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Ultra-processed foods and risk of declined renal function: a dose–response meta-analysis of 786,216 participants

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Abstract

Objectives Earlier investigations have documented an association between elevated consumption of Ultra-Processed Foods (UPFs) and adverse renal outcomes. To explore this relationship further, we executed a comprehensive dose–response meta-analysis to examine the link between UPFs intake and the risk of declined renal function.

Setting.

A systematic search was completed utilizing the ISI Web of Science, Scopus, Embase as well as PubMed/MEDLINE databases (without any restrictions), up until September 5, 2024. Effect sizes of declined renal function were recalculated by applying a random effects model. The GRADE tool was adopted to assess the certainty of the evidence, while study quality and potential publication bias were examined via validated methods such as the Newcastle–Ottawa Scale, Egger's regression asymmetry and Begg's rank correlation test.

Results Thirty-three studies (comprising 786,216 participants) were incorporated in the quantitative analysis. The results demonstrated that a greater UPFs intake was significantly associated with an enhanced risk of declined renal function (RR = 1.16; 95% CI: 1.09, 1.23; $I^2 = 68.8\%$; $p < 0.001$; $n = 37$). Additionally, we observed that each 1-serving-per-day increase in UPFs consumption was associated to a 5% greater risk of reduced renal function (RR = 1.05; 95% CI: 1.02, 1.09; $I^2 = 80.9\%$; $p = 0.013$; $n = 9$). A positive, linear association between UPF intake and the risk of declined renal function ($P_{nonlinearity} = 0.107$, $P_{dose-response} < 0.001$) was further displayed in the non-linear dose–response analysis.

Conclusion Greater exposure to UPFs is positively associated with the risk of declined renal function. The information emphasizes the importance of considering UPFs in the prevention and management of adverse renal outcomes.

Keywords Food processing, Kidney function, Meta-analysis, Renal

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Introduction

Declined renal function (often referred to as renal insufficiency) signifies a gradual deterioration in the kidneys' ability to filter waste and maintain fluid balance in the body. This decrement in renal capacity is often age-related, with notable acceleration due to cardiovascular risk factors that may precipitate Chronic Kidney Disease (CKD) [1, 2]. The progression from diminished renal function to end-stage renal disease (ESRD) necessitates life-sustaining interventions such as dialysis or transplantation [3]. Globally, CKD affects an estimated 10% of the population, equating to over 800 million individuals [4]. Prevalence rates vary, with figures ranging from 9.5 to 13% across different studies and regions [5]. Consequences of CKD include cognitive impairment [6], decreased life expectancy, diminished quality of life [7], as well as significant economic burden on individuals and healthcare systems [8].

Emerging evidence underscores the impact of lifestyle factors on renal health, particularly the role of dietary habits, physical inactivity and smoking [9]. Among these, dietary choices represent a significant modifiable risk factor [10]. The NOVA classification system has identified four distinct categories of food: (1) Unprocessed or minimally processed foods, which are mostly whole foods in their natural state or with minimal processing that does not add or significantly alter their nutritional content; (2) Processed culinary ingredients, like sugar and oils, which are derived from natural foods but intended to cook and season; (3) Processed foods, which are simple products made by adding salt, oil, sugar or other culinary ingredients to unprocessed foods; and (4) Ultra-Processed Foods (UPFs), which differ markedly as they are not merely processed foods but are formulated from industrial ingredients and additives such as stabilizers, preservatives, and artificial colors to enhance flavor, extend shelf life or modify texture [11]. UPFs stand out in this regard, constituting a massive portion of the daily energy consumption in certain high-income countries [12]. Despite their palatability, ease of consumption and affordability, UPFs are notorious for their minimal micronutrient and fiber content, compensating with an overload of refined sugars, unhealthy fats, sodium and additives [13–15]. Furthermore, UPFs are shown to disproportionately contain higher proportions of unhealthy nutrients. For instance, a study in Argentina revealed that all UPFs examined surpassed the recommended limits for at least one critical nutrient, with 94.4% containing an excessive amount of free sugars, 47.9% having an disproportionate amount of total fats and 59.2% having an excessive amount of saturated fat [16]. A series of studies has found that higher consumption of UPFs is associated with an increased risk of CKD [17–19], although some studies did not find a clear connection [20–24]. Consequently, there are variations in current findings, and a thorough analysis could aid in clarifying these inconsistencies.

Review of existing scientific databases and literature indicates that only two meta-analyses have explored the association between UPF intake and the risk of CKD. These analyses, however, are constrained by their limited scope; Xiao et al. [25] included only four studies, and He et al. [26] comprised eight studies, both sets offering low power and lacking subgroup analyses. In light of these limitations (and to encapsulate the entirety of available evidence), we conducted an extensive systematic review and dose–response meta-analysis. Our investigation aims to integrate findings from all relevant observational studies to assess the potential association between UPFs consumption and the risk of declining renal function in adults aged 18 years and older.

