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REVIEW ARTICLE

Ultra-processed foods and cancer risk: from global food systems to individual exposures and mechanisms

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Ultra-processed foods (UPFs) have become increasingly dominant globally, contributing to as much as 60% of total daily energy intake in some settings. Epidemiological evidence suggests this worldwide shift in food processing may partly be responsible for the global obesity epidemic and chronic disease burden. However, prospective studies examining the association between UPF consumption and cancer outcomes are limited. Available evidence suggests that UPFs may increase cancer risk via their obesogenic properties as well as through exposure to potentially carcinogenic compounds such as certain food additives and neoformed processing contaminants. We identify priority areas for future research and policy implications, including improved understanding of the potential dual harms of UPFs on the environment and cancer risk. The prevention of cancers related to the consumption of UPFs could be tackled using different strategies, including behaviour change interventions among consumers as well as bolder public health policies needed to improve food environments.

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BACKGROUND

Food systems in high-income countries, such as Canada, Australia, the United States and the United Kingdom, became dominated by packaged, ready-to-consume, ultra-processed foods (UPFs) from the second half of the twentieth century onwards [1]. UPFs are also increasingly displacing traditional food cultures in middle-income countries [1–8]. The growth in UPFs consumption which contributes to as much as 25–60% of total daily energy intake, depending on the region [9–14], has been increasingly linked with the global obesity epidemic. Positive associations between increased UPF volume sales/capita and population-level Body Mass Index (BMI) trajectories worldwide have been reported [15]. UPF intake has been associated with greater increases in adiposity from childhood to early adulthood [16] and a greater risk of overweight and obesity in adults [17–23]. Recent data highlight associations between high UPF consumption and health outcomes, including a higher risk of hypertension, type 2 diabetes, cardiovascular diseases and depressive symptoms [24–29]. The consumption of UPFs has also shown marked socio-economic patterning with important implications for its potential impacts on health inequalities [30]. Although research investigating associations between the consumption of UPFs and cancer risk is still very limited, recent results from the French NutriNet-Santé cohort support the association between high consumption of UPFs and the risk of developing overall cancer and breast cancer [31]. Different potential pathways have been suggested, with the primary one the high energy density and low nutritious value of many UPFs. However, the increase in UPF intake may also increase the potential risk for exposures to contaminants or other potential carcinogenic components, including certain additives such as Titanium dioxide (TiO_2), that has been commonly used in UPFs and is no longer considered safe for humans health according to more recent evidence [32].

It is of paramount importance to better understand the potential role of ultra-processing on the cancer burden globally. Therefore, we undertook a review with the aim to describe and appraise published articles about the relationship between the consumption of ultra-processed foods and cancer risk, including potential and probable biological mechanisms and the role of the global food system in this suggested relationship.

FOOD PROCESSING IN THE GLOBAL FOOD SYSTEM

Our ancestors faced difficulties in obtaining and preserving foods. Since then, humans have sought to ensure food availability and security as well as food safety through different means, tools and technologies. Nowadays, food processing plays an important role in ensuring a safe, functional and nutritional food supply [33]. Food processing can enable food preservation to avoid spoilage and foodborne illness. It can also enhance the palatability of food as well as food diversity leading to better taste, improved digestibility and bioavailability of nutrients. Additionally, it ensures transportation stability through heat (e.g. appertisation) or cold treatment (4 °C, freezing −18 °C) and allows the production of pre-prepared meals saving time and energy that cooking requires [34].

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Technological developments and the industrialisation and globalisation of the food system, however, have changed the purpose of processing over the last decades. Industrialised processes, the use of additives and preservatives and packaging allow food manufacturers to massively produce a wide variety of highly palatable foods with long shelf lives from cheap ingredients [6]. The profitability and convenience of these highly processed foods which are usually high-calorie and of low nutritional value, has made them widely available and consumed, replacing traditional diets that are mainly composed of a variety of fresh or minimally processed foods. As a consequence, a profound change in food purchasing and consumption patterns has been observed globally [35, 36].

Highly processed foods are part of a large and complex system [37, 38] that not only covers production and consumption but the whole food supply chain (from "farm to fork"). Several actors and their interlinked value-adding activities are involved in the production, aggregation, processing, packaging, distribution (transport, retail and food services), cooking, consumption and disposal of these food products [35]. By considering the entire food system we are better positioned to understand issues related to processed foods and to address them in a more integrated way.

FOOD PROCESSING CLASSIFICATION FRAMEWORKS AND DEFINITIONS

In line with this, recently several food processing frameworks have been developed, radically transforming how we think about the relationship between diet and health. Examples of new food processing frameworks are the NOVA system, the International Food Information Council and the Food Standards Australian New Zealand [39–41]. Although most of them make similar basic food classifications as processed or unprocessed, those with more levels of classifications seem to be more useful for tracking changes in the food supply and for assessing health outcome associations [40].

The NOVA system has been endorsed by the World Health Organization (WHO) and the Food and Agriculture Organization and is most widely accepted and used in scientific studies [42, 43]. The development of the NOVA classification in 2009 also coined the term ultra-processed foods (UPFs), defined as «*industrially-derived food and drink formulations of chemical compounds which, beyond substances of common culinary use, include substances derived from foods but not used in culinary preparations, such as hydrogenated fats, and cosmetic additives added to make it more palatable or appealing (such as flavours, sweeteners, emulsifiers) and are packed using sophisticated packaging usually of synthetic materials* » [44, 45]. Examples of ultra-processed foods are processed meats (reconstituted meat products or sausage, ham and other meat products), carbonated soft drinks, packaged bread and buns, sweet or savoury packaged snacks, chocolate and ready-to-eat-meals.

