to disproportionately high energy intakes, and thereby to the obesity epidemic, the type and degree of food processing play an important role. Ultraprocessed foods (UPFs) are industrialized and quite often high-energy-dense products with added sugar, salt, unhealthy fats and food additives formulated to be palatable or hyperpalatable. UPFs can trigger an addictive eating behaviour and is typically characterized by an increase in energy intake. Furthermore, high consumption of UPFs, a hallmark of a Western diet, results in diets with poor quality. A high UPF intake is associated with higher risk for CKD. In addition, UPF consumption by patients with CKD is likely to predispose and/or to exacerbate uraemic metabolic derangements, such as insulin resistance, metabolic acidosis, hypertension, dysbiosis, hyperkalaemia and hyperphosphatemia. Global sales of UPFs per capita increased in all continents in recent decades. This is an important factor responsible for the nutrition transition, with home-made meals being replaced by ready-to-eat products. In this review we discuss the potential risk of UPFs in activating hedonic eating and their main implications for health, especially for kidney health and metabolic complications of CKD. We also present various aspects of consequences of UPFs on planetary health and discuss future directions for research to bring awareness of the harms of UPFs within the CKD scenario.

LAY SUMMARY

When the diet we eat has more calories than the energy spent by the body, obesity may develop. Obesity increases the risk of developing chronic kidney disease (CKD). Ultraprocessed foods (UPFs) are among the products that can increase energy intake. UPFs include industrialized foods such as carbonated soft drinks, candies, ice cream, mass-produced packaged breads and buns, margarines and other ready-to-eat foods. In some UPFs, sugar is replaced for non-caloric artificial sweeteners, which may not add as many calories, but are still unhealthy. For individuals with CKD, a diet with large amounts of UPFs can trigger or worsen blood pressure and increase blood concentrations of glucose, potassium and phosphate. Therefore we recommend that patients with CKD avoid or reduce the use of UPFs in their diet and prefer home-made meals.

Received: 30.12.2022; Editorial decision: 30.3.2023

Keywords: chronic kidney disease, high energy intake, non-communicable diseases, ultraprocessed food

INTRODUCTION

In the long past, our foraging ancestors had to rely on hunting and gathering to find food and fulfil the body's needs for energy and nutrients. This triggered metabolic adaptations to save energy in the form of adipose tissue for the sometimes long periods without food [1]. As the food supply became more predictable and more easily available, energy intake increased, and this metabolic adaptation became less needed; however, the acquired ability of the body to save a surplus of calories from the diet in the form of adipose tissue remains [1]. Concomitantly, the physical activity level has decreased substantially, with the lifestyle of modern civilization creating a condition of positive energy balance that favours the accumulation of fat and the development of obesity [1]. Obesity is highly present, and its prevalence has increased substantially in the past 40 years. In 2010, obesity [body mass index (BMI) >30 kg/m^2] was present in 11.4% of adults worldwide while the estimated prevalence for 2025 is 16.1%, with an expected increase to 17.5% by 2030 [2]. This increase in obesity prevalence has an important impact on the incidence of non-communicable diseases (NCDs), including chronic kidney disease (CKD).

Obesity has been linked to the development of CKD in epidemiological studies as well as in experimental and observational studies and in clinical trials. Systematic reviews show that obesity is associated with an increased risk of proteinuria, CKD and end-stage kidney disease (ESKD) in persons with comorbidities predisposing to CKD and also in healthy individuals without these comorbidities [3, 4]. In contrast, weight loss is normally accompanied by a decrease in proteinuria, which may indicate a protective effect on glomerular hyperfiltration [5, 6]. Altogether, it is plausible to assume that maintaining a positive energy balance from high caloric intake combined with low physical activity is an important factor leading to obesity and to increasing risk of developing CKD.

Among components leading to a positive energy balance, a higher energy intake is a common finding [1]. As food became more available with techniques that preserve foods, such as cooking, salting, pickling, smoking and fermenting [7], energy intake increased substantially ≈2000 years ago. Industrial processing started with canning and pasteurization in the 1800s and with a rapid development in the 1900s of ready-to-eat packaged meals aiming to serve soldiers in wars [7]. There is no doubt that food processing has had a positive role in decreasing hunger by delivering ready-to-eat food that can be stored for long periods of time, but it has evolved to a degree where its benefits to our overall health can be argued [8].

So-called ultraprocessed foods (UPFs), a concept initially developed by the Brazilian nutrition researcher Carlos Monteiro at the University of São Paulo, Brazil, are defined as products containing ingredients exclusive to industrial processing using sophisticated equipment and technology for production (Table 1). To produce UPFs, the food is subjected to chemical modifications with industrial techniques and the inclusion of additives that can modify the texture, consistency, colour and taste, resulting in products that are palatable or hyperpalatable, normally with high energy density. In addition, UPFs can have added sugar, oils, fructose, corn syrup, fats, salt, protein isolates and even non-caloric artificial sweeteners to replace sugar. Another characteristic of UPFs is sophisticated packaging and being relatively safe from a microbiological perspective. Altogether, UPFs trigger an addictive eating behaviour that is a reason of concern for overall health [9]. UPFs have become more affordable in recent decades and, as a result, sales have increased tremendously over time [10–12]. In Sweden, a 142% increase in the consumption of UPFs was observed between 1960 and 2010, with the greatest increase observed after 1995 [13]. Similarly, global sales of UPFs (kg) per capita increased in all continents from 2006 to 2019, with the highest sales of UPFs observed in Australia and North America and the lowest in South and Southeast Asia [12]. Of note, the increase in UPFs was followed by a decrease in minimally processed foods [12, 13]. This change points to the consumption of UPFs as a pivotal factor in the nutrition transition, with a shift from traditional local diets to a Western dietary pattern containing energy-dense food with increased sodium, saturated fat, sugar, animal-sourced foods, refined carbohydrates and non-caloric artificial sweeteners that may not add calories, but are still unhealthy, and relying on heavy industrial machinery and processing [12]. Therefore, it is not surprising that the consumption of UPFs is directly associated with an increase in the prevalence of obesity and of other NCDs such as cardiovascular disease (CVD), type 2 diabetes mellitus (T2DM), hypertension, cancer, dementia, depression, CKD and non-alcoholic liver disease [14–22]. Furthermore, hypothetically, the consumption of UPFs by CKD patients can also be harmful by predisposing and/or exacerbating metabolic derangements present in CKD.

In this review, we call attention to the potential harms of a high intake of UPFs for the development of CKD and its sequalae and the potential risks of UPFs further worsening metabolic complications in CKD, such as insulin resistance, hyperkalaemia, hyperphosphatemia, metabolic acidosis, dyslipidaemia and dysbiosis. Despite the increasing consumption of UPFs and increased evidence of their potential harmful effects on health, their role in CKD has not yet been included in guidelines dedicated to the treatment of CKD. This review aims to bring awareness of the harms of UPF consumption and the need to consider UPFs in the agenda of future studies and guidelines for CKD.

ENERGY HOMEOSTASIS CONTROL: INFLUENCE OF UPFS IN ACTIVATING HEDONIC EATING

In a simplistic way, the energy balance of an individual is based on the assumption that the energy intake must be similar to energy expenditure [1]. This theory is well accepted, but different factors interfere in this balance, including the neuro-endocrine regulation system. One important finding is that increased adiposity caused by failure to maintain stable body weight due to high energy intake with concomitant low energy expenditure could be the result of individuals overcoming the natural set points of neuro-endocrine regulation, shifting the energy equilibrium and making body weight maintenance more difficult [1]. In this regard, high fat and high sugar foods that are characteristic of UPFs, activate mesolimbic reward, gustatory and oral somatosensory brain regions, contributing to overeating [23]. Based on pooled data from five published studies that measured energy intake rates across a sample of 327 foods, Forde *et al.* [24] found that going from unprocessed (36 ± 4 kcal/min) and processed (54 ± 4 kcal/min) foods to UPFs (69 ± 3 kcal/min), the

Table 1: The NOVA food classification system according to the degree of industrial processing [27].