Methods

The current study was implemented complying with the guidelines specified in the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [27]. We registered our study protocol in the International Prospective Register of Systematic Reviews Database (PROSPERO) under the registration number CRD42023456417. The PECOS tool for each study was illustrated in Supplementary Table 1.

Literature search and selection

A systematic search was completed utilizing the Scopus, PubMed/MEDLINE, Embase, and ISI Web of Science databases (without any restriction), up until September 5 2024. Supplementary Table 2 presents the detailed search strategy. Additionally, manual examination of the references cited in the retrieved articles was undertaken to include data from non-peer-reviewed sources (commonly referred to as grey literature). This encompasses a variety of documents such as conference proceedings, letters, brief surveys, abstracts, notes and reports.

Inclusion and exclusion criteria

The inclusion criteria comprised the following: observational research (cross-sectional, cohort, or case–control studies) on adults (≥ 18 years) that presented data on the association between UPFs intake and the risk of CKD (estimated GFR of < 60 mL/min/1.73 m^2) [28], showing effect estimates as odds ratios (OR), relative risk (RR), or hazard ratio (HR) with at least 95% confidence interval (95% CI). The exclusion criteria encompassed investigations that: (a) were conducted in pediatric and adolescent populations (< 18 years), (b) lacked sufficient data to be

utilized in our analysis, (c) did not present relevant exposure, or (d) with overlapping exposure and outcome variables, leading to duplication of variables (e.g., duplicate reports from the same cohort study). In cases where multiple publications reported the same dataset, the study with a larger sample size or longer follow-up period was picked. Article titles and abstracts, followed by full-text reviews sourced from database searches that matched the inclusion criteria were evaluated by two investigators (SM and SP). Discrepancies over eligibility were resolved through mutual discussion.

Data extraction

Two investigators independently retrieved the following data from studies meeting the inclusion criteria, which included the following elements: (a) first author's name, publication year and originating country; (b) study-specific details, such as design, follow-up duration and source of health status data; (c) characteristics of the participants, including the sample size, age and sex distribution; (d) CKD defining criteria; (e) UPFs assessment method; (f) CKD outcomes; (g) primary findings of the study (outcomes), and (h) covariates implemented for adjustment in multivariate analyses. Any divergence in data extraction was settled through dialogue.

Quality assessment

Employing the Newcastle–Ottawa Scale (NOS) [29], two independent investigators conducted an appraisal of the quality of each selected article. The NOS is designed to evaluate the risk of bias in non-randomized prospective cohort investigations within the context of systematic reviews or meta-analyses. It assigns a maximum of 9 points distributed across three main domains: selection of study groups (up to 4 points), comparability of study groups (up to 2 points,) in addition to ascertainment of exposure and outcomes in case–control or cohort studies (up to 3 points). Studies that achieve scores between 7 and 9 points are classified as high quality with a low risk of bias, while those scoring between 0 and 3 are considered to have a high risk of bias.

Statistical analyses and data synthesis

Statistical analyses were executed applying STATA version 14.0 (StataCorp, College Station, TX, USA). In this meta-analysis, relative risk (RR) with 95% CIs was calculated as the overall effect size, consistent with the effect estimates reported by the original studies that met the inclusion criteria [30]. Pooled effect estimates were derived via the DerSimonian-Laird random-effects model, which accounts for variability between studies [31]. A pairwise meta-analysis was first performed by aggregating the effect sizes for the extreme categories of UPF consumption (i.e. the highest and lowest levels). The heterogeneity across the included investigations was examined via the Cochran's Q test and the I-squared (I^2) statistic. The I^2 value was computed based on the formula: $[(Q-df)/Q \times 100\%]$, where Q represents the χ^2 value and *df* signifies degrees of freedom. Significant between-study heterogeneity was defined as either a Cochran Q statistic with a p value of < 0.01 or an I^2 value exceeding 50%. To delineate further, thresholds for I^2 statistics were outlined to categorize heterogeneity levels as follows: low ($< 25\%$), moderate (25–50%), high (50–75%) and extreme ($> 75\%$). Additionally, subgroup analyses were undertaken to assess potential effects on outcomes based on various study characteristics, including research design (cross-sectional or cohort), UPF classification method (NOVA food classification system, Western dietary pattern, fast food intake or sweets consumption), geographical origin (USA, Europe, and Asia), number of participants (< 1000 or ≥ 1000), gender distribution (male, female, and both), dietary assessment tool (food frequency questionnaires [FFQ], 24 h recall or a brief diet history questionnaire), age (≤ 50 or > 50 years), BMI [body mass index] (≤ 25 or > 25 kg/m^2) and other covariate adjustments to data (BMI, smoking status, physical activity level, alcohol consumption, energy intake, sex, diabetes mellitus and hypertension). We completed sensitivity analysis by sequentially excluding individual studies and recalculating the pooled effect estimates to test the robustness of the findings. Moreover, publication bias was appraised through the visual scrutiny of funnel plots and formally by Egger's regression asymmetry and Begg's rank correlation tests [32, 33], with results regarded as significant when $p < 0.05$.