ULTRA-PROCESSED FOODS AND CANCER RISK: EPIDEMIOLOGICAL EVIDENCE

Since the food processing frameworks have been only recently developed [39–41], the majority of evidence for the association between ultra-processed foods intake and cancer risk comes from epidemiological studies evaluating the association between intake of specific food groups and cancer risk. In 2018, the World Cancer Research Fund's (WCRF) continuous update project (CUP), the world's largest source of scientific research on cancer prevention and survivorship through diet, nutrition and physical activity, reviewed the latest global research on how diet affects the risk of developing cancer, including methods of preservation and processing of food [46]. Findings from this review suggest there is strong evidence that consuming processed meat increased the risk of colorectal cancer. There is also convincing evidence suggesting that higher consumption of cantonese-style salted fish increases the risk of nasopharyngeal cancer and of foods preserved by salting increase the risk of stomach cancer; however, these may be considered as processed foods instead of ultra-processed foods depending on the food classification [42]. It was also reported that alcoholic drinks are strong risk factors for mouth, pharynx and larynx cancers; oesophageal cancer; breast cancer; colorectal cancer; stomach cancer; liver cancer and kidney cancer. The evidence suggests that alcoholic drinks of all types have a similar impact on cancer risk [42].

UPF intake has been associated with a greater risk of overweight and obesity in many epidemiological studies [16–23], and in turn obesity has been linked to the risk of various cancers in the WCRF report [46]. This led to some cancer prevention recommendations by the WCRF related to ultra-processed foods, for example, to limit the consumption of sugary drinks and of processed foods high in fat, starches or sugar (e.g. 'fast foods'; many pre-prepared dishes, snacks; bakery foods and desserts; and confectionery), due to their contribution to weight gain, overweight and obesity [46]. In line with this, a recent systematic review, published in 2018, assessing the associations between dietary sugars and lifestyle-related cancer risk from longitudinal studies, reported that added sugars and sugary beverages may increase cancer risk [38]. Similarly, in 2019, an analysis conducted within the French NutriNet-Santé cohort ($N = 101,257$ participants) reported a positive association between consumption of sugary drinks and risk of overall cancer (Hazard ratio (HR) for a 100 mL/d increase: 1.18; 95% confidence interval (CI) 1.10–1.27) and breast cancer (HR: 1.22; 95% CI 1.07–1.39) [47]. Higher sugary drink intake has also been associated with early-onset of colorectal cancer (≥7 vs. <1 drinks/week, Odds ratio (OR): 2.99; 95% CI 1.57–5.68) in a population-based case-control study conducted in Ontario, Canada during 2018–2019 [48].

Recent review studies aiming to assess the association between ultra-processed foods intake as defined by the NOVA framework and health outcomes, identified two studies related to cancer risk [49, 50]. One of the studies was conducted within the French NutriNet-Santé cohort ($N = 104,980$ participants) and examined the association between UPF intake and risk of overall, breast, prostate and colorectal cancers [31]. Findings from this study suggested that a 10-point increment in the proportion of UPFs consumed in the diet was associated with a 12% (95% CI 1.06–1.18) higher risk of overall cancer and an 11% (95% CI 1.02–1.22) higher risk of breast cancer, while no association was observed for colorectal and prostate cancers [31]. Conversely, a 10-point increment in the proportion of "minimally/unprocessed foods" in the diet was inversely associated with overall cancer risk (HR: 0.91; 95% CI 0.87–0.95) and breast cancer risk (HR: 0.42; 95% CI 0.19–0.91) [31]. The second one was a case-control study conducted with 59 cases of breast cancer and 59 matched controls in Brazil [51]. Findings from this study suggested higher UPF intake was associated with an increased risk of breast cancer (OR: 2.35; 95% CI 1.08–5.12).

Less consistent associations between UPF consumption and cancer have been identified in more recent studies. A study using data from the Multicentric population-based case-control study (MCC-Spain) conducted in 12 Spanish provinces, including individuals with diagnoses of colorectal ($n = 1852$), breast ($n = 1486$) or prostate cancer ($n = 953$), and population-based controls ($n = 3543$), observed only a positive association between UPFs intake and colorectal cancer risk (OR for an increment of 10% in consumption: 1.11; 95% CI 1.04–1.18), while no statistically significant associations were observed for breast and prostate cancers [52]. Another study conducted within MCC-Spain (230 cases and 1634 population-based controls) found no association between UPF intake and chronic lymphocytic leukemia [53].

However, when the results were restricted to cases diagnosed within <1 year, a positive association was observed (OR of 10% increment: 1.22; 95% CI 1.02–1.47). The authors argued this may indicate people change their diet habits after cancer diagnoses.

The PROtEuS study also assessed the association between dietary intake, based on the extent of food processing, and prostate cancer risk [54]. The study was conducted in Montreal between 2005 and 2012 with 1919 prostate cancer cases and 1991 controls. Findings from this study suggested higher prostate cancer risk was associated with higher intake of processed foods (OR: 1.29, 95% CI 1.05–1.59; highest vs. lowest quartile), but not with the consumption of ultra-processed food and drinks.

Although prospective studies examining the association between UPF consumption and cancer outcomes are still limited, the current evidence suggests UPFs intake may increase the risk for specific cancers. However, conflicting results were observed, which may reflect differences in methodology for defining and classifying UPFs. Most recent studies have used the NOVA framework to classify food intake, which has been subject to some criticism for being imprecise, vague and qualitative [55]. However, recently published work has sought to address these criticisms and improve the consistent application of the NOVA classification in future studies [42]. It is paramount that future studies investigate the association between UPF intake and cancer risk following a valid and standardised food classification framework, facilitating comparison with other studies.