NOVA food group	Definition	Examples
(Group 1) Unprocessed or minimally processed foods	Unprocessed: edible parts of plants, fungi, algae or from animals after separation from nature or animals	Plant origin: fruits, seeds, leaves, stems, roots, tubers Animal origin: eggs, milk, fat, meat
	Minimally processed: minimal food processing, such as pasteurization, freezing, placing in containers, vacuum packing, non-alcoholic fermentation, no addition of sugar, fat, salt or oils to the food	Tea, coffee, herbs, dried fruits, pasteurized milk, powdered milk
(Group 2) Processed culinary ingredients	Foods with industrial processes such as pressing, centrifuging, refining or extracting. Used to prepare, season, and cook group 1 foods. May contain additives	Vegetable oils, butter, sugar, honey, syrup, starches; vegetable oils with added antioxidants; salt mined or from seawater and table salt with added drying agents
(Group 3) Processed foods	Products made by adding salt, oil, sugar or other group 2 ingredients to group 1 foods. Uses preservation methods such as canning and bottling, and in the case of breads and cheeses, using non-alcoholic fermentation. May contain additives	Canned or bottled vegetables and legumes; salted or sugared nuts and seeds; salted, dried, cured or smoked meats and fish; canned fish; fruit in syrup; freshly made unpackaged breads and cheeses
(Group 4) UPFs	Product with the use of ingredients exclusive to the industrial processing with sophisticated equipment and technology Foods pass by chemical modifications with industrial techniques; use of additives Foods are palatable or hyperpalatable and sophisticated packaging with added sugar, oils or fats or salt, with high fructose corn syrup, interesterified oils and protein isolates	Carbonated soft drinks; sweet or savoury packaged snacks; chocolate, candies; ice-cream; mass-produced packaged breads and buns; margarines and other spreads; cookies (biscuits), pastries, cakes and cake mixes; breakfast 'cereals' 'Energy' bars; 'energy' drinks; milk drinks, 'instant' sauces
	Foods are designed to be affordable, long shelf- life and convenient (ready to consume)	Pies, pasta and pizza dishes; poultry and fish 'nuggets', sausages, peanut butter, hamburgers, powdered and packaged 'instant' soups, noodles and desserts. Infant formulas, follow-on milks, replacement shakes and powders

average energy intake rate increases significantly [24]. In addition, an investigation that analysed 98 ready-to-eat foods found that the higher the degree of industrial food processing, the higher the glycaemic response and the lower its satiety potential [25]. These findings are aligned with the discovery that in addition to the 'metabolic brain', in which regulation of energy intake is carried out by homeostatic mechanisms (glucostatic, lipostatic and others), humans developed a 'hedonic brain', responsible for the motivational control of food intake, with a complex reward system involving expression of opioid receptors, cannabinoid receptors type 1 and several neurotransmitters such as dopamine and serotonin, further influencing appetite and energy intake according to the palatability of foods and the pleasure sensation [1]. Therefore UPFs are a potential contributor to obesity by inducing hedonic eating through overriding the homeostatic control of food intake [26].

AN OVERVIEW OF UPFs AND THEIR MAIN IMPLICATIONS FOR HEALTH

The term UPF was created for the new classification of foods called NOVA that is based on the nature, extent and purposes of the industrial processes that foods undergo [27]. These industrial processes involve sophisticated techniques such as extrusion, moulding and pre-frying, with inclusion of artificial sweeteners and additives to add colour, enhance flavour, change food consistency and increase shelf life [27]. All those procedures are possible only with high-tech industrial machinery [27]. UPFs are packed with synthetic materials and the final product is palatable or highly palatable and can create an addictive eating pattern [9]. Therefore the food processing itself may not be the problem, since most food consumed today has had some degree of processing that shifts the food so that it no longer resembles the form of the original food [27]. The NOVA food classification system [27] is summarized in Table 1. Other food classification systems are discussed in detail elsewhere [27]. For the current review, the NOVA classification system will be described in more detail since it has been the most used in epidemiological studies.

The main harm that UPFs represent to health is that due to its poor nutritional value, the increase in the proportion of UPFs in the diet is associated with a decrease in dietary quality indexes and to lower adherence to a healthy dietary pattern, such as the Mediterranean diet [16]. This means that the higher the proportion of UPFs, the worse the dietary quality [17, 28, 29], even among pesco-vegetarians, vegetarians and vegans that replace regular milk and meat for plant-based drinks and textured soy protein foods, respectively [30]. The assessment of UPF intake in the diet varies depending on how it is expressed, e.g. as a percentage of total energy intake (TEI), as grams/day or grams/kg/day or as a percentage of total food weight in the diet. Other variables contributing to variations of UPFs in the diet include the geographical region, age group, social and educational inequalities and, to a lower extent, gender [28]. In a systematic review of studies from 21 countries estimating the UPF intake as a proportion of the TEI using the NOVA classification, it was found that the highest percentage of UPF intake was from the USA and UK (≈50%) and the lowest was from Italy and Portugal (≈10%) [28]. A similar finding was observed in studies from European countries, where the UK and Germany had the highest average household availability of UPFs, while Portugal and Italy had the lowest [31]. Regarding age group, the percentage of UPF intake from the TEI is higher in children and teenagers, since UPFs are served in school cafeterias [28]. A higher UPF intake was observed in young adults as compared with older adults, a result that is believed to reflect lifestyle patterns, such as the habit of eating out, which is associated with higher UPF intake [28]. Other factors shown to influence UPF consumption are social and economic inequality, lower education level and unemployment, which may lead to a preference for more affordable and less nutritious foods, such as UPFs [28].

The most consumed UPFs are in general baked goods, dairy products, reconstituted meat products, sugary products and sugar-sweetened beverages [14, 17, 28, 31]. As plant-based UPFs and substitutes for meat and dairy products may be used by vegans and vegetarians, UPFs could be a concern also among those categories [32]. In fact, it was shown in a French cohort that avoidance of animal-based food was associated with an increase in UPF consumption among pesco-vegetarians, vegetarians and vegans, with plant-based drinks, soy products, salty snacks and biscuits being examples of commonly consumed UPFs [30]. In addition, among the Adventist population, with many vegetarians, those in the 90th percentile of UPF consumption (47.7% of energy intake from UPFs) had a higher mortality risk than those in the lower 10^{th} percentile (12.1% of energy intake from UPFs), while the same comparison between high and low animal-based food intake (6.2% versus 0% of dietary energy with meats, diary and eggs from the 90^{th} and 10^{th} percentiles, respectively) was not associated with a higher mortality risk [33]. These recent findings indicate that plant-based UPFs also require attention.

Altogether, it is not surprising that in the past 10 years a plethora of studies have showed a consistent finding—the higher the consumption of UPFs, the higher the chances of developing NCDs [14–19, 22]. Of note, a Brazilian ecological study showed that people from areas offering more UPFs were at higher risk of death from cardiovascular diseases as compared with people from areas with fewer available UPFs [34]. The most important factors leading to these associations are summarized in Fig. 1. First, UPFs are considered less satiating foods than minimally processed foods due to alteration of the food matrix through fractioning and recombination of ingredients [35]. This property of UPFs promotes hedonic eating and overrides homeostatic control of food intake, increases TEI and consequently leads to obesity [26]. There is evidence showing that UPFs lead to higher caloric intake and to obesity in an animal experimental study [36] and in a randomized clinical trial [37]. In rats fed a cafeteria diet (comprised mostly by UPFs), an obesity phenotype accompanied by impaired serum fatty acids was found, with significantly higher proportions of total saturated fatty acids [36]. Furthermore, the cafeteria diet induced gut dysbiosis with increased levels of *bacteroidetes* [36].

In a randomized clinical trial, Hall *et al.* [37] demonstrated that when healthy individuals with normal body weight were exposed to a UPF-based diet for 2 weeks, there was a significant increase in *ad libitum* energy intake with a consequent increase in body weight and body fat as compared with when the same individuals were exposed during the same period to a diet of unprocessed food [37]. In another study with a cohort comprised of older individuals from Spain, it was shown that those with higher UPF consumption (>3 servings/day) had almost twice the odds of having short telomeres than the others with lower UPF consumption [38]. Since telomere shortening is associated with inflammation and oxidative stress and with higher biological age, this finding adds to the list of potential harms of UPFs to human health. Also of importance, the presence of non-caloric artificial sweeteners in UPFs, such as saccharin and aspartame, has been implicated in the development of glucose intolerance, central obesity and poor glucose control through changes of composition and function of the gut microbiota [39].