To quantify the RRs per 1 serving/day increment in UPF consumption, a dose–response meta-analysis was conducted according to the methodological framework proposed by Greenland et al. [34, 35]. Studies were incorporated if they reported case numbers, non-case numbers or person-years, along with the median UPF intake across more than three categories. Ultimately, a one-stage linear mixed-effects meta-analysis was completed to display dose–response associations, via a combination of study-specific slopes to produce an average slope across studies.

Quality of evidence

The quality of evidence across the studies was appraised utilizing the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group

guidelines. According to the GRADE framework, evidence is categorized into 1 of 4 levels: high, moderate, low or very low quality [36].

Results

Study characteristics

In a systematic database search and scrutiny of reference lists, 4700 records were identified. After removing duplicates, 3418 studies were shortlisted for further review (Fig. 1). Of these, 3374 were excluded based on their titles and abstracts. An in-depth evaluation of the remaining 44 full-text studies resulted in the exclusion of 11 studies; nine due to non-relevant exposure and two due to overlapping exposure and outcome variables (Supplementary Table 3). Ultimately, 33 studies satisfied our inclusion criteria and were incorporated into the current meta-analysis [17, 18, 20, 21, 37–65].

The overall characteristics of the included studies are reported in Supplementary Table 4: fourteen employed a cohort design [17, 21, 40, 42, 43, 46, 48, 51–54, 58–60, 62, 65], thirteen were cross-sectional [18, 20, 38, 39, 41, 44, 45, 47, 49, 50, 55–57, 61, 63, 64] and one was case–control [37]. These studies were conducted between 2007 and 2024, and spanned multiple nations: United States