POTENTIAL BIOLOGICAL MECHANISMS LINKING ULTRA-PROCESSING OF FOODS WITH CANCER RISK

Ultra-processed foods intake may hypothetically increase cancer risk through obesogenic properties as well as through exposure to food additives and contaminants. Several studies have confirmed that UPFs can have a poorer dietary quality when compared to minimally processed foods [9–14]. Diets rich in UPFs tend to be higher in energy density, free sugar and overall fat content, saturated fat and trans-fat content, as well as lower in fiber, protein, sodium and potassium [9–13]. According to Hall and collaborators [56], individuals that consume a diet rich in UPFs tend to eat more calories and gain more weight when compared to an unprocessed diet. In this study, the excess of calories came mainly from carbohydrates and fats; which shows up the hyperpalatability and attractiveness of UPF products. In fact, diets rich in UPFs have been associated with obesity [17–20], an established risk factor for at least 13 cancer sites, including colorectal and breast cancers mentioned previously to be associated with cancer risk [29, 30, 38].

Food contaminants, such as neoformed processing contaminants, have also been suggested as potential mechanisms linking UPFs to higher cancer risk. Foods in their natural form go through different types of transformations (chemical, biological and physical) to generate the final processed product. Throughout these operations, reactions occur and the chemical structure of the food changes, inducing the creation of neoformed processing contaminants, such as trans-fat and acrylamide (derived from the heat-inducing reactions between the amino group of the amino acid asparagine and carbonyl groups of glucose and fructose) [57]. Recent evidence has shown a positive link between higher industrial trans-fat intakes and cancer risk [37, 58, 59]. Other neoformed processing contaminants may also be created, such as heterocyclic amines, polycyclic aromatic hydrocarbons, oxyhalides and haloacetic acids, which have also been linked to cancer risk [60].

Certain 'indirect' contaminants may also be found in UPFs, such as substances derived from food packaging. Indeed, it has been reported that food contact materials are an underestimated source of contaminants that could have potential endocrine-disrupting effects [61]. For example, the urinary concentrations of Di(ethylhexyl) phthalate (DEHP), an endocrine-disruptor chemical widely used as a plasticiser [62], have been positively associated with ultra-processed food consumption [63]. Both human and animal studies have indicated that exposure to DEHP may induce cancer through multiple molecular signals, including DNA damage [64]. A recent study also suggested that exposure to DEHP may promote colon cancer metastasis by increasing cancer stemness [65]. Similarly, exposure to bisphenol-A (BPA), another endocrine-disrupting chemical used in a variety of food packaging [66, 67] has been suggested to increase cancer risk [68]. BPA exposure has been shown to deregulate signalling pathways implicated in head and neck cancers [69].

Ultra-processed foods may also contain an extensive list of additives such as preservatives and cosmetic additives (e.g. dyes and emulsifiers) [44]. Although all food additives used in food production are evaluated and authorised for general safety, their cumulative effect on long-term human health remains largely unknown (most literature is currently derived from animal/cellular experimental models). Several food additives have been suggested to have carcinogenic properties in experimental studies [70–72]. Sodium nitrate, for example, is currently used by manufacturers to preserve processed meat and poultry meats. Some studies suggested that this compound may increase cancer risk [73] due to formation of certain nitroso-compounds that could yield carcinogenic nitrosamines [74]. A meta-analysis of 49 studies also showed an increased risk of gastric cancer among those with higher intakes of nitrites (OR: 1.31; 95% CI, 1.13–1.52) and nitrosamines (OR: 1.34; 95% CI, 1.02–1.76) [75]. Supporting this, there is currently evidence suggesting that processed meat intake increases colorectal cancer risk, with stronger associations for colon cancer [46]. Similarly, titanium dioxide (TiO_2), which has been commonly used as a preservative to improve texture and as a colouring agent in UPFs, is no longer considered safe when used as a food additive according to more recent evidence [32]. It has been suggested to be a possible carcinogen to humans [76] and to promote gene expression changes in the colon in mouse models [77]. Another area of concern is the effect of artificial sweeteners on cancer risk, which is still controversial. Although the European Food Safety Authority has declared aspartame, the most commonly used artificial sweetener, as safe to human health [78], other studies still suggest carcinogenic potential of aspartame [70]. Additionally, some emulsifiers have been postulated to promote inflammation in the gut [79], a metabolic alteration also associated with cancer aetiology [80].

Alcoholic drinks, more specifically the distillated drinks, are also considered ultra-processed drinks and have been consistently associated with cancer development [46]. There's a large body of experimental evidence suggesting that acetaldehyde, a toxic metabolite of alcohol has carcinogenic properties, as it disrupts DNA synthesis and repair [46, 81]. Other potential underlying mechanisms involve the oxidative stressed induced by ethanol consumption and its probable function as a solvent for cellular penetration of carcinogens [82, 83].

Many epidemiological studies investigating associations between ultra-processed food intake and health outcomes have adjusted for nutritional quality [27, 28, 31], suggesting that other characteristics of UPFs may be contributing to associations found. However, residual confounding cannot be ruled out and further research is needed to confirm this. Although the precise mechanisms underlying the relationship between UPF consumption and certain cancers are not completely understood, current evidence suggests UPFs may increase cancer risk, possibly via obesogenic, alcoholic intake and dietary quality factors, as well as non-nutritional food processing compounds.