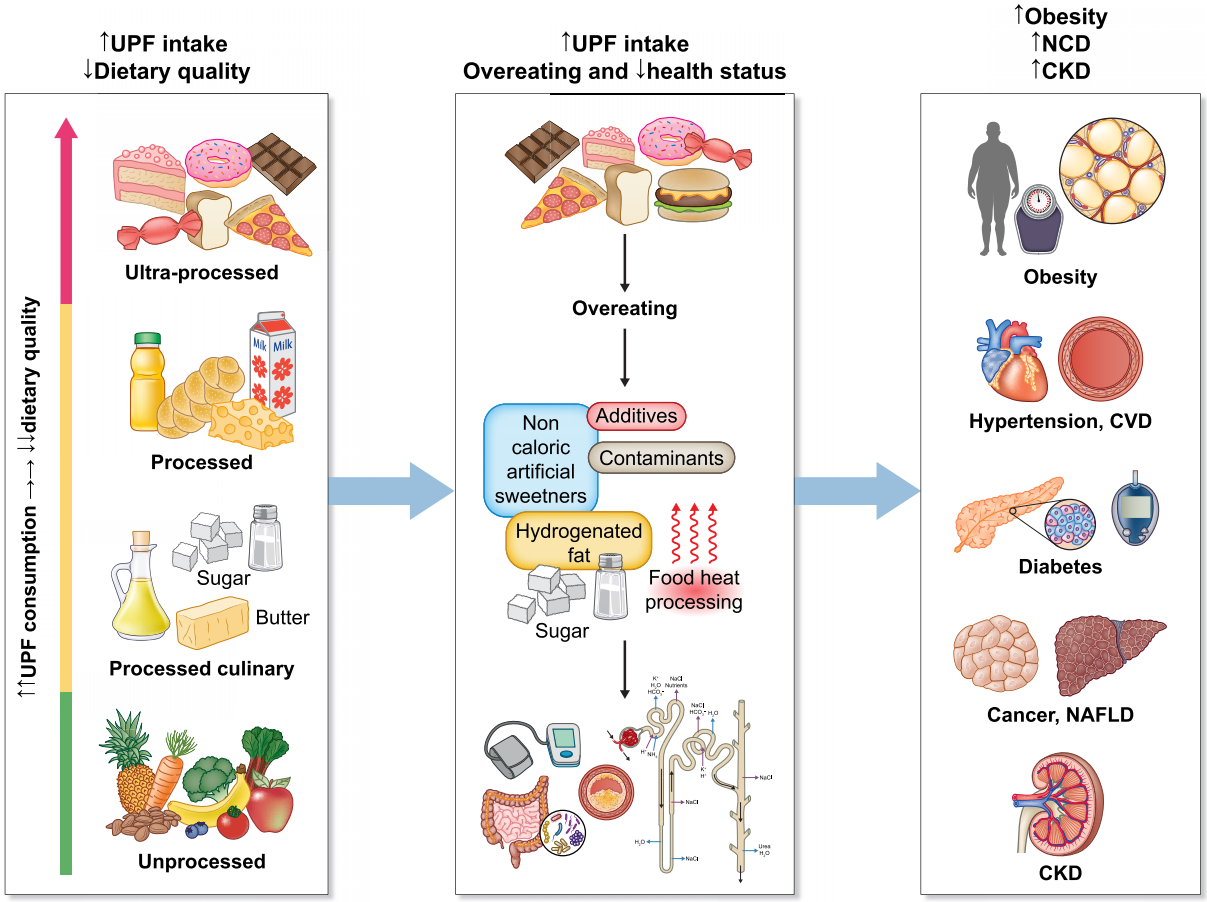

Figure 1: Plausible links between higher consumption of UPFs and higher risk of developing NCDs.
Higher UPF consumption is associated with lower dietary quality (first square). A high consumption of UPFs results in overeating a diet with high density food, with added sugar, salt, unhealthy fats, non-caloric artificial sweeteners, food additives and contaminants and molecular alterations of food components due food processing such as heating. UPFs lead to an increase in factors that are detrimental for health (second square). The conditions and factors listed in the first and second squares lead to an increased risk for obesity and NCDs, such as hypertension, cardiovascular disease (CVD), non-alcoholic fat liver disease (NAFLD) and CKD (third square). CKD: chronic kidney disease; NCD: non-communicable diseases; UPF: ultraprocessed food.

Beyond the nutritional features, the industrial processing of UPFs includes browning, caramelization and other changes caused by a chemical reaction between amino acids and reducing sugars at high temperatures, called the Maillard reaction. This reaction, which is a key feature of cooking and also one of the formulas to enhance flavouring, leads to the generation of high levels of neo-formed contaminants (e.g. acrylamide, furans, heterocyclic amines and others) [40, 41] that are considered potentially carcinogenic, explaining the association between UPF consumption and the increased risk of cancer [42]. Other products with carcinogenic properties used in UPFs include additives, such as sodium nitrite (used in processed meat), titanium dioxide (food pigment banned in Europe) and bisphenol (used in packing) [43]. Moreover, these contaminants and many other food additives have been shown to negatively affect components of the intestinal microbiota that may lead to a disruption of the intestinal barrier with increased abdominal bacterial exposure and systemic inflammation [44, 45].

CONSUMPTION OF UPF AND KIDNEY HEALTH

Recently published observational studies from cohorts of different geographic regions (Table 2) consistently show a significant association between increased UPF intake and the risk of developing CKD or a more rapid kidney function decline, independent of how UPF consumption was evaluated [22, 46–51]. In general, the higher risk for CKD was found with UPF intakes >30% TEI (Table 2). Considering the consistency of these findings, one can hypothesize that limiting UPF intake can prevent CKD development. Among the potential explanations behind these associations are the effect of a high sodium diet in altering the renal and vascular systems and by increasing oxidative stress regardless of changes in blood pressure [52, 53]. Moreover, in animals with normal kidney function fed a high sodium diet, there were increases in markers of oxidative stress in skeletal muscle arterioles and vessels, blood pressure, protein excretion and renal fibrosis and worsened kidney function [54]. Other mechanisms could be that UPFs contain increased amounts of advanced glycation end products (AGEs) [55]. AGEs and their respective precursors are produced in food manufacturing during high-temperature and dry cooking methods (frying, baking, broiling) [55]. The kidneys are the major site for clearance of AGEs and, when in excess, AGEs can promote damage in kidney structures [55]. In rodents, exposure to diets with AGEs led to injury in the glomerulus with albuminuria [56]. This condition can be worsened in animals with T2DM [45]. In

Table 2: Observational studies showing the association between the intake of UPFs and CKD.

Author, year	Aim	Methods	Main findings	Comments
Gu *et al.*, 2022 [51]	To evaluate the association between UPF intake and risk of CKD in two large cohorts	Observational and longitudinal study Cohort: two cohorts from China ($n = 23\,775$) and UK ($n = 102\,332$) UPF intake: obtained from validated FFQ in the first cohort and from 24-hour dietary recall using the NOVA system. UPF expressed as quartiles of energy-adjusted UPF (g/1000 kcal) CKD definition: eGFR <60 ml/min/1.73 m^2 or albumin:creatinine ratio ≥30 mg/g or having a diagnosis of CKD	After a median of 4 years (China) and 10 years (UK) of follow-up, the HR for CKD adjusted for multiple cofounders across the UPF quartiles was: China cohort: 1 (reference); 1.24 (95% CI 0.89–1.72); 1.30 (95% CI 0.91–1.87); 1.58 (95% CI 1.07–2.34); *P* for trend = .02. UK cohort: 1 (reference); 1.14 (95% CI 1.00–1.31); 1.16 (95% CI 1.01–1.33); 1.25 (95% CI 1.09–1.43); *P* for trend < .01	Pooled HRs show that per SD increase in UPF consumption there is a 9% increase in risk of CKD in the two cohorts combined [HR 1.09 (95% CI 1.04–1.15), $P = .001$]
Kityo and Lee, 2022 [49]	To evaluate the association between UPF intake and the prevalence of CKD and the eGFR in the general population	Observational cross-sectional cohort study Cohort: $n = 134\,544$ from Korea. Age: 40–68 years with plausible dietary records UPF intake: assessed by FFQ using the NOVA system classification. UPF expressed as quartiles of percentage of UPF from total food weight. CKD definition: eGFR <60 ml/min/1.73 m^2	Median UPF intake: 5.6% of food weight The prevalence of CKD increased in parallel with UPF intake increase (*P* for trend = .003) (adjusted analysis for confounding variables) Every IQR increase of UPF was associated with a 6% increase in the prevalence of CKD [prevalence ratio 1.06 (CI 1.03–1.09)]. High glucose was associated with an increase in UPF IQR. Analysis adjusted for confounders	A low median UPF percentage of total food intake was observed as compared with other studies A single measure of eGFR was used The FFQ used was not designed to evaluate UPF
Du *et al.*, 2022 [48]	To evaluate the association between UPF consumption and development of CKD in the general population	Observational and longitudinal study	The mean of energy-adjusted servings of UPF consumption in the four quartiles were 3.6, 5.2, 6.2 and 8.4 servings/day	