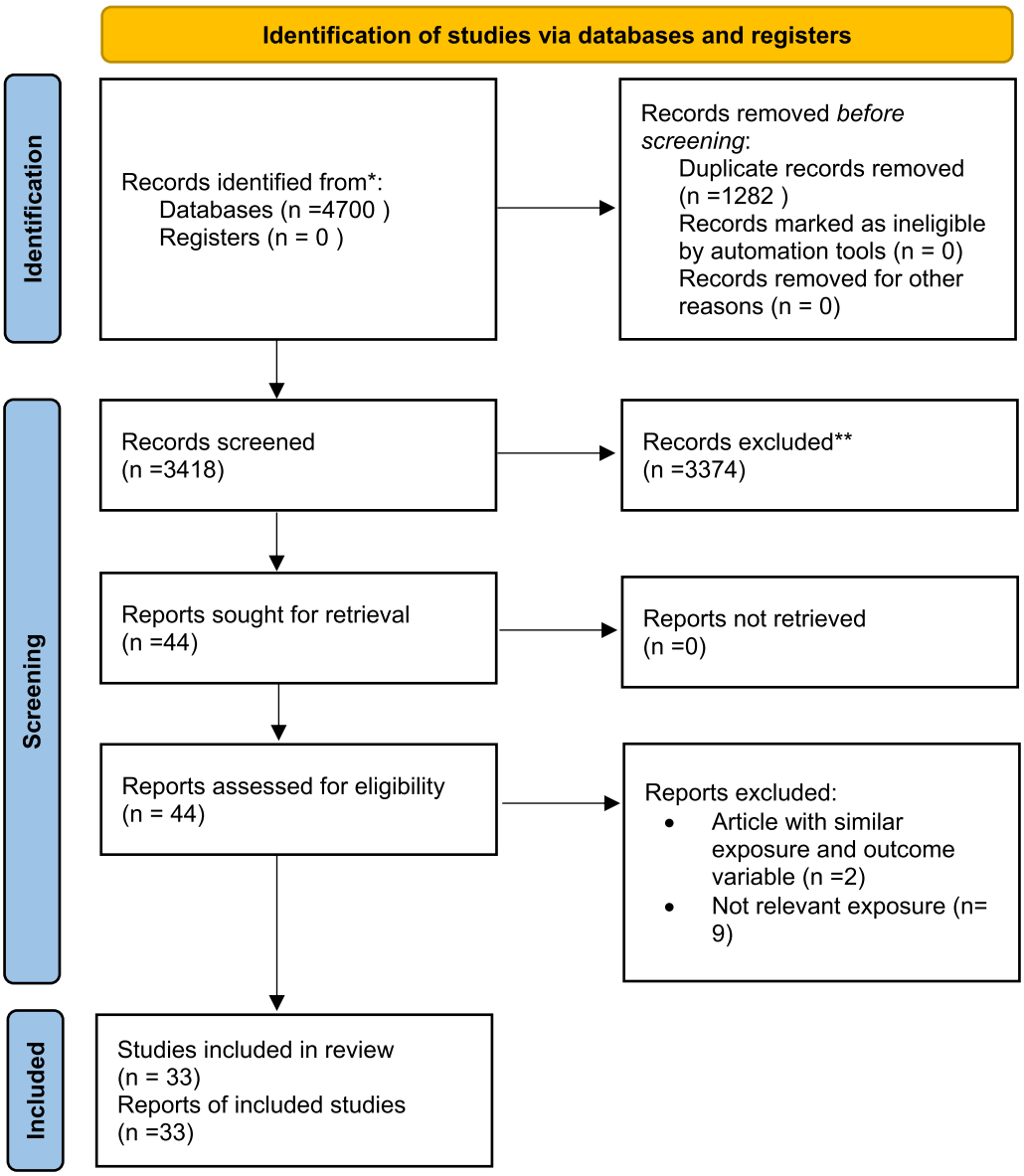

Fig. 1 Flow chart of the process of the study selection

Table 1 Dietary ultra-processed food and the risk of chronic kidney disease

	Highest vs. lowest category meta-analysis						Dose–response meta-analysis					
	Studies, *n*	**RR (95% CI)**	***p* value**	**I^2, %**	**$P_{heterogeneity}$**	**Dose, unit**	**Studies, *n***	**RR (95% CI)**	***p* value**	**I^2, %**	**$P_{heterogeneity}$**	**Quality of evidence**
CKD	37	1.16 (1.09, 1.23)	< 0.001	68.8	< 0.001	1 serving/day	9	1.05 (1.02, 1.09)	0.004	80.9	< 0.001	⊕⊕◯◯LOW

RR relative risk, *CI* Confidence Interval, *CKD* chronic kidney disease

[17, 21, 37, 40, 42, 46, 54, 60, 61, 65], United Kingdom [59], China [20, 43, 44, 50, 58, 64], Iran [18, 41, 47, 49], Taiwan [38, 45, 48, 56], the Netherlands [53], Spain [51, 52, 62], Croatia [57], Korea [55], Japan[63] and Thailand [39]. The maximally adjusted RR specific to each study was recorded for a total of 786,216 individuals across the included publications and was subsequently pooled for a meta-analysis aimed at evaluating the relationship between UPFs and CKD risk. In the quality assessment, the Newcastle–Ottawa scale designated 23 articles as high [17, 18, 20, 21, 39–46, 49–56, 58–65] and 5 as medium [37, 38, 47, 48, 57] quality. Inter-rater consistency for data collection and quality assessment was appropriate (Kappa = 0.881).

UPFs and chronic kidney disease

A greater UPFs intake was significantly associated with a higher risk of CKD (RR = 1.16; 95% CI: 1.09, 1.23; $I^2 = 68.8\%$; $p < 0.001$; $n = 37$) (Table 1, Fig. 2). Subgroup analyses also suggested that a higher UPFs intake was significantly related with an increased risk of CKD in those employing the NOVA food classification (RR = 1.18; 95% CI: 1.10, 1.25; $I^2 = 33.7\%$; $p < 0.001$; $n = 8$) as well as Western dietary pattern for UPF valuation (RR = 1.37; 95% CI: 1.16, 1.62; $I^2 = 14.0\%$; $p < 0.001$; $n = 5$) in comparison with others (Supplementary Table 5). Noteworthy was also the significant relationship seen in investigations completed in the United States (RR = 1.10; 95% CI: 1.02, 1.19; $I^2 = 49.7\%$; $p = 0.045$; $n = 10$) and Asian nations (RR = 1.20; 95% CI: 1.09, 1.33; $I^2 = 76.1\%$; $p < 0.001$; $n = 18$; vs. European countries), those with > 1000 participants (RR = 1.18; 95% CI: 1.11, 1.25; $I^2 = 58.0\%$; $p < 0.001$; $n = 28$; vs. studies with less than 1000 participants), and those using FFQ for dietary measurement (RR = 1.21; 95% CI: 1.13, 1.30; $I^2 = 75.5\%$; $p < 0.001$; $n = 20$) or diet history questionnaire (RR = 1.24; 95% CI: 1.00, 1.52; $I^2 = 64.8\%$; $p = 0.047$; $n = 6$). Furthermore, our outcomes exposed that greater UPFs consumption was significantly related to a superior risk of CKD in overweight and obese participants (RR = 1.19; 95% CI: 1.07, 1.32; $I^2 = 70.7\%$; $p = 0.001$; $n = 16$) but not others. Moreover, subgroup analysis for covariates adjustment revealed that smoke status, physical activity, BMI, intake of energy, diabetes mellitus and hypertension adjustment may have an effect on the relationship between UPFs intake and risk of CKD (Supplementary Table 5).

Dose–response analysis

The outcomes corresponding to the linear dose–response analysis are shown in Table 1 and Fig. 3. We found that a 1 serving/day increment in UPFs intake was associated to a 5% greater risk of CKD (RR = 1.05; 95% CI: 1.02, 1.09; $I^2 = 80.9\%$; $p = 0.013$; $n = 9$). The non-linear dose–response relationship further revealed a positive linear correlation between the consumption of UPFs and the heightened risk of developing CKD ($P_{nonlinearity} = 0.107$, $P_{dose-response} < 0.001$, Fig. 4).

Sensitivity analyses and publication bias

The sensitivity analysis established that no single study prominently affected the risk assessments for CKD, as denoted in Supplementary Fig. 1. The assessment of Publication bias ($p = 0.268$, Egger's test; $p = 0.178$, Begg's) indicated no significant bias. The symmetry of the funnel plot for UPFs intake and CKD can be visualized in Fig. 5.