THE GLOBAL FOOD SYSTEM, ULTRA-PROCESSED FOOD CONSUMPTION AND CANCER RISK

The global food system [35, 37, 38] plays an important role in driving growth in UPF production and consumption and associated cancer

risk. While the relationship between the food system and cancer risk is complex, here we discuss two hypothesised pathways. The first potential pathway is the environmental pathway. Food industries are now capable, due to advanced technologies, to increase their production of UPF products by exploiting finite environmental resources: the land is used extensively to meet the needs through non-environmentally friendly agriculture practices such as overuse of pesticides and deforestation. Globalisation of UPFs threatens the local food cultures and culinary traditions. It endangers animal/plant biodiversity. Mega production of ingredients to produce cheap UPF jeopardize small scale farmers and shifts agriculture towards monoculture. Those products require longer transport distances which worsen global warming. In addition, UPFs are known to have sophisticated and attractive packaging, contributing to an important source of plastic waste. This overproduction puts the material resources under pressure and leads to increased air, water and land pollution. These environmental changes and exposures are known to negatively impact people's health, including their risk of developing cancer [84, 85].

A second potential pathway is the consumption pathway. UPFs are characterised by their hyperpalatability and attractiveness due to different factors: their hyper-palatable nutrient profile (e.g. high energy, salt, sugar and low in fibers and vitamins minerals), the use of cosmetic additives (e.g. colours and taste enhancers) and their attractive packaging. These UPFs properties alongside the UPFs' extensive marketing and cheap prices are resulting in increased energy consumption coming from UPFs worldwide [86–88], increasing obesity [6, 43] and associated cancer risk worldwide [46, 89]. The increase in UPF intake may also increase the potential risk for exposures to contaminants or other potential carcinogenic components, including certain additives that may no longer be considered safe for humans health, for example, Titanium dioxide (TiO_2) [32]. In line with this, it has been suggested that between 30 and 50% of all cancers can be prevented by avoiding exposure to environmental pollution and improving healthy lifestyles [46]. This highlights the importance of public health policies promoting environments that are conducive to health to reduce the burden of cancer.

POLICY ACTIONS

Public health authorities in Brazil, Uruguay, Ecuador, Peru, France and Canada have included specific recommendations to limit UPFs in their national dietary guidelines [4]. Recommendations from the Food and Agriculture Organization [43] and the World Cancer Research Fund [46] state that people should aim to limit their consumption of UPFs and replace those foods with minimally processed foods options, such as fruit and vegetables, whole grains and beans and drink mostly water and unsweetened drinks in order to reduce their risk for cancer and other chronic diseases. While minimising consumption of UPFs should be the principal goal, food reformulation may have a modest role to play to reduce their harms. This includes limiting the generation of compounds with potential adverse health effects (e.g. acrylamide and nitrosamines), which could potentially assist in the transition from ultra-processed food environment towards healthier food environments driven by fresh and minimally processed foods. According to recent evidence, new technologies could potentially also be leveraged for the development of healthier processed foods that are environmentally friendly [90–92] and at the same time beneficial for our human health through an improved nutritional composition of foods and reduced contamination levels of suggested toxic components [65, 66]. Nevertheless, any benefits that could be realised from reformulation need strong oversight from governments and other authorities as there is an established evidence base that voluntary agreements with industry for product reformulations are ineffective [4, 93–96]. Other potential public policies and actions involve restricting the widespread marketing promotion of UPFs and support of cooperative, small and family farmers and producers of fresh foods, which may ensure that healthy foods and freshly prepared meals are affordable by and available to all [44]. Policies should be developed and assessed on their effectiveness to reduce both the health and environmental harms of UPFs [97].

RESEARCH GAPS AND NEEDS

Although results from previously published studies assessing the associations between UPF intake and cancer risk suggest a positive association, they need to be confirmed in future cohort studies and in different settings. Some conflicting results were observed, which may reflect the lack of standardisation on the definition and classification of UPFs. Future studies should aim to use a valid and standardised food processing classification framework, facilitating comparison with other studies and the consideration of the entire food system. Improved understanding about which mechanisms may explain associations between food processing and cancer risk is needed. There is also a need for studies investigating the associations between lower degrees of food processing and cancer risk. Longitudinal data with repeated dietary intake measurements may also advance understanding of the effect of changes in the degree of food processing in our diets and cancer risk. There is also a lack of studies testing the potential mediation effect of each factor (overconsumption and weight gain, dietary quality, contaminants related to food processing, food additives etc.) in the associations between UPFs intake and cancer risk. Short-term dietary interventions and substitution analysis assessing the replacement of specific groups (e.g. processed meat by a minimally processed meat) will also be relevant to inform public health recommendations.

Further research is warranted to better understand the role of chemical compounds in the association between UPFs and cancer risk, since epidemiological studies have reported inconsistent findings so far. This is the case with nitrates and nitrite [98], and artificial sweeteners [99], for example. Furthermore, additional studies are needed to understand the chemical structural changes in the food matrix and additives when exposed to physical, chemical and enzymatic reactions during processing. Synergistic effects between multiple additives in the same product should also be explored. This synergistic effect can be explored via in vivo/in vitro experiments, and it can also be investigated through collecting detailed ultra-processed food consumption data. Additionally, discovering biological markers related to each additive can be a promising method since it avoids the memory bias and social desirability found in reporting the quantity of UPF consumed [100, 101]. In order to gather causality arguments, targeted experimental studies are urgently needed to investigate not only the additives effect but also the effect of all the suggested putative mechanisms involved in these associations between cancer risk and the consumption of UPFs.

