Cite this article:
Khandpur, N., Geleijnse, J.M., Kamphuis, C.B.M. *et al.* The validity and utility of Nova and the concept of ultra-processed foods for science and policy. *Nature Food* (2026). https://doi.org/10.1038/s43016-026-01371-8

Ultra-Processed Diet as a Distinct Dietary Exposure: Addressing Common Critiques to Underscore the Reliability, Validity and Utility of Nova and Ultra-Processed Foods for Science and Policy

Neha Khandpur[1,2,3]*, Johanna M. Geleijnse[1,] Carlijn B.M Kamphuis[4], Elizabeth Velema[5], Maartje P. Poelman[6], Rik Eshuis[7], Sanne K. Djojosoeparto[6], Marcel Verweij[8], Alyssa Moran[9,10]

[1] Division of Human Nutrition and Health, Wageningen University, Wageningen, the Netherlands
[2] Center for Epidemiological Research in Nutrition and Health, University of Sao Paulo, Sao Paulo, Brazil
[3] Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, US
[4] Department of Interdisciplinary Social Science, Utrecht University, Utrecht, the Netherlands
[5] Netherlands Nutrition Centre, the Hague, the Netherlands
[6] Chair group Consumption and Healthy Lifestyles, Wageningen University & Research, Wageningen, the Netherlands
[7] Department of Industrial Engineering & Innovation Sciences, Eindhoven University of Technology, Eindhoven, the Netherlands
[8] Ethics Institute, Department of Philosophy and Religious Studies, Utrecht University, Utrecht, the Netherlands
[9] Division of Medical Ethics and Health Policy, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, US
[10] Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, US
*Corresponding author [neha.khandpur@wur.nl]

Abstract

In this perspective, we address four critiques of Nova and ultra-processed foods (UPF) common in the public discourse, analyzing their implications for research and policy, and drawing parallels with other dietary exposures and their evidence base. In responding to these critiques, our aim is to underscore the conceptual clarity, validity, utility of the Nova framework and its underlying constructs, encouraging engagement and continued scrutiny for scientific research and policy. UPF represent the aggregate of ready-to-heat/eat products manufactured by the industrial food system. Epidemiology frequently relies on such conceptual categories to elucidate diet-disease relationships, providing precendent for the framework. Operational criteria used to identify UPF for research tend to provide a conservative estimate of true intake – a pattern of misclassification that is likely to bias diet-disease relationships toward the null. As with other aggregated constructs, UPF represents a multidimensional exposure, encompassing variation in nutritional composition, ingredients, processing methods, and additive profiles. This complexity is common and does not diminish the construct's analytic or predictive utility for science or policy. The evidence on the ultra-processed diet complements the evidence from established nutrient-based parameters. The perspective also raises broader questions about where the burden of proof should lie and how responsibility for diet-related disease should be assigned.

Introduction

Nutrition scientists have long acknowledged that the non-nutritive properties of food may impact health. Such properties are inherent to both naturally occurring and industrially produced food. Compared to just a century ago, industrially produced food dominate the current global food supply. Many of these foods have undergone multiple processing techniques (e.g., hydrolysis, extrusion), contain multiple additives (e.g., dyes, non-nutritive sweeteners) not typically used in home cooking, and are packaged using synthetic materials (e.g., plastics). Although there is value in understanding how each processing technique, additive, and material impacts biological processes on its own, these attributes of food never present as isolated exposures – they occurr in combination and the foods that serve as a vector for these exposures are consumed in combination with other foods and over extended periods of time. Thus, measuring the extent to which chronic consumption of industrially produced food and the combination of nutritive and non-nutritive properties they contain impact the risk of disease when compared to naturally occuring food, is a relevant question for nutrition science.