Table 2: Continued

Author, year	Aim	Methods	Main findings	Comments
		Cohort: 14 679 adults from USA without CKD at baseline followed for 24 years UPF intake: assessed by FFQ at visits 1 and 3. The NOVA system was used to classify UPFs. UPFs were expressed as servings/day adjusted for energy intake. Quartiles of energy adjusted UPF servings/day were calculated CKD definition: presence of at least one of four criteria: eGFR <60 ml/min/1.73 m^2 accompanied by 25% eGFR decline; CKD-related hospitalization; death involving CKD; kidney failure with KRT	The highest quartile of UPF consumption had a 24% higher risk [HR 1.24 (95% CI 1.15–1.35)] of developing CKD compared with those in the lowest quartile There was an approximately linear relationship between UPF intake and the risk of CKD By substituting one serving of UPFs with minimally processed foods, there was a 6% lower risk of CKD [HR 0.94 (95% CI 0.93–0.96), $P < .001$]	
Montero-Salazar *et al.*, 2022 [50]	To evaluate the association between dietary quality index and kidney function in older adults Cohort: 1312 older adults (≥60 years of age) from Spain followed up to 6 years Kidney function decline definition: increase in SCr or decrease in eGFR beyond changes expected for age Food intake: assessed by food history. Dietary quality index was categorized based on Nutri-score. The higher the Nutri-score score, the lower the dietary quality.	Observational and longitudinal study using a cohort of older adults	Each 10-point increase in the Nutri-score dietary index was associated with odds for a decrease in kidney function by 27% (CI 6–52). Analysis adjusted for confounding variables	This study does not assess the consumption of UPF *per se*, but the higher Nutri-score index was characterized by containing least healthy foods and more UPFs
Cai *et al.*, 2022 [22]	To evaluate the association between UPF consumption and risk of kidney function decline in the general population	Observational and longitudinal study with a mean follow-up of 3.6 years Cohort: 78 346 adults from the Netherlands with normal renal function and plausible dietary records	UPF consumption in the diet was 37.7 ± 12.3% The Mediterranean diet score decreased as quartiles of UPF% increased	The FFQ used was not designed to evaluate UPF
		UPF intake: assessed from FFQ using the NOVA classification system. UPF expressed as percentage of total diet weight in grams. Sex-specific quartiles of UPF (% of total diet weight) were calculated Mediterranean diet score was used to evaluate the dietary quality	In the follow-up analysis, participants in the highest quartile of UPF% had a higher risk of incident CKD or 30% eGFR decline as compared with those in the lowest UPF% quartile [OR 1.27% (95% CI 1.09–1.47), $P = .003$] Participants in the highest UPF% had a more rapid eGFR decline compared with those in the lower quartile [$\beta = -0.17$ (95% CI −0.23 to −0.11), $P < .011$] Analysis adjusted for confounding variables	

Table 2: continued

Author, year	Aim	Methods	Main findings	Comments
Osté *et al.*, 2022 [47]	To study the association between UPF consumption and all-cause mortality in KTR	Observational longitudinal study in adult KTRs that were followed for a median of 5.7 years after transplantation for all-cause mortality Cohort: 632 KTRs from the Netherlands with functioning graft after 1 year. Patients with diabetes or history of diabetes at baseline were not included UPF intake: assessed from FFQ using the NOVA classification system. UPF expressed as a percentage of total diet weight in grams Sex-specific tertiles of UPF (% total diet weight) were calculated Primary outcome: all-cause mortalitySecondary outcomes: death-censored graft failure, renal function decline (doubling serum creatine in the follow-up) and PTDM	The mean UPF consumption in the diet was 28% of total food weight/day Adherence to the Mediterranean diet and DASH diet was lower in the RTRs with higher UPF consumption UPF consumption was associated with all-cause mortality [HR 2.13 (95% CI 1.46–3.10), $P < .001$]. Analysis adjusted for confounding variablesUPF consumption was associated with faster decline of kidney function but not with death-censored graft failure and PTDM	
Rey-García *et al.*, 2021 [46]	To assess the association between UPF consumption and kidney function decline in the general population	Observational and longitudinal study in individuals >60 years of age Cohort: 1312 older adults from Spain ≥60 years of age followed up to 6.2 years Food intake: assessed by food history. UPF was identified using the NOVA classification system. Sex-specific tertiles of UPF expressed as % TEI and UPF expressed in g/kg/day were calculated A combined endpoint of kidney function decline was considered when SCr increased or eGFR decreased beyond that expected for age from baseline to follow-up	Participants with higher UPF consumption at baseline had higher risk of kidney function decline over time than those with lower UPF consumption UPF intake by %TEI: Men: tertile 1, 8.6%; tertile 2, 18.7%; tertile 3, 33% Women: tertile 1, 6.8%; tertile 2, 16.2%; tertile 3, 29.8% Analysis: UPF intake by % TEI: tertile 3, OR 1.74 (95% CI 1.14–2.66), $P = .023$; UPF intake by g/kg/day: tertile 3, OR 1.62 (95% CI 1.06–2.49), $P = .043$	This is the same cohort as that studied by Montero-Salazar *et al.* 2022 [50] The associations between UPF consumption and kidney function decline were stronger among patients with diabetes and without obesity

CI: confidence interval; eGFR: estimated glomerular filtration rate; FFQ: Food Frequency Questionnaire; HR: hazard ratio; KRT: kidney replacement therapy; KTR: kidney transplant recipient; OR: odds ratio; PTDM: post-transplant diabetes; PR: prevalence ratio; SCr: serum creatinine.

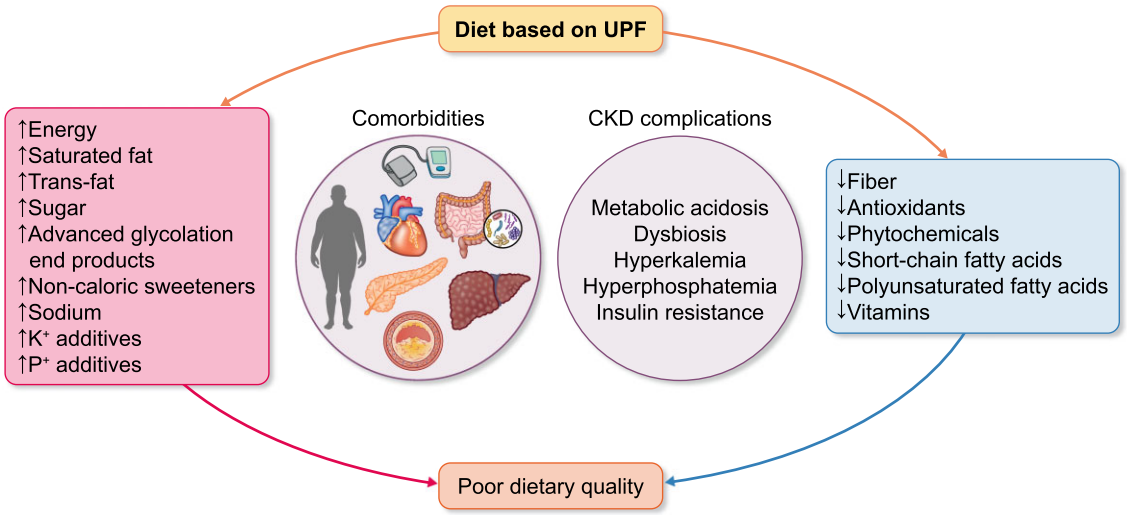

Figure 2: Intersection of a diet based on UPFs in driving complications related to CKD.
UPFs are characterized by poor dietary quality. This type of diet can further exacerbate comorbidities and contribute to the development of metabolic complications already present in CKD. UPF: ultraprocessed food.

humans, consumption of diets with excessive amounts of AGEs was associated with serum biomarkers of inflammation, oxidative stress, hyperglycaemia, hyperlipidaemia and endothelial dysfunction [57]. In addition, in a randomized crossover trial, 10 healthy subjects were assigned to a 1-day high protein diet with low AGEs content (10 cooked large chicken eggs) and to a 1-day diet with high AGEs content (industrialized fried chicken nuggets). The study showed that renal perfusion and oxygen consumption increased significantly after the high AGEs diet. Despite the short-term diet, this trial demonstrated that the AGEs content of UPFs can modify kidney haemodynamics [58]. Therefore, several pathophysiological explanations may justify the higher predisposition of developing CKD or the faster decline in kidney function in subjects with higher UPF intake.