Last but not least, we should not lose sight of the fact that the global food system can have an important role in this association. More studies are needed to explore the effect of UPFs on food sustainability. To date, many studies tackle the effect of diets on food system sustainability, but few take into consideration the repercussion of the processing degree of diets on our environment [1].

CONCLUSIONS

In conclusion, the current epidemiological evidence, although still limited, suggests a positive association between UPFs and the risk of some cancers. More population-based and experimental studies are needed to confirm these associations. The potential mechanisms underlying these associations are not completely clear, but they may involve the obesogenic properties of UPFs, alcohol

intake and the exposure to potentially carcinogenic compounds such as certain food additives and neoformed processing contaminants. The global food system plays an important role by promoting overconsumption of UPFs and through the environmental impact of their production (e.g. monocultures, pesticides, pollution and global warming), which may in turn increase cancer risk.

While growing evidence indicates that reducing the consumption of ultra-processed foods should be an integral component of cancer prevention strategies in public health, further research is needed to understand the best way to achieve this. However bold fiscal and regulatory action which reduces the widespread access, affordability and attractiveness of these products are likely to be needed to reduce the global burden of non-communicable diseases, including the cancer burden.

DISCLAIMER

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer /World Health Organization.

DATA AVAILABILITY

Not applicable.

REFERENCES

1. Popkin BM. Global nutrition dynamics: the world is shifting rapidly toward a diet linked with noncommunicable diseases. Am J Clin Nutr. 2006;84:289–98.
2. El Kinany K, Mint Sidi Deoula M, Hatime Z, Boudouaya HA, Huybrechts I, El Asri A, et al. Consumption of modern and traditional Moroccan dairy products and colorectal cancer risk: a large case control study. Eur J Nutr. 2020;59:953–63.
3. Deoula MS, El Kinany K, Huybrechts I, Gunter MJ, Hatime Z, Boudouaya HA, et al. Consumption of meat, traditional and modern processed meat and colorectal cancer risk among the Moroccan population: a large-scale case-control study. Int J Can. 2020;146:1333–45.
4. Baker P, Machado P, Santos T, Sievert K, Backholer K, Hadjikakou M, et al. Ultra-processed foods and the nutrition transition: Global, regional and national trends, food systems transformations and political economy drivers. Obes Rev. 2021;21:e13126.
5. Popkin BM. Measuring the nutrition transition and its dynamics. Public Health Nutr. 2021;24:318–20.
6. Monteiro CA, Moubarac J-C, Cannon G, Ng SW, Popkin B. Ultra-processed products are becoming dominant in the global food system. Obes Rev. 2013; 14:21–8.
7. Baker P, Friel S. Food systems transformations, ultra-processed food markets and the nutrition transition in Asia. Glob Health. 2016;12:80.
8. Vilar-Compte M, Burrola-Méndez S, Lozano-Marrufo A, Ferré-Eguiluz I, Flores D, Gaitán-Rossi P, et al. Urban poverty and nutrition challenges associated with accessibility to a healthy diet: a global systematic literature review. Int J Equity Health. 2021;20:40.
9. Cediel G, Reyes M, Corvalán C, Levy RB, Uauy R, Monteiro CA. Ultra-processed foods drive to unhealthy diets: evidence from Chile. Public Health Nutr. 2020; 27:1–10.
10. Steele EM, Popkin BM, Swinburn B, Monteiro CA. The share of ultra-processed foods and the overall nutritional quality of diets in the US: evidence from a nationally representative cross-sectional study. Popul Health Metr. 2017;14:15.
11. Rauber F, da Costa Louzada ML, Steele EM, Millett C, Monteiro CA, Levy RB. Ultra-processed food consumption and chronic non-communicable diseases-related dietary nutrient profile in the UK (2008–2014). Nutrients. 2018;9:10.
12. Moubarac JC, Batal M, da Costa Louzada ML, Steele EM, Monteiro CA. Consumption of ultra-processed foods predicts diet quality in Canada. Appetite. 2017;1:512–20.
13. da Costa Louzada ML, Ricardo CZ, Steele EM, Levy RB, Cannon G, Monteiro CA. The share of ultra-processed foods determines the overall nutritional quality of diets in Brazil. Public Health Nutr. 2018;21:94–102.
14. Machado PP, Steele EM, Levy RB, Sui Z, Rangan A, Woods J, et al. Ultra-processed foods and recommended intake levels of nutrients linked to non-communicable diseases in Australia: evidence from a nationally representative cross-sectional study. BMJ Open. 2019;9:e029544.
15. Vandevijvere S, Jaacks LM, Monteiro CA, Moubarac JC, Girling-Butcher M, Lee AC, et al. Global trends in ultraprocessed food and drink product sales and their association with adult body mass index trajectories. Obes Rev. 2019;20:10–19.
16. Chang K, Khandpur N, Neri D, Touvier M, Huybrechts I, Millett C, et al. Association between childhood consumption of ultraprocessed food and adiposity trajectories in the avon longitudinal study of parents and children birth cohort. JAMA Pediatr. 2021;14:e211573.
17. Juul F, Martinez-Steele E, Parekh N, Monteiro CA, Chang VW. Ultra-processed food consumption and excess weight among US adults. Br J Nutr. 2018;120:90–100.
18. Mendonca RD, Pimenta AM, Gea A, de la Fuente-Arrillaga C, Martinez-Gonzalez MA, Lopes AC, et al. Ultraprocessed food consumption and risk of overweight and obesity: the University of Navarra Follow-Up (SUN) cohort study. Am J Clin Nutr. 2016;104:1433–40.
19. Rauber F, Chang K, Vamos EP, da Costa Louzada ML, Monteiro CA, Millett C, et al. Ultra-processed food consumption and risk of obesity: a prospective cohort study of UK Biobank. Eur J Nutr. 2020;60:2169–80.
20. Canhada SL, Luft VC, Giatti L, Duncan BB, Chor D, Fonseca M, et al. Ultra-processed foods, incident overweight and obesity, and longitudinal changes in weight and waist circumference: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Public Health Nutr. 2020;23:1076–86.
21. Canella DS, Levy RB, Martins APB, Claro RM, Moubarac J-C, Baraldi LG, et al. Ultra-processed food products and obesity in Brazilian households (2008-2009). PLoS ONE. 2014;9:e92752.
22. Beslay M, Srour B, Méjean C, Allès B, Fiolet T, Debras C, et al. Ultra-processed food intake in association with BMI change and risk of overweight and obesity: a prospective analysis of the French NutriNet-Santé cohort. PLoS Med. 2020;17:1003256.
23. Nardocci M, Leclerc B-S, da Costa Louzada ML, Monteiro CA, Batal M, Moubarac J-C. Consumption of ultra-processed foods and obesity in Canada. Can J Public Health. 2018;110:4–14.
24. Lavigne-Robichaud M, Moubarac J-C, Lantagne-Lopez S, Johnson-Down L, Batal M, Laouan Sidi EA, et al. Diet quality indices in relation to metabolic syndrome in an Indigenous Cree (Eeyouch) population in northern Québec, Canada. Public Health Nutr. 2018;21:172–80.
25. Mendonca RD, Lopes AC, Pimenta AM, Gea A, Martinez-Gonzalez MA, Bes-Rastrollo M. Ultra-processed food consumption and the incidence of hypertension in a Mediterranean cohort: The Seguimiento Universidad de Navarra Project. Am J Hyper. 2017;30:358–66.
26. Srour B, Touvier M. Processed and ultra-processed foods: coming to a health problem? Int J Food Sci Nutr. 2020;6:653–5.
27. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Debras C, Druesne-Pecollo N, et al. Ultraprocessed food consumption and risk of type 2 diabetes among participants of the NutriNet-Santé Prospective Cohort. JAMA Intern Med. 2020;2:283.
28. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Méjean C, Andrianasolo RM, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). BMJ. 2019;365:l1451.
29. Adjibade M, Julia C, Alles B, Touvier M, Lemogne C, Srour B, et al. Prospective association between ultra-processed food consumption and incident depressive symptoms in the French NutriNet-Sante cohort. BMC Med. 2019;17:78.
30. Baraldi LG, Steele EM, Canella DS, Monteiro CA. Consumption of ultra-processed foods and associated sociodemographic factors in the USA between 2007 and 2012: evidence from a nationally representative cross-sectional study. BMJ Open. 2018;8:e020574.
31. Fiolet T, Srour B, Sellem L, Kesse-Guyot E, Allès B, Méjean C, et al. Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort. BMJ. 2018;360:k322.
32. EFSA. Titanium dioxide: E171 no longer considered safe when used as a food additive. 2021. https://www.efsa.europa.eu/en/news/titanium-dioxide-e171-no-longer-considered-safe-when-used-food-additive.
33. Cole MB, Augustin MA, Robertson MJ, Manners JM. The science of food security. npj Sci Food. 2018;2:14.
34. Knorr D, Watzke H. Food processing at a crossroad. Front Nutr. 2019;6:85.
35. Food and Agriculture Organization of the United Nations (FAO). Sustainable Food Systems. Concept and framework. 2021. http://www.fao.org/3/ca2079en/CA2079EN.pdf.
36. Stuckler D, Nestle M. Big food,food systems, and global health. PLoS Med. 2012; 9:e1001242.
37. Michels N, Specht IO, Heitmann BL, Chajès V, Huybrechts I. Dietary trans-fatty acid intake in relation to cancer risk: a systematic review and meta-analysis. Nutr Rev. 2020;79:758–76.