The Nova food classification system was designed to advance this field of scientific inquiry by measuring human exposure to industrially produced food. Nova classifies food into four mutually exclusive groups based on the extent and purpose of their processing, and includes unprocessed or minimally processed food (group 1), processed culinary ingredients (group 2), processed food (group 3) and ultra-processed food and beverages (UPF, group 4) [1]. UPF comprise industrial formulations of refined ingredients and cosmetic additives containing little, if any, whole food [1]. UPF often undergo several chemical and physical processing techniques to extract their ingredients (e.g., hydrolysis, hydrogenation, extrusion, pulverization), combine them (e.g., by using additives, pre-frying, moulding), and package them, often using synthetic materials. Nova groups 1, 2 and 3 (non-UPF groups) form the basis of scratch-cooked meals, while UPF represent their ready-to-heat/eat equivalents. In categorizing groups in this way Nova allows for testing hypothesis on the displacement of freshly prepared, scratch-cooked meals by UPF, and in comparing both their nutritive and their non-nutritive properties.

Epidemiologists apply Nova to categorise food items into mutually exclusive categories. This method can be used with a range of tools including food frequency questionnaires (FFQs), dietary recalls, diet records, or retail sales data [2]. Since 2015, Nova has been applied to dietary data or household purchases in more than 50 countries to quantify human exposure to UPF. Global estimates from sales, household purchases, and dietary intake data suggest that UPF sale and consumption has increased in the past two decades [3, 4]. A large and growing body of evidence demonstrates that a UPF-dominant diet compared to a non-UPF diet is associated with adverse health outcomes, including a higher risk of mortality and cardiometabolic diseases [4, 5]. Yet, many scientists, national governments, and health organizations dismiss the health risks associated with UPF-dominent diets, often arguing that the evidence base is immature, or biologically implausible. A substantial portion of this debate reflects a limited or incomplete understanding of the UPF construct itself. Misinterpretations of what the construct captures - its purpose, scope, and the type of exposure it is designed to represent - promote misplaced critiques of the evidence. Instead of stimulating further research on UPF, such circumspection has the effect, intended or unintended, of undermining the validity and utility of the UPF construct and of constraining future research and innovation. It also slows the development of recommendations and policy measures that would shift dietary patterns toward minimally processed, whole-foods and meals – a shift which is strongly supported by decades of nutrition science and consistently recommended in public health guidance. Delays in advancing such policies not only hinder efforts to improve diets at the population-level but also entrench reliance on food environments and food systems dominated by UPF, and limit the potential for meaningful improvements in health outcomes.

In this perspective, we argue that UPF as defined within Nova is a useful, reliable and valid scientific concept for research and policy and ought to be held to the same standard as other nutritional exposures. We identified critiques of Nova or the concept of UPF, as these were often interlinked, through a multi-method approach that included a scoping review of peer-reviewed literature indexed in PubMed, an examination of position statements and consensus reports issued by scientific committees, and a rapid review of online print journalism available to the general public in the US and Europe. Critiques with similar themes were grouped and synthesized, and their core arguments were distilled. For each argument, the implications for scientific inquiry and policy - often implicit, ambiguous, or entirely absent in the original critique - were systematically inferred and articulated. We discarded some critiques where no implication for science was identified (for instance, the critique that Nova has evolved over time, was discarded). We responded to the critiques by providing a comparative assessment of conceptual coherence and empirical support by drawing parallels with the evidence base for other dietary exposures. This comparison underscores both the precedent, the validity and the scientific utility of the UPF construct and demonstrates that the evidence aligns with - and in several respects exceeds - the standards typically applied to analogous dietary exposure frameworks.

In responding to these critiques, our aim is to provide conceptual clarity, while underscoring the validity, and utility of the Nova framework as well as complementarity to established nutrient-based measures of dietary exposure. We seek to encourage constructive engagement and ongoing scientific scrutiny, both of which are essential for strengthening research, refining methods, and informing evidence-based policy.