Quality of evidence

The GRADE scale assessment revealed the evidence elucidating relationships between UPFs intake and CKD risk to be of low quality (Table 1).

Discussion

UPFs that have been heavily modified and are now easily accessible have surged in global popularity. The habitual consumption of such heavily processed foods can lead to negative health effects. Studies that were part of the current analysis used a variety of UPFs, such as sweets, fast food, and other foods that were classified as UPFs by the NOVA-food classification, such as margarine, ultra-processed meats, ice cream, sugary snacks, fried foods, cake, biscuits, croissants, cookies, cereals, sauces, sprits, among others. The outcomes of the current investigation clearly indicate that consuming higher levels of UPFs is significantly associated with an enhanced risk of CKD, a result consistent even after subgroup analyses. Additionally, the results of the linear dose–response observed that a 1 serving/day increment in UPFs intake was related to a 5% greater risk of CKD.

In recent decades, the worldwide preference for UPFs, often rich in sugars, fats, and additives but deficient in essential nutrients, has been on the rise [66]. Such foods have been previously linked to a myriad of health issues [67]. The current study's outcomes confirm that greater UPFs consumption, particularly when classified under the NOVA food system and Western dietary pattern, is significantly related to an increased risk of CKD. This contrasts with studies focused on fast foods and sweets intake. The NOVA system arranges UPFs according to the type, extent, and reason for their industrial food processing instead of their nutrient content [68]. This distinction might explain the current observations: assessments predicated on the NOVA classification and Western dietary patterns capture a broader spectrum of

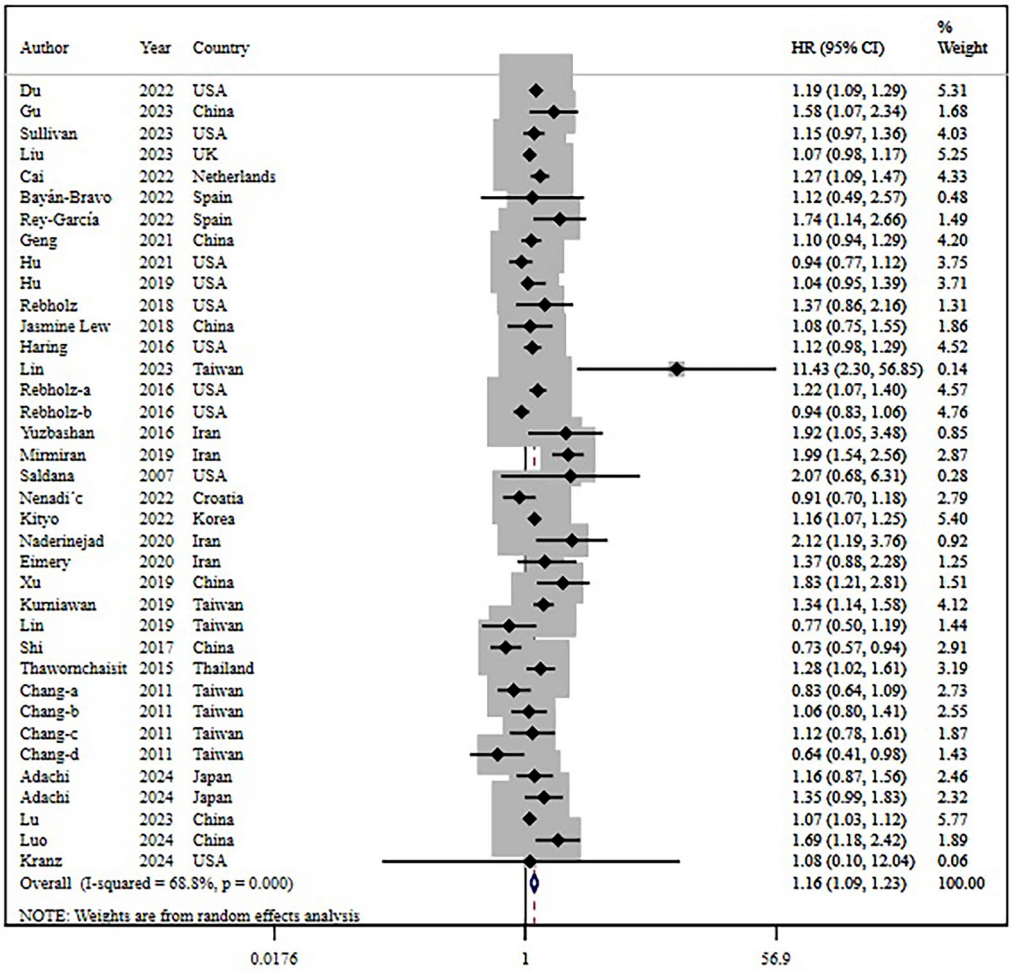

Fig. 2 Forest plots demonstrating RR and 95% CI of pooled results from the random-effects models to evaluate the relationship between ultra-processed foods consumption and risk of chronic kidney disease

UPFs consumed by participants, whereas other methodologies assess only single foods such as sweets and fast foods.