38. Makarem N, Nicholson JM, Bandera EV, McKeown NM, Parekh N. Consumption of whole grains and cereal fiber in relation to cancer risk: a systematic review of longitudinal studies. Nutr Rev. 2016;74:353–73.
39. Bleiweiss-Sande R, Chui K, Evans EW, Goldberg J, Amin S, Sacheck J. Robustness of food processing classification systems. Nutrients. 2019;11:1344.
40. Crino M, Barakat T, Trevena H, Neal B. Systematic review and comparison of classification frameworks describing the degree of food processing. Nutr Food Technol. 2017;3:1–12.
41. Moubarac J-C, Parra DC, Cannon G, Monteiro CA. Food classification systems based on food processing: significance and implications for policies and actions: a systematic literature review and assessment. Curr Obes Rep. 2014;3:256–72.
42. Monteiro CA, Cannon G, Levy RB, Moubarac JC, da Costa Louzada ML, Rauber F, et al. Ultra-processed foods: what they are and how to identify them. Public Health Nutr. 2019;22:936–41.
43. Popkin BM. Ultra-processed foods' impacts on health. Santiago de Chile: Food and Agriculture Organization of the United Nations; (2030: Food, Agriculture and rural development in Latin America and the Caribbean). 2019. Report No.: 34.
44. Monteiro CA. Ultra-processed foods, diet quality, and health using the NOVA classification system. Rome: FAO: 2019.
45. Moodie R, Stuckler D, Monteiro C, Sheron N, Neal B, Thamarangsi T, et al. Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. Lancet. 2013;381:670–9.
46. World Cancer Research Fund/ American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. 2021. https://www.wcrf.org/wp-content/uploads/2021/02/Summary-of-Third-Expert-Report-2018.pdf.
47. Chazelas E, Srour B, Desmetz E, Kesse-Guyot E, Julia C, Deschamps V, et al. Sugary drink consumption and risk of cancer: results from NutriNet-Santé prospective cohort. BMJ. 2019;366:l2408.
48. Chang VC, Cotterchio M, De P, Tinmouth J. Risk factors for early-onset colorectal cancer: a population-based case–control study in Ontario, Canada. Cancer Causes Control. 2021;32:1063–83.
49. Pagliai G, Dinu M, Madarena MG, Bonaccio M, Iacoviello L, Sofi F. Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. Br J Nutr. 2021;125:308–18.
50. Elizabeth L, Machado P, Zinöcker M, Baker P, Lawrence M. Ultra-processed foods and health outcomes: a narrative review. Nutrients. 2020;12:1955.
51. Queiroz SA, de Sousa IM, Silva FRM, Lyra CO, Fayh APT. Nutritional and environmental risk factors for breast cancer: a case-control study. Sci Med. 2018;28:287239.
52. Romaguera D, Fernández-Barrés S, Gracia-Levadán E, Vendrell,. E, Azpiri M, Ruiz-Moreno E, et al. Consumption of ultra-processed foods and drinks and colorectal, breast and prostate cancer. Clin Nutr. 2021;40:1537–45.
53. Solans M, Fernández-Barrés S, Romaguera D, Benavente Y, Marcos-Gragera R, Gracia-Lavedan E, et al. Consumption of ultra-processed food and drinks and chronic lymphocytic leukemia in the MCC-spain study. Int J Environ Res Public Health. 2021;18:5457.
54. Trudeau K, Rousseau M-C, Parent M-É. Extent of food processing and risk of prostate cancer: The PROtEuS Study in Montreal, Canada. Nutrients. 2020;12:637.
55. Fardet A, Rock E. Ultra-processed foods: a new holistic paradigm? Trends Food Sci Technol. 2019;93:174–84.
56. Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, 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.
57. Friedman M. Acrylamide: inhibition of formation in processed food and mitigation of toxicity in cells, animals, and humans. Food Func. 2015;6:1752–72.
58. Yammine S, Huybrechts I, Biessy C, Dossus L, Aglago EK, Naudin S, et al. Dietary and circulating fatty acids and ovarian cancer risk in the European prospective investigation into cancer and nutrition. Cancer Epidemiol Biomark Prev. 2020;29:1739–49.
59. Matta M, Huybrechts I, Biessy C, Casagrande C, Yammine S, Fournier A, et al. Dietary intake of trans fatty acids and breast cancer risk in 9 European Countries. BMC Med. 2021;19:81.
60. Pouzou JG, Costard S, Zagmutt FJ. Probabilistic assessment of dietary exposure to heterocyclic amines and polycyclic aromatic hydrocarbons from consumption of meats and breads in the United States. Food Chem Toxicol. 2018;114:361–74.
61. Muncke J. Endocrine disrupting chemicals and other substances of concern in food contact materials: an updated review of exposure, effect and risk assessment. J Steroid Biochem. 2011;127:118–27.
62. Chen ML, Chen JS, Tang CL, Mao IF. The internal exposure of Taiwanese to phthalate-an evidence of intensive use of plastic materials. Environ Int. 2008;34:79–85.
63. Buckley JP, Kim H, Wong E, Rebholz CM. Ultra-processed food consumption and exposure to phthalates and bisphenols in the US National Health and Nutrition Examination Survey, 2013-2014. Environ Int. 2019;131:105057.