When it comes to the intake of UPFs in patients with CKD, the data are still scarce. In older adults (>60 years) on haemodialysis (HD), the intake of UPFs (expressed as a percentage of TEI) was significantly higher than in non-CKD older adults [59]. Of note, when further investigating the HD group, the UPF intake (percentage of TEI) of the dialysis day was significantly higher than that of the weekend day and non-dialysis day. The long hours away from home that makes it more difficult to eat homemade meals may account for this. The dietary quality index of the older adults on HD was also worse than that of older non-CKD individuals [59]. In another study investigating kidney recipients with stable graft function, it was observed that the mean UPF consumption was equivalent to 28% of the total food weight/day and adherence to the Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) diet was lower in patients with higher UPF consumption. Furthermore, UPF consumption was associated with a 2-fold increased mortality risk [47]. One point that requires future investigation is the use of plant-based products to replace animal protein in UPFs and other foods. It may be that patients with CKD following low-protein diets erroneously believe that plant-based dairy products and textured soy protein foods can be freely used because of lower protein content.

The benefits of reducing the UPF intake to levels similar to that observed in countries with low UPF consumers was shown in a study where the estimated dietary inadequacy for energy density, free sugars and saturated fat and fibre would decrease from 9.5% to 76.8% depending on the nutrient and country in question [60]. This extrapolation is an example of the potential benefits that lowering UPF intake can exert to prevent NCDs, including CKD. In summary, the high consumption of UPFs in the general population seems to be a determining factor leading to a higher risk of CKD. In individuals with CKD, the consumption of UPFs follows the high intake levels observed in the general population. The effects of UPFs in CKD require attention due to their potential in worsening of uraemic metabolic complications.

UPFs AS DRIVERS OF METABOLIC COMPLICATIONS IN CKD

Recent evidence suggests that UPF consumption can contribute to metabolic acidosis, dysbiosis, hyperphosphatemia and hyperkalaemia (Fig. 2). Metabolic acidosis is a common complication of CKD [61] that can lead to bone demineralization, muscle mass loss and CKD progression [62]. Due to the preponderance of animal-sourced food components, including many of the UPFs, the modern Western-type diet is considered H^+-producing as compared with base-producing plant-sourced diets [63]. In addition, proteins from animal sources contains sulphur amino acids, such as methionine and cysteine, that when metabolized yield sulphuric acid. The content of these amino acids is 2–5-fold higher in meat and eggs than in grains and legumes. In contrast, most fruits and vegetables have fewer sulphur-containing amino acids and they contain organic salts (e.g. potassium citrate and malate) that, when metabolized, release bicarbonate and thus provide alkali to the body [63]. Therefore a preponderance of UPFs in the diet mainly from processed meat may increase acid retention in CKD. Furthermore, the additives present in UPFs, such as salt (sodium chloride), can independently increase acid load and lower bicarbonate, accounting for 50–100% of the dietary acid load [64]. Carbonated drinks containing carbonic acid and those containing phosphoric acid, such as cola-based sodas, have some of the highest levels of acidity among soft drinks.

Other widely used phosphate-based additives in UPFs, such as calcium acid pyrophosphate used in processed meat and potato products, are also a source of acids [65].

Another problem with high UPF intake is that it associates with low intake of foods with a high fibre content (fruits, vegetables, grains and whole cereals). The high intake of protein and fat is harmful for the gut, leading to detrimental protein and choline fermentation instead of beneficial fermentation coming from fibre carbohydrates [66]. In addition, this type of diet augments the colonic transit time, which also has a negative impact on colonic microbiome composition. Under this condition, there is growth of proteolytic species (proteolytic bacteria), resulting in increased generation and uptake of end products of bacterial protein fermentation (ammonia, amines, thiols, phenols and indoles) and to gut dysbiosis [67–69]. However, a recent study in mice has raised the possibility that some of the uraemic toxins generated by bacterial fermentation of amino acids, including hydrogen sulphide, seem to have a physiological and potentially beneficial effect on the progression of CKD [70]. Moreover, since the uraemic milieu can lead to gut dysbiosis by increasing the influx of circulating urea and other toxins to the gut lumen, the combination with poor fibre intake can increase gut production of uraemic toxins, such as p-cresyl sulphate, indoxyl sulphate and trimethylamine-N-oxide [68, 69, 71]. In HD patients, increased adherence to an unhealthy plant-based diet containing UPFs such as processed fruit juices, sugar-sweetened beverages, refined grains, chips and crisps and sweets and deserts was associated with an increase in free and total indoxyl sulphate. Moreover, an increase in the intake of these UPFs was linked to higher circulating concentrations of indoxyl sulphate and p-cresyl sulphate [72], suggesting an indirect effect of UPFs in worsening gut microbiotic uraemic toxin production.

Phosphate-based and potassium-based additives present in UPFs may worsen hyperphosphatemia and hyperkalaemia [73, 74]. Compared with similar food items without additives, phosphorus and potassium content is ≈70–100% higher in food that contain additives [75–77]. In addition, the intestinal absorption of inorganic phosphorus and potassium additives is close to 100%, compared with plant- (20–50%) and animal-based sources (40–60%) [78]. So far, studies evaluating the association between higher intake of UPFs and hyperphosphatemia and hyperkalaemia are lacking in CKD. Limiting the consumption of UPFs may be especially important in the large group of patients with both T2DM and CKD, as part of a holistic approach for improving management and outcomes in these patients [79, 80].

SEEKING PLANETARY HEALTH: ANOTHER REASON TO AVOID UPF

Adding to the harms of high UPF intake for overall and kidney health, UPFs tend to be harmful for the environment [81]. The food system, including all processes in the food chain, production, processing, packing, distributing, consumption and recycling, contributes to ≈30% of total greenhouse gas emissions [82], the major risk factor for global warming and climate change [82]. The EAT-*Lancet* commission launched a healthy mainly plant-based diet that is safe for the environment and for overall health [83]. This type of diet relies on fresh, preferably locally produced products (such as fruits, vegetables, whole grains and nuts); vegetable protein (from beans), with lower amounts of red meat, eggs and dairy products [84]; and no use of UPFs. In addition, the production of UPFs depends on a system that requires large amounts of energy, land and water, with land degradation, biodiversity loss and plastics and metals pollution [84]. In other words, the food chain of UPFs is highly unsustainable and leads to a 'lose–lose' situation, meaning bad for the environment and bad for human health [84]. A recent study by da Silva *et al.* [85] showed that the environmental effects of the Brazilian diet have increased over the past 3 decades along with increased effects from UPFs, indicating that dietary patterns in Brazil are becoming potentially more harmful to both human and planetary health. Thus the negative effects of UPFs on planetary health are another strong argument to diminish the consumption of UPFs and the kidney care community needs to educate healthcare professionals, patients and the population at large about the perils of UPFs [81]. As recently discussed by Lawrence [86], the UPF concept challenges several traditional nutrition research and policy undertakings as well as the political economy of the industrial food system.