Moreover, our subgroup analysis also identified significant associations in the United States and Asian countries compared to Europe. This disparity may be attributed to a greater volume of research exploring the association between UPFs consumption and CKD risk conducted in Asian and American regions as opposed to European territories. Moreover, it is critical to acknowledge that UPF consumption is significantly higher in the United States [17, 21, 37, 40, 42, 46, 54, 60]; indeed, extant literature suggests that upwards of 50% of the energy intake in the American diet is derived from UPFs [69].

Our subgroup findings also demonstrated that a greater UPFs intake was associated to a heightened risk of CKD in overweight or obese subjects. The pathogenesis of CKD in the context of obesity is frequently attributed to inflammatory mechanisms. Specifically, obesity-induced inflammation has been acknowledged as a pivotal contributor in the etiology and progression of CKD. Elevated levels of the inflammatory cytokine TNF-α, commonly found in obese individuals [70, 71], are linked to glomerulonephritis and tubulointerstitial damage, as prior studies have highlighted [72]. Experimental models have demonstrated that endothelial cell dysfunction is exacerbated by increased dosages of recombinant TNF-α infusion [73]. Moreover, the consumption of UPFs may exacerbate the inflammatory milieu through various mechanisms. UPFs, characterized by their high simple sugar content, precipitate acute postprandial hyperglycemia, thereby fostering a pro-inflammatory state [74, 75]. Additionally, the elevated salt content in UPFs has been posited to induce an inflammatory response [76, 77]. The presence of significant amounts of trans and saturated fats in heavily processed foods is known to

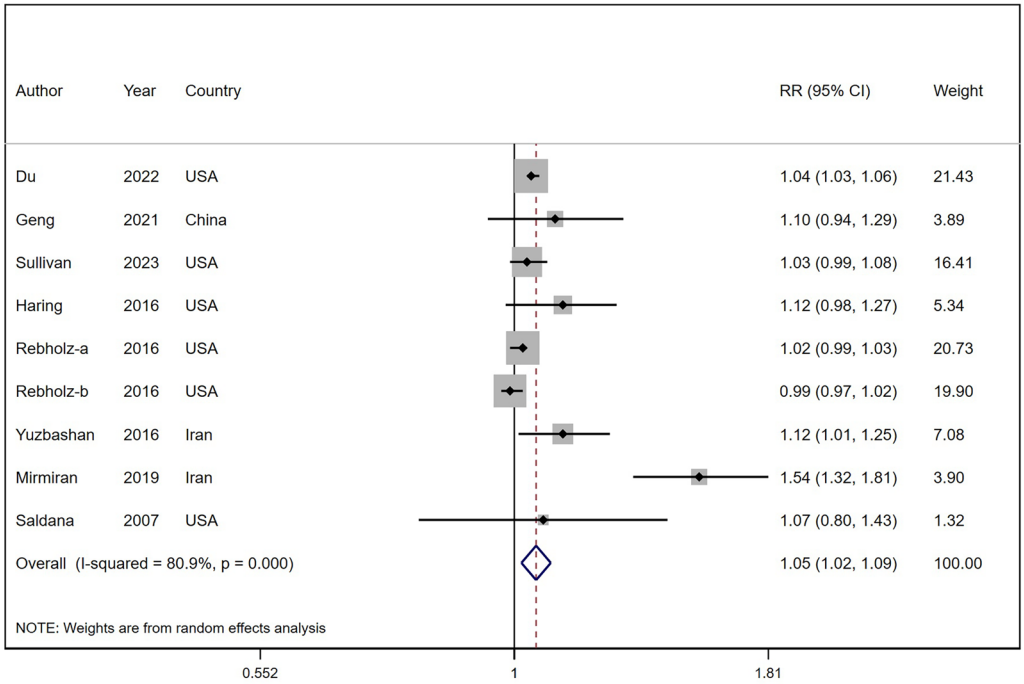

Fig. 3 Forest plots showing the linear dose–response meta-analysis of mortality risk for 100 g change in ultra-processed food consumption in daily intake and risk of chronic kidney disease

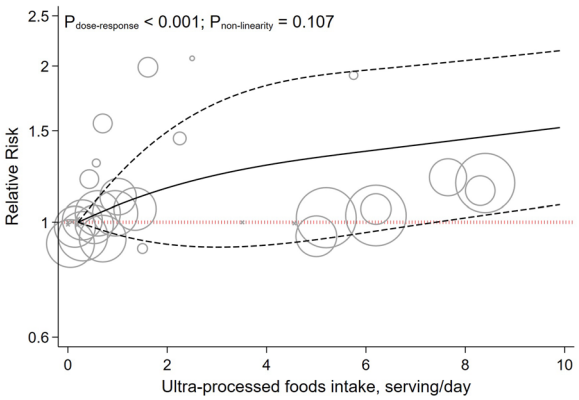

Fig. 4 Non-linear dose–response indicated associations between UPF intake and the risk of chronic kidney disease