64. Caldwell JC. DEHP: genotoxicity and potential carcinogenic mechanisms-a review. Mutat Res. 2012;751:82–157.
65. Chen HP, Lee YK, Huang SY, Shi PC, Hsu PC, Chang CF. Phthalate exposure promotes chemotherapeutic drug resistance in colon cancer cells. Oncotarget. 2018;9:13167–80.
66. Carwile JL, Ye X, Zhou X, Calafat AM, Michels KB. Canned soup consumption and urinary bisphenol A: a randomized crossover trial. JAMA. 2011;306:2218–20.
67. Adeyi AA, Babalola BA. Bisphenol-A (BPA) in Foods commonly consumed in Southwest Nigeria and its Human Health Risk. Sci Rep. 2019;9:17458.
68. Seachrist DD, Bonk KW, Ho SM, Prins GS, Soto AM, Keri RA. A review of the carcinogenic potential of bisphenol A. Reprod Toxicol. 2016;59:167–82.
69. Emfietzoglou R, Spyrou N, Mantzoros CS, Dalamaga M. Could the endocrine disruptor bisphenol-A be implicated in the pathogenesis of oral and oropharyngeal cancer? Metabolic considerations and future directions. Metabolism. 2019;91:61–9.
70. Soffritti M, Padovani M, Tibaldi E, Falcioni L, Manservisi F, Belpoggi F. The carcinogenic effects of aspartame: The urgent need for regulatory re-evaluation. Am J Ind Med. 2014;57:383–97.
71. Proquin H, Jetten MJ, Jonkhout MCM, Garduno-Balderas LG, Briede. JJ, de Kok TM, et al. Gene expression profiling in colon of mice exposed to food additive titanium dioxide (E171). Food Chem Toxicol. 2018;111:153–65.
72. Abnet CC. Carcinogenic food contaminants. Cancer Invest. 2007;25:189–96.
73. Goldman R, Shields PG. Food mutagens. J Nutr. 2003;133:965S–973S.
74. Sindelar JJ, Milkowski AL. Sodium nitrite in processed meat and poultry meats: a review of curing and examining the risk/benefit of its use. 2016. http://info-nitrites.fr/wp-content/uploads/2016/06/nitrite_report.pdf.
75. Song P, Wu L, Guan W. Dietary nitrates, nitrites, and nitrosamines intake and the risk of gastric cancer: a meta-analysis. Nutrients. 2015;7:9872–95.
76. IARC. Carbon Black, Titanium Dioxide, and Talc. International Agency for Research on Cancer; 2010. pp. 1–413. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans).
77. Bettini S, Boutet-Robinet E, Cartier C, Coméra C, Gaultier E, Dupuy J, et al. Food-grade TiO2 impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon. Sci Rep. 2017;7:40373.
78. EFSA Panel on Food Additives and Nutrient Sources Added to Food. Scientific Opinion on the re-evaluation of aspartame (E 951) as a food additive. EFSA J. 2013;11:3496.
79. Viennois E, Bretin A, Dubé PE, Maue AC, Dauriat CJG, Barnich N, et al. Dietary emulsifiers directly impact adherent-invasive E. coli gene expression to drive chronic intestinal inflammation. Cell Rep. 2020;33:108229.
80. Viennois E, Merlin D, Gewirtz AT, Chassaing B. Dietary emulsifier–induced low-grade inflammation promotes colon carcinogenesis. Cancer Res. 2017;77:27–40.
81. Seitz HK, Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. Nat Rev Cancer. 2007;7:599–612.
82. Albano E. Alcohol, oxidative stress and free radical damage. Proc Nutr Soc. 2006;65:278–90.
83. Boffetta P, Hashibe M. Alcohol and cancer. Lancet Oncol. 2006;7:149–56.
84. Alsaffar AA. Sustainable diets: the interaction between food industry, nutrition, health and the environment. Food Sci Technol Int. 2016;222:102–11.
85. Fardet A, Rock E. Ultra-processed foods and food system sustainability: what are the links? Sustainability. 2020;12:6280.
86. Moubarac J-C, Martins AP, Claro RM, Levy RB, Cannon G, Monteiro CA. Consumption of ultra-processed foods and likely impact on human health. Evidence from Canada. Public Health Nutr. 2013;16:2240–8.
87. Poti JM, Mendez MA, Ng SW, Popkin BM. Is the degree of food processing and convenience linked with the nutritional quality of foods purchased by US households? Am J Clin Nutr. 2015;101:1251–62.
88. Slimani N, Deharveng G, Southgate DAT, Biessy C, Chajès V, van Bakel MME, et al. Contribution of highly industrially processed foods to the nutrient intakes and patterns of middle-aged populations in the European Prospective Investigation into Cancer and Nutrition study. Eur J Clin Nutr. 2009;63:S206–225.
89. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K, et al. Body fatness and cancer-viewpoint of the IARC working group. N Engl J Med. 2016;375:794–8.
90. Poore J, Nemecek T. Reducing food's environmental impacts through producers and consumers. Science. 2018;360:987–92.
91. McClements DJ, Barrangou R, Hill C, Kokini JL, Ann Lila. M, Meyer AS, et al. Building a resilient, sustainable, and healthier food supply through innovation and technology. Annu Rev Food Sci Technol. 2020;12:1–28.
92. Ozyurt VH, Ötles S. Effect of food processing on the physicochemical properties of dietary fibre. Acta Sci Pol Technol Aliment. 2016;15:233–45.