CONCLUSIONS AND FUTURE DIRECTIONS

Excessive energy intake is a main factor driving the worldwide epidemic of obesity, which in turn is linked to the increase of NCDs, including CKD. A better understanding of the underlying driving factors is needed to halt this unfortunate development. Perhaps among the factors contributing to high energy intake, the most important one is UPFs, which are energy dense foods with low nutritional value. The increasing consumption of diets with a high UPF content (often >30% of TEI), a hallmark of the modern Western diet, reflects global trends—supported by industrial food production, processing and marketing—towards hedonic dietary patterns replacing more healthy home-made diets often based on locally produced food and benefiting from the use of traditional methods such as fermentation. This change is leading to diets with poor quality and increased amounts of food additives that may be harmful for human and planetary health. Table 3 summarizes attractive and harmful factors of UPFs in the diet. For a high-risk patient group like those with CKD, high consumption of UPFs has the potential to further worsen the metabolic risk factor profile and progression. We suggest the inclusion of statements regarding UPFs in dietary CKD guidelines to guide healthcare professionals and patients [87]. The Brazilian nutrition guidelines [88] and the 2021 dietary guidance to improve cardiovascular health [89] are examples of how to emphasize the importance of advocating healthy dietary patterns rather than recommendations based on advantages or restrictions of individual nutrients. Finally, there is a need for increased public awareness regarding the potential perils of UPFs, and all data regarding the human and planetary health concerns related to increased use of UPFs need to reach policymakers. We suggest a traffic light food labelling system (green–yellow–red) to be used in grocery stores so that the public, and especially risk groups with NCDs, can make healthier food consumption decisions, with the hope that this also may have an impact on the food industry and pave the way for more sustainable and healthier food production.

FUNDING

C.M.A. and P.S. received a grant from the Erasmus+ funding programme of the European Union (ePlanet 2021-1-NL01-KA220-HED-000032029). C.M.A. acknowledges the Stig and Gunborg Westman Foundation for Research and the Martin Rind Foundation. L.C. receives a stipend from Conselho Nacional de Desenvolvimento Científico e Tecnológico (302765/2017-

Table 3: Main potential attractive and harmful factors concerning the consumption of UPFs.

Attractive factors	Harmful factors
More affordable	Low in nutritional quality
Relatively safe	High energy density
Long shelf-life	High in added sugar, salt, fat, artificial sweeteners and additives
Palatable or highly palatable	Can trigger addictive eating pattern
Ease of use: ready to eat or easily prepared foods	Lead to overeating
Attractive marketing and packaging	Increased risk of obesity and development of NCDs
	Globalized diet that is replacing the culturally based home-made meals
	UPF production relies on food systems that are not sustainable for the planet

4). B.L. acknowledges support from Baxter Healthcare. P.S. acknowledges support from the Center for Innovative Medicine, Karolinska Institutet; the Stig and Gunborg Westman Foundation for Research; the Heart and Lung Foundation; Njurfonden and the Swedish Medical Research Council.

AUTHORS' CONTRIBUTIONS

C.M.A., L.C. and F.B.N. were responsible for conception of the review, drafting and/or revision of the manuscript and approval of the final version of the manuscript. B.L. and P.S. were responsible for drafting and/or revision of the manuscript and approval of the final version of the manuscript.

DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Vettor R, Di Vincenzo A, Maffei P *et al*. Regulation of energy intake and mechanisms of metabolic adaptation or maladaptation after caloric restriction. *Rev Endocr Metab Disord* 2020;**21**:399–409. https://doi.org/10.1007/s11154-020-09565-6
2. World Obesity Federation. *World Obesity Atlas 2022*. London: Ludgate House; 2022.
3. Garofalo C, Borrelli S, Minutolo R *et al*. A systematic review and meta-analysis suggests obesity predicts onset of chronic kidney disease in the general population. *Kidney Int* 2017;**91**:1224–35. https://doi.org/10.1016/j.kint.2016.12.013
4. Friedman AN, Kaplan LM, le Roux CW *et al*. Management of obesity in adults with CKD. *J Am Soc Nephrol* 2021;**32**:777–90. https://doi.org/10.1681/ASN.2020101472
5. Li K, Zou J, Ye Z *et al*. Effects of bariatric surgery on renal function in obese patients: a systematic review and meta analysis. *PLoS One* 2016;**11**:e0163907. https://doi.org/10.1371/journal.pone.0163907
6. Afshinnia F, Wilt TJ, Duval S *et al*. Weight loss and proteinuria: systematic review of clinical trials and comparative cohorts. *Nephrol Dial Transplant* 2010;**25**:1173–83. https://doi.org/10.1093/ndt/gfp640
7. Knorr D, Watzke H. Food processing at a crossroad. *Front Nutr* 2019;**6**:85. https://doi.org/10.3389/fnut.2019.00085
8. Dicken SJ, Batterham RL. Ultra-processed food: a global problem requiring a global solution. *Lancet Diabetes Endocrinol* 2022;**10**:691–4. https://doi.org/10.1016/S2213-8587(22)00248-0
9. Monteiro CA, Cannon G, Levy RB *et al*. Ultra-processed foods: what they are and how to identify them. *Public Health Nutr* 2019;**22**:936–41. https://doi.org/10.1017/S1368980018003762
10. Maia EG, Dos Passos CM, Levy RB *et al*. What to expect from the price of healthy and unhealthy foods over time? The case from Brazil. *Public Health Nutr* 2020;**23**:579–88. https://doi.org/10.1017/S1368980019003586
11. Moodie R, Bennett E, Kwong EJL *et al*. Ultra-processed profits: the political economy of countering the global spread of ultra-processed foods – a synthesis review on the market and political practices of transnational food corporations and strategic public health responses. *Int J Health Policy Manag* 2021;**10**:968–82. https://www.ijhpm.com/article_4050.html
12. Baker P, Machado P, Santos T *et al*. Ultra-processed foods and the nutrition transition: global, regional and national trends, food systems transformations and political economy drivers. *Obes Rev* 2020;**21**:e13126. https://doi.org/10.1111/obr.13126
13. Juul F, Hemmingsson E. Trends in consumption of ultra-processed foods and obesity in Sweden between 1960 and 2010. *Public Health Nutr* 2015;**18**:3096–107. https://doi.org/10.1017/S1368980015000506
14. Vandevijvere S, Jaacks LM, Monteiro CA *et al*. Global trends in ultraprocessed food and drink product sales and their association with adult body mass index trajectories. *Obes Rev* 2019;**20**:10–9. https://doi.org/10.1111/obr.12860
15. Lane MM, Davis JA, Beattie S *et al*. Ultraprocessed food and chronic noncommunicable diseases: a systematic review and meta-analysis of 43 observational studies. *Obes Rev* 2021;**22**:e13146. https://doi.org/10.1111/obr.13146
16. Dicken SJ, Batterham RL. The role of diet quality in mediating the association between ultra-processed food intake, obesity and health-related outcomes: a review of prospective cohort studies. *Nutrients* 2021;**14**:23. https://doi.org/10.3390/nu14010023
17. Srour B, Fezeu LK, Kesse-Guyot E *et al*. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). *BMJ* 2019;**365**:l1451. https://doi.org/10.1136/bmj.l1451
18. Fiolet T, Srour B, Sellem L *et al*. Consumption of ultra-processed foods and cancer risk: results from