Table 1: Responses to the critiques of Nova and the concept of ultra-processed food

Critique	Description of critique	Implications of the critique	Our response to the critique
1. Nova imprecisely differentiates between processing techniques which may lead to misclasification of non-ultra-processed and ultraprocessed foods.	Nova does not precisely nor comprehensively identify the additive compounds and processing techniques, aggregating them instead.	Researchers must rely on proxy indicators to make an ultra-processed food determination and risk misclassifying products. This could bias diet-disease effect estimates.	Nova provides the conceptual framework for distingishing between ready-to-eat/heat products manufactured by the industrial food complex and their less processed scratch-cooked equivalents. Objective proxy markers that are disclosed by manufacturers are used to identify ultra-processed foods. The relability and validity of identifying Nova food groups for research has been well established. Epidemiology frequently relies on such dietary categories to provide valuable insights into the diet-disease relationship.
2. The criteria used to differentiate between ultra-processed food and non-ultra-processed foods are arbitrary, limiting research and policy utility.	Nova categorizes nutritionally diverse products with a wide range of additives as ultra-processed. Also, it does not account for the nutritional similarities between homemade and premade products, often categorizing them in different groups.	Nova has limited utility for research and policy as some foods with balanced nutrient profiles are ultra-processed, and vice versa. Researchers and consumers may incorrectly assume that all ultra-processed foods have similar health effects.	The criteria used to distinguish between ultra-processed foods and non-ultra-processed foods for research is independent of a product's nutrient profile. The nutrient composition of a product alone does not explain all physiological responses, health impacts, preferences, or behavioral patterns. Like other aggregated dietary variables, ultra-processed food reflect a composite exposure with components that vary across multiple dimensions, including nutritional composition. Its value ultimately lies in its demonstrated ability to predict meaningful health outcomes.
3. The biological mechanisms underpinning the health impacts of the ultra-processed diet are unclear and what is known is not unique, raising questions about construct utility.	The biological mechanisms underlying the health impacts from the wide range of additives and processing techniques encompassed within the ultra-processed diet have yet to be elucidated.	Researchers cannot definitively say that "ultra-processing", per se, causes poor health outcomes. Instead it is likely to be the nutrient profile or strucutral changes.	Mechanistic uncertainty does not undermine conceptual validity, predictive utility or epidemiologic consistency. Multiple dietary components, both nutrient-based and non-nutritive, that are excessive or insufficient in the ultra-processed diet relative to a minimally processed diet have been hypothesized to impact health, through several plausible biological pathways acting simultaneously. Some of these dietary components and their biological responses are already known. Others warrant investigation.
4. The evidence of health harms from observational studies is inconclusive, limiting the utility of the ultra-processed food construct to infer causality.	Evidence on the health harms of an ultra-processed diet comes primarily from observational studies.	Researchers cannot make causal determinations about the health harms of an ultra-processed diet, limiting the utility of the construct.	The reliability, validity and utility of a scientific construct are not determined by the limitations of observational evidence. The association between an ultra-processed diet and adverse health outcomes has been consistently replicated across diverse populations with different dietary patterns and socio-demographic characteristics, controlled for possible confounders, and supported by dose-response relationships.

Critique 1. Nova imprecisely differentiates between processing techniques which may lead to misclasification of non-ultra-processed and ultraprocessed foods.

Description of critique 1: Nova does not identify precise additive compounds or processing techniques across the four groups, but rather aggregates them into broad categories (e.g., Nova flags cosmetic additives instead of signalling out specific compounds like synthetic food dye Red 3). Foods must be classified using proxy indicators such as the presence and the primary purpose of a particular additive or processing technique. Additives have multiple uses, and their purposes are not always publicly known, available, or directly measurable. Processing techniques are not required to be listed on food labels. Such broad groupings of additives and processing techniques, and reliance on proxy indicators, make it difficult to accurately and reliably differentiate between non-UPF and UPF [6-9]. The risk of misclassifying foods biases diet-disease estimates and limits Nova's reliability, validity and utility for research and policy.