93. Seferidi P, Millett C, Laverty AA. Industry self-regulation fails to deliver healthier diets, again. BMJ. 2021;372:m4762.
94. Scrinis G. Reformulation, fortification and functionalization: Big Food corporations' nutritional engineering and marketing strategies. J Peasant Stud. 2016;43:17–37.
95. Scrinis G, Monteiro CA. Ultra-processed foods and the limits of product reformulation. Public Health Nutr. 2018;21:247–52.
96. Laverty AA, Kypridemos C, Seferidi P, Vamos EP, Pearson-Stuttard J, Collins B, et al. Quantifying the impact of the Public Health Responsibility Deal on salt intake, cardiovascular disease and gastric cancer burdens: interrupted time series and microsimulation study. J Epidemiol Community Health. 2019;73:881–7.
97. Seferidi P, Scrinis G, Huybrechts I, Woods J, Vineis P, Millett C. The neglected environmental impacts of ultra-processed foods. Lancet Planet Health. 2020;4:e437–8.
98. Xie L, Mo M, Jia H-X, Liang F, Yuan J, Zhu J. Association between dietary nitrate and nitrite intake and site-specific cancer risk: evidence from observational studies. Oncotarget. 2016;7:56915–32.
99. Singh N, Singh Lubana S, Arora S, Sachmechi I. A study of artificial sweeteners and thyroid cancer risk. J Clin Med Res. 2020;12:492–8.
100. Gultekin F. Food additives of public concern for their carcinogenicity. J Nutriton Health Food Sci. 2015;3:1–6.
101. Chazelas E, Deschasaux M, Srour B, Kesse-Guyot E, Julia C, Alles B, et al. Food additives: distribution and co-occurrence in 126,000 food products of the French market. Sci Rep. 2020;10:3980.

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NK, AAN and IH conceived the content of the paper and wrote the paper. EPV, MT, EKG, MJG and CM critically reviewed it.

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Not applicable.

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ADDITIONAL INFORMATION

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