NutriNet-Santé prospective cohort. *BMJ* 2018;**360**:k322. https://doi.org/10.1136/bmj.k322
19. Cai Q, Duan MJ, Dekker LH *et al*. Ultra-processed food consumption and kidney function decline in a population-based cohort in the Netherlands. *Am J Clin Nutr* 2022;**116**:263–73. https://doi.org/10.1093/ajcn/nqac073
20. Gomes Gonçalves N, Vidal Ferreira N, Khandpur N *et al*. Association between consumption of ultraprocessed foods and cognitive decline. *JAMA Neurol* 2023;**80**:142–50. https://jamanetwork.com/journals/jamaneurology/article-abstract/2799140
21. Gómez-Donoso C, Sánchez-Villegas A, Martínez-González MA *et al*. Ultra-processed food consumption and the incidence of depression in a Mediterranean cohort: the SUN Project. *Eur J Nutr* 2020;**59**:1093–103. https://doi.org/10.1007/s00394-019-01970-1
22. Cai Q, Duan MJ, Dekker LH *et al*. Ultraprocessed food consumption and kidney function decline in a population-based cohort in the Netherlands. *Am J Clin Nutr* 2022;**116**:263–73. https://doi.org/10.1093/ajcn/nqac073
23. Stice E, Burger KS, Yokum S. Relative ability of fat and sugar tastes to activate reward, gustatory, and somatosensory regions. *Am J Clin Nutr* 2013;**98**:1377–84. https://doi.org/10.3945/ajcn.113.069443
24. Forde CG, Mars M, de Graaf K. Ultra-processing or oral processing? A role for energy density and eating rate in moderating energy intake from processed foods. *Curr Dev Nutr* 2020;**4**:nzaa019. https://doi.org/10.1093/cdn/nzaa019
25. Fardet A. Minimally processed foods are more satiating and less hyperglycemic than ultra-processed foods: a preliminary study with 98 ready-to-eat foods. *Food Funct* 2016;**7**:2338–46. https://doi.org/10.1039/C6FO00107F
26. Neumann NJ, Fasshauer M. Added flavors: potential contributors to body weight gain and obesity? *BMC Med* 2022;**20**:417. https://doi.org/10.1186/s12916-022-02619-3
27. Monteiro CA, Cannon G, Lawrence M *et al*. *Ultra-processed foods, diet quality, and health using the NOVA classification system*. Rome: Food and Agriculture Organization; 2019.
28. Marino M, Puppo F, Del Bo' C *et al*. A systematic review of worldwide consumption of ultra-processed foods: findings and criticisms. *Nutrients* 2021;**13**:2778. https://doi.org/10.3390/nu13082778
29. Julia C, Martinez L, Allès B *et al*. Contribution of ultra-processed foods in the diet of adults from the French NutriNet-Santé study. *Public Health Nutr* 2018;**21**:27–37. https://doi.org/10.1017/S1368980017001367
30. Gehring J, Touvier M, Baudry J *et al*. Consumption of ultra-processed foods by pesco-vegetarians, vegetarians, and vegans: associations with duration and age at diet initiation. *J Nutr* 2021;**151**:120–31. https://doi.org/10.1093/jn/nxaa196
31. Monteiro CA, Moubarac JC, Levy RB *et al*. Household availability of ultra-processed foods and obesity in nineteen European countries. *Public Health Nutr* 2018;**21**:18–26. https://doi.org/10.1017/S1368980017001379
32. Orlich MJ, Jaceldo-Siegl K, Sabaté J *et al*. Patterns of food consumption among vegetarians and non-vegetarians. *Br J Nutr* 2014;**112**:1644–53. https://doi.org/10.1017/S000711451400261X
33. Orlich MJ, Sabaté J, Mashchak A *et al*. Ultra-processed food intake and animal-based food intake and mortality in the Adventist Health Study-2. *Am J Clin Nutr* 2022;**115**:1589–601. https://doi.org/10.1093/ajcn/nqac043
34. Victor A, Silva RCR, Silva NJ *et al*. Influence of unhealthy food environment on premature cardiovascular disease mortality in Brazil: an ecologic approach. *Am J Prev Med* 2023;**64**:285–92. https://doi.org/10.1016/j.amepre.2022.09.018
35. Fardet A, Lakhssassi S, Briffaz A. Beyond nutrient-based food indices: a data mining approach to search for a quantitative holistic index reflecting the degree of food processing and including physicochemical properties. *Food Funct* 2018;**9**:561–72. https://doi.org/10.1039/C7FO01423F
36. de la Garza AL, Martínez-Tamez AM, Mellado-Negrete A *et al*. Characterization of the cafeteria diet as simulation of the human Western diet and its impact on the lipidomic profile and gut microbiota in obese rats. *Nutrients* 2022;**15**:86. https://doi.org/10.3390/nu15010086
37. Hall KD, Ayuketah A, Brychta R *et al*. Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. *Cell Metab* 2019;**30**:67–77.e3. https://doi.org/10.1016/j.cmet.2019.05.008
38. Alonso-Pedrero L, Ojeda-Rodríguez A, Martínez-González MA *et al*. Ultra-processed food consumption and the risk of short telomeres in an elderly population of the Seguimiento Universidad de Navarra (SUN) Project. *Am J Clin Nutr* 2020;**111**:1259–66. https://doi.org/10.1093/ajcn/nqaa075
39. Suez J, Korem T, Zeevi D *et al*. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature* 2014;**514**:181–6. https://doi.org/10.1038/nature13793
40. Birlouez-Aragon I, Morales F, Fogliano V *et al*. The health and technological implications of a better control of neoformed contaminants by the food industry. *Pathol Biol (Paris)* 2010;**58**:232–8. https://doi.org/10.1016/j.patbio.2009.09.015
41. Mariotti MS, Granby K, Rozowski J *et al*. Furan: a critical heat induced dietary contaminant. *Food Funct* 2013;**4**:1001–15. https://doi.org/10.1039/c3fo30375f
42. Dybing E, Sanner T. Risk assessment of acrylamide in foods. *Toxicol Sci* 2003;**75**:7–15. https://doi.org/10.1093/toxsci/kfg165
43. World Health Organization International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans. Volume 93. Carbon black, titanium dioxide and talc*. Geneva: World Health Organization Press; 2010.
44. Vissers E, Wellens J, Sabino J. Ultra-processed foods as a possible culprit for the rising prevalence of inflammatory bowel diseases. *Front Med* 2022;**9**:1058373. https://doi.org/10.3389/fmed.2022.1058373
45. Snelson M, Tan SM, Clarke RE *et al*. Processed foods drive intestinal barrier permeability and microvascular diseases. *Sci Adv* 2021;**7**:eabe4841. https://doi.org/10.1126/sciadv.abe4841
46. Rey-García J, Donat-Vargas C, Sandoval-Insausti H *et al*. Ultra-processed food consumption is associated with renal function decline in older adults: a prospective cohort study. *Nutrients* 2021;**13**:428. https://doi.org/10.3390/nu13020428
47. Osté MCJ, Duan MJ, Gomes-Neto AW *et al*. Ultra-processed foods and risk of all-cause mortality in renal transplant recipients. *Am J Clin Nutr* 2022;**115**:1646–57. https://doi.org/10.1093/ajcn/nqac053
48. Du S, Kim H, Crews DC *et al*. Association between ultra-processed food consumption and risk of incident CKD: a prospective cohort study. *Am J Kidney Dis* 2022;**80**:589–98.e1. https://doi.org/10.1053/j.ajkd.2022.03.016
49. Kityo A, Lee SA. The intake of ultra-processed foods and prevalence of chronic kidney disease: the Health Examinees Study. *Nutrients* 2022;**14**:3548. https://doi.org/10.3390/nu14173548