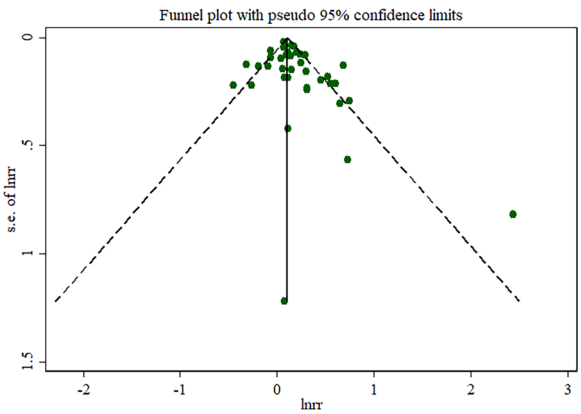

Fig. 5 Funnel plot for evaluation publication bias among studies reported risk of chronic kidney disease

promote chronic inflammatory processes [78, 79]. Furthermore, UPFs are rich in advanced glycation end-products (AGEs), primarily sourced from foods high in animal fats, proteins, and saturated fatty acids subjected to high-temperature cooking methods [80, 81]. AGEs have been associated with oxidative stress and inflammation, mediated through the interaction with the receptor for AGEs (RAGE), leading to an upsurge in pro-inflammatory cytokines production [82, 83]. AGEs also activate several intracellular signaling pathways, including nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), culminating in the augmented synthesis of pro-inflammatory mediators [84, 85].

The impact of food processing on the composition of the gut microbiota has been negatively perceived, with alterations in the gut flora linked to various health conditions, including inflammation [86, 87]. UPFs often contain additives such as emulsifiers, which may influence the gut microbiota composition, contribute to intestinal dysbiosis, augment intestinal permeability, and promote

inflammatory states [88, 89]. Additionally, the existence of non-nutritive constituents like phthalates and bisphenol, derived from food packaging materials, has been associated with augmented concentrations of inflammatory cytokines [90].

The role of obesity in CKD etiology is further supported by the observation of elevated leptin levels, a pro-inflammatory adipokine more abundant in obese individuals, which correlates with reduced renal function and increased CKD risk [91, 92]. Moreover, the intricate link between obesity and insulin resistance is noteworthy, as insulin resistance is a known risk factor for CKD [93]. Insulin resistance and ensuing hyperinsulinemia lead to a cascade of pathophysiological events including albuminuria, glomerular hyperfiltration, impaired endothelial function, oxidative stress and enlarged vascular permeability [94–96]. Moreover, gut dysbiosis related with obesity can promote kidney dysfunction by inducing inflammation [97]. It is also worth noting that the Renin–Angiotensin–Aldosterone System (RAAS) components circulate at elevated levels in obese individuals. Key actors within the RAAS, including aldosterone and Ang II, have been previously shown to induce hypertension that is one of the risk factor for CKD [98, 99].

The association between UPFs intake and CKD may be clarified by different pathways. Elements within UPFs, such as excessive sodium, sugar and additives, may propel progression of CKD. Prior meta-analytic work established a significant correlation between heightened sodium consumption and increased risk of CKD [100]. Excessive sodium consumption increases oxidative stress and protein excretion through urine, harming the kidneys and vascular structures [101, 102]. Moreover, consuming UPFs like processed meats and colas can inadvertently raise the intake of inorganic phosphate as an additive [103]. Dietary overconsumption of phosphates can accelerate kidney function decline [104] and heighten blood pressure, another CKD risk factor [105]. Animal studies have further showcased the dangers of high phosphorus intake, linking it to vascular and renal system calcifications, as well as renal tubular injuries [106]. Furthermore, packaging materials of some UPFs are known to contain endocrine-disrupting chemicals (EDCs) such as Bisphenol A, with studies illustrating the correlation between elevated Bisphenol A levels and kidney disease indicators [107]. EDCs can also contribute to the inflammatory markers elevation [90], emphasizing their role as a CKD risk predictor [108]. Additionally, excessive simple sugar consumption has been implicated in the deterioration of renal function through the promotion of dyslipidemia, insulin resistance, hyperglycemia, oxidative stress and increased uric acid levels [109–112].

The current systematic review and dose–response meta-analysis has several strengths. Among these is the comprehensive examination of the relationship between UPF intake and CKD by analyzing all available observational data. Moreover, this review is underpinned by a meticulously devised and transparent methodological framework, characterized by a highly systematic and reproducible search strategy that rigorously adhered to predetermined inclusion and exclusion criteria and conformed to the PRISMA guidelines. Additionally, a dose–response analysis was conducted to elucidate the association between UPF dosage and the risk of CKD, thereby providing a detailed understanding of how differential consumption rates might impact CKD risk. In line with the rigorous criteria we deployed, a review of the high-quality investigations and the large number of participants included (786,216 participants) suggests a robust foundation for the conclusions of this investigation. Furthermore, the included studies were adjusted for multiple potential confounders. Despite the inherent limitations associated with observational studies, this analysis considered a majority of prevalent confounders, including age, sex, body mass index (BMI), energy intake, educational levels, smoking status, among others. An additional strength of this systematic review and meta-analysis is the absence of evidence indicating publication bias, which lends further credence to the validity of our findings.

However, it is important to take into account the following limitations when interpreting the current outcomes. One included study, conducted in Taiwan [59], presented an unusually high RR value of 11.43. Despite its notable deviation, this investigation contributed only 0.14 to the overall weight of the analysis, indicative of its relatively small sample size. To assess the impact of this outlier, we conducted a sensitivity analysis by excluding the Taiwanese study from our meta-analysis. The results remained consistent with our main findings, thereby indicating that this outlier does not substantially alter the overall conclusions. We have accounted for between-study heterogeneity by employing a random-effects model, which ensures that variations across studies, including extreme estimates like this, do not disproportionately influence the pooled effect size. Additionally, the reliance on self-reported dietary data in many nutritional epidemiological studies presents inherent challenges, chief among them the possibility of recall bias. Several of the investigations integrated into our analysis employed the FFQ, a tool not specifically tailored to measure UPFs consumption. The FFQ's lack of detailed descriptions for certain foods means there is potential for inadvertent misclassification of some food items. This limitation could result in the underestimation of actual

UPF intake. Furthermore, the methodology employed in data collection, notably the usage of dietary assessment tools such as FFQs or 24-h dietary recalls, critically influences the research outcomes concerning the relationship between UPFs and health outcomes, including CKD. FFQs, by asking respondents to report their usual food intake over an extended period, typically the preceding year, are advantageous for assessing long-term dietary patterns. However, the accuracy of these recollections is susceptible to recall bias. Conversely, 24-h dietary recalls, which require participants to detail their food and beverage intake over the prior 24 h, provide more precise information on specific food items and quantities but may not accurately embody habitual dietary intake. The variation in accuracy of these dietary assessment tools can significantly affect the elucidated relationship between CKD and diet. Opting for a combined approach in these tools, along with conducting studies of longer duration that utilize these methods more frequently, may offer a more accurate depiction of dietary consumption patterns than shorter-duration studies with fewer measurement instances. Moreover, in a cross-sectional study, dietary records collected during the measurement period of study may not adequately represent the usual dietary pattern of the respondents.

A further limitation of the current research was the inability to conduct subgroup analyses by CKD status and stages, as the datasets procured from the included studies lacked the requisite detail to differentiate between CKD stages or to reliably contrast individuals with versus without CKD. It is also imperative to note that while the included studies took into account various confounding factors, one must remain vigilant to the possibility of residual confounders influencing the outcomes. Moreover, although the current meta-analysis study encompassed a large population, ethnicity as an important factor that can affect the eating habits and vulnerabilities to CKD was not considered. These types of studies are inherently limited in their capacity to establish causal associations. As such, there is a pressing need for more methodologically rigorous interventional investigations to decisively establish any causal impact.

Conclusion

The results of this meta-analysis reveal a significant association between the consumption of UPFs and an increased incidence of CKD. Specifically, for each additional serving of UPFs consumed daily, there is a 5% increase in the likelihood of developing CKD. Subgroup analyses further underscore key patterns: cohort studies show stronger relationships than cross-sectional designs, and investigations using the NOVA classification and Western diet patterns exhibit more robust correlations. Geographical variations were also evident, with studies conducted in the U.S. and Asia showing a stronger association than those from Europe. Moreover, larger studies with over 1000 participants demonstrated more consistent results.

Clinically, these findings underscore the potential health risks associated with high consumption of UPFs and suggest that dietary interventions focusing on reducing UPF intake could be an effective strategy for lowering CKD risk. This is especially relevant for populations that are already at higher risk, such as those who are overweight or obese. Healthcare professionals should consider these results when advising patients on dietary choices, particularly in regions where UPFs are heavily consumed. Furthermore, the distinct relationships identified in specific subgroups highlight the importance of tailored dietary recommendations that consider individual and regional dietary patterns. The significant impact of diet on CKD risk also supports the need for public health initiatives aimed at improving food quality and accessibility to healthier food choices.

Given the robust associations found in diverse populations and dietary patterns, it is crucial to continue research in this area. Future observational studies should expand to include a wider range of ethnicities, geographical regions and stages of CKD. Employing more precise tools to accurately assess UPF intake will further elucidate the relationship between diet and CKD, paving the way for more effective prevention and management strategies.

Supplementary Information

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Supplementary 1.
Supplementary 2.
Supplementary 3.
Supplementary 4.
Supplementary 5.
Supplementary 6.

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Author contributions
SM and ST designed this research. MA-HK, MZ and PA contributed to the conduct of the search. SM and ST performed the statistical analysis and interpreted the outcomes. SM, SM-GH, Sanaz Merabani, and MA-HK wrote the initial manuscript. AW and FH-A critically revised the manuscript and contributed to the subsequent drafts of the manuscript. All authors approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval
This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication
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Competing interests
The authors declare no competing interests.

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