50. Montero-Salazar H, Guallar-Castillón P, Banegas JR *et al*. Food consumption based on the nutrient profile system underlying the Nutri-Score and renal function in older adults. *Clin Nutr* 2022;**41**:1541–8. https://doi.org/10.1016/j.clnu.2022.05.004
51. Gu Y, Li H, Ma H *et al*. Consumption of ultraprocessed food and development of chronic kidney disease: the Tianjin Chronic Low-Grade Systemic Inflammation and Health and UK Biobank Cohort Studies. *Am J Clin Nutr* 2023;**117**:373–82.
52. Nerbass FB, Calice-Silva V, Pecoits-Filho R. Sodium intake and blood pressure in patients with chronic kidney disease: a salty relationship. *Blood Purif* 2018;**45**:166–72. https://doi.org/10.1159/000485154
53. He FJ, Tan M, Ma Y *et al*. Salt reduction to prevent hypertension and cardiovascular disease: *JACC* state-of-the-art review. *J Am Coll Cardiol* 2020;**75**:632–47. https://doi.org/10.1016/j.jacc.2019.11.055
54. Kitiyakara C, Chabrashvili T, Chen Y *et al*. Salt intake, oxidative stress, and renal expression of NADPH oxidase and superoxide dismutase. *J Am Soc Nephrol* 2003;**14**:2775–82. https://doi.org/10.1097/01.ASN.0000092145.90389.65
55. Fotheringham AK, Gallo LA, Borg DJ *et al*. Advanced glycation end products (AGEs) and chronic kidney disease: does the modern diet AGE the kidney? *Nutrients* 2022;**14**:2675. https://doi.org/10.3390/nu14132675
56. Vlassara H, Striker LJ, Teichberg S*et al*. Advanced glycation end products induce glomerular sclerosis and albuminuria in normal rats. *Proc. Natl Acad Sci USA* 1994;**91**:11704–8. https://doi.org/10.1073/pnas.91.24.11704
57. Chao PC, Huang CN, Hsu CC *et al*. Association of dietary AGEs with circulating AGEs, glycated LDL, IL-1α and MCP-1 levels in type 2 diabetic patients. *Eur J Nutr* 2010;**49**:429–34. https://doi.org/10.1007/s00394-010-0101-3
58. Normand G, Lemoine S, Villien M *et al*. AGE content of a protein load is responsible for renal performances: a pilot study. *Diabetes Care* 2018;**41**:1292–4. https://doi.org/10.2337/dc18-0131
59. Martins AM, Bello Moreira AS, Canella DS *et al*. Elderly patients on hemodialysis have worse dietary quality and higher consumption of ultraprocessed food than elderly without chronic kidney disease. *Nutrition* 2017;**41**:73–9. https://doi.org/10.1016/j.nut.2017.03.013
60. Martinez Steele E, Marrón Ponce JA, Cediel G *et al*. Potential reductions in ultra-processed food consumption substantially improve population cardiometabolic-related dietary nutrient profiles in eight countries. *Nutr Metab Cardiovasc Dis* 2022;**32**:2739–50. https://doi.org/10.1016/j.numecd.2022.08.018
61. Raphael KL, Zhang Y, Ying J *et al*. Prevalence of and risk factors for reduced serum bicarbonate in chronic kidney disease. *Nephrology* 2014;**19**:648–54. https://doi.org/10.1111/nep.12315
62. Raphael KL. Metabolic acidosis in CKD: Core Curriculum 2019. *Am J Kidney Dis* 2019;**74**:263–75. https://doi.org/10.1053/j.ajkd.2019.01.036
63. Remer T, Manz F. Potential renal acid load of foods and its influence on urine pH. *J Am Diet Assoc* 1995;**95**:791–7. https://doi.org/10.1016/S0002-8223(95)00219-7
64. Frassetto LA, Morris RC, Sebastian A. Dietary sodium chloride intake independently predicts the degree of hyperchloremic metabolic acidosis in healthy humans consuming a net acid-producing diet. *Am J Physiol Renal Physiol* 2007;**293**:F521–5. https://doi.org/10.1152/ajprenal.00048.2007
65. Passey C. Reducing the dietary acid load: how a more alkaline diet benefits patients with chronic kidney disease. *J Ren Nutr* 2017;**27**:151–60. https://doi.org/10.1053/j.jrn.2016.11.006
66. Su G, Qin X, Yang C *et al*. Fiber intake and health in people with chronic kidney disease. *Clin Kidney J* 2022;**15**:213–25. https://doi.org/10.1093/ckj/sfab169
67. Andrade LSRC, Cuppari L. The cross-talk between the kidney and the gut: implications for chronic kidney disease. *Nutrire* 2017;**42**:27.
68. Montemurno E, Cosola C, Dalfino G *et al*. What would you like to eat, Mr CKD Microbiota? *Kidney Blood Press Res* 2014;**39**:114–23. https://doi.org/10.1159/000355785
69. Mafra D, Borges N, Alvarenga L *et al*. Dietary components that may influence the disturbed gut microbiota in chronic kidney disease. *Nutrients* 2019;**11**:496. https://doi.org/10.3390/nu11030496
70. Lobel L, Cao YG, Fenn K *et al*. Diet posttranslationally modifies the mouse gut microbial proteome to modulate renal function. *Science* 2020;**369**:1518–24. https://doi.org/10.1126/science.abb3763
71. Lau WL, Kalantar-Zadeh K, Vaziri ND. The gut as a source of inflammation in chronic kidney disease. *Nephron* 2015;**130**:92–8. https://doi.org/10.1159/000381990
72. Stanford J, Charlton K, Stefoska-Needham A *et al*. Associations among plant-based diet quality, uremic toxins, and gut microbiota profile in adults undergoing hemodialysis therapy. *J Ren Nutr* 2021;**31**:177–88. https://doi.org/10.1053/j.jrn.2020.07.008
73. Parpia AS, L'Abbé M, Goldstein M *et al*. The Impact of additives on the phosphorus, potassium, and sodium content of commonly consumed meat, poultry, and fish products among patients with chronic kidney disease. *J Ren Nutr* 2018;**28**:83–90. https://doi.org/10.1053/j.jrn.2017.08.013
74. Picard K, Mager D, Richard C. How food processing impacts hyperkalemia and hyperphosphatemia management in chronic kidney disease. *Can J Diet Pract Res* 2020;**81**:132–6. https://doi.org/10.3148/cjdpr-2020-003
75. Benini O, D'Alessandro C, Gianfaldoni D *et al*. Extra-phosphate load from food additives in commonly eaten foods: a real and insidious danger for renal patients. *J Ren Nutr* 2011;**21**:303–8. https://doi.org/10.1053/j.jrn.2010.06.021
76. Watanabe MT, Araujo RM, Vogt BP *et al*. Most consumed processed foods by patients on hemodialysis: alert for phosphate-containing additives and the phosphate-to-protein ratio. *Clin Nutr ESPEN* 2016;**14**:37–41. https://doi.org/10.1016/j.clnesp.2016.05.001
77. Picard K, Picard C, Mager DR *et al*. Potassium content of the American food supply and implications for the management of hyperkalemia in dialysis: an analysis of the Branded Product Database. *Semin Dial* 2021. https://doi.org/10.1111/sdi.13007
78. Kalantar-Zadeh K, Gutekunst L, Mehrotra R *et al*. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. *Clin J Am Soc Nephrol* 2010;**5**:519–30. https://doi.org/10.2215/CJN.06080809
79. de Boer IH, Khunti K, Sadusky T *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* 2022;**102**:974–89. https://doi.org/10.1016/j.kint.2022.08.012
80. Rossing P, Caramori ML, Chan JCN *et al*. Executive summary of the KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease: an update based

on rapidly emerging new evidence. *Kidney Int* 2022;**102**:990–9. https://doi.org/10.1016/j.kint.2022.06.013

81. Avesani CM, Cardozo LF, Yee-Moon Wang A *et al*. Planetary health, nutrition and chronic kidney disease: connecting the dots for a sustainable future. *J Ren Nutr* 2022. https://doi.org/10.1053/j.jrn.2022.09.003
82. Willett W, Rockström J, Loken B *et al*. Food in the Anthropocene: the EAT-*Lancet* Commission on healthy diets from sustainable food systems. *Lancet* 2019;**393**:447–92. https://doi.org/10.1016/S0140-6736(18)31788-4
83. EAT-*Lancet* Commission. *Healthy diets from sustainable food systems. Food Planet Health. Summary report*. 2020. https://eatforum.org/content/uploads/2019/01/EAT-Lancet_Commission_Summary_Report.pdf
84. Leite FHM, Khandpur N, Andrade GC *et al*. Ultra-processed foods should be central to global food systems dialogue and action on biodiversity. *BMJ Glob Health* 2022;**7**:e008269. https://doi.org/10.1136/bmjgh-2021-008269
85. da Silva JT, Garzillo JMF, Rauber F *et al*. Greenhouse gas emissions, water footprint, and ecological footprint of food purchases according to their degree of processing in Brazilian metropolitan areas: a time-series study from 1987 to 2018. *Lancet Planet Health* 2021;**5**:e775–85. https://doi.org/10.1016/S2542-5196(21)00254-0
86. Lawrence M. Ultra-processed foods: a fit-for-purpose concept for nutrition policy activities to tackle unhealthy and unsustainable diets. *Br J Nutr* 2022. https://doi.org/10.1017/S000711452200280X
87. Monteiro CA, Astrup A. Does the concept of "ultra-processed foods" help inform dietary guidelines, beyond conventional classification systems? YES. *Am J Clin Nutr* 2022;**116**:1476–81. https://doi.org/10.1093/ajcn/nqac122
88. Ministry of Health of Brazil. Dietary guidelines for the Brazilian population. Brasilia: *Ministry of Health*, 2014.
89. Lichtenstein AH, Appel LJ, Vadiveloo M *et al*. 2021 dietary guidance to improve cardiovascular health: a scientific statement from the American Heart Association. *Circulation* 2021;**144**:e472–87. https://doi.org/10.1161/CIR.0000000000001031