Our response: Nova provides the conceptual framework for distingishing between ready-to-eat/heat products manufactured by the industrial food complex and their less processed, scratch-cooked equivalents. The relability and validity of identifying Nova food groups for research has been well established, highlighting the utility of the framework. Efforts to establish the relability and validity of identifying Nova food groups for policy are ongoing. There is precedent in nutritional science and epidemiology for characterizing dietary exposures using similar approaches, which supports continued scientific inquiry and efforts for translation into practise and policy.

Nova does not aim to group products according to their precise chemical composition, but to distingish between industrially manufactured ready-to-eat/heat products and their less processed, scratch-cooked equivalents made from processed ingredients, and processed and minimally/unprocessed food. Epidemiological research frequently relies on such functional categories of foods for providing valuable insights into the diet-disease relationship, often aggregating multiple unique compounds that share common attributes into a single exposure. Doing so increases explanatory power, helps scientists communicate health risks to the public, and provides a basis for conceptualizing interventions. Dietary fiber, whole foods, sugary drinks, plant-based foods, red meat, the Mediterranean diet, the Western diet, and the ultra-processed diet are all examples of complex dietary exposures that aggregate many distinct compounds and food items. For each of these exposures, researchers routinely set operational criteria for what to include and exclude (e.g., amount of sugar or calories required for a drink to be sugary), based on several factors including limitations of the diet assessment method and the context. Thus, exposures may be operationalized differently across studies.

Nova clearly defines the concept of UPF and operationalizes the concept for research within Nova. The operational criteria for research is based on the presence of cosmetic additive classes intended to enhance organoleptic properties including the texture, flavor, aroma, mouth-feel and color of the product; and ingredients of rare culinary use like protein isolates that distinguish UPF from processed foods [2]. These proxy markers are currently disclosed by UPF manufacturers. The identification of UPF could be expanded to include other markers, should this information be made available by manufacturers. The iterative approach for reliably identifying UPF - including the need for training and discussion, documenting assumptions for complex food categories with different levels of processing (e.g., mixed dishes or bread) and conservatively identifying UPF only when clear evidence supports the decision (e.g., consistent presence of cosmetic additives), have been previously documented [2,10]. These assumptions have been used to reliably determine UPF exposure from FFQs, 24-hour dietary recalls, diet records, food supply data, and menus. Discrepancies are likely to arise without such approaches, much as they do for all other aggregated dietary and non-dietary exposures [9, 11-14].

The approach for identifying UPFs and other Nova groups has also been validated. By comparing UPF estimates from FFQs - which aggregate foods into broad categories - with those from 24-hour dietary recalls that provide more detailed food item-level information, validation studies have found UPF intakes to be conservative and underestimated [15]. As with other dietary exposures that FFQs were not originally designed to capture, aggregated food categories lose specificity, masking substantial variation (e.g., an FFQ may capture intake of 'whole grain cereals' or 'seafood' but not 'Cornflakes' and 'Cheerios' or 'salmon' or 'prawns'). This limitation, common in nutrition research, is typically addressed using a weighted average of the nutritional composition foods within each FFQ item which, depending on the exposure of interest and context, may be quite heterogenous (e.g., grams of sugar in US varies compared to European whole grain cereals). Estimates of UPF from FFQs may be imprecise but like other nutritional exposures are very useful to rank individuals based on their usual dietary intake (e.g., low' consumers of UPF versus 'high' consumers) [16,17]. Several other studies have demonstrated acceptable reliability, validity and reproducibility of the FFQ in ranking energy intake across Nova groups among adults and children [18-20].

Imprecise Nova group and UPF identification can lead to misclassification errors, which may bias effect estimates towards the null. In large prospective cohort studies of UPF intake, misclassification errors are likely to be non-differential and independent - that is, independent of errors in other variables in the analysis, and unlikely to interact with other sources of systematic errors [21]. Also, the probability of the UPF exposure misclassification is very likely to be independent of the status of the disease, having been determined before disease diagnosis. Such non-differential and independent misclassification errors typically bias estimates of diet-disease associations towards the null [22]. The large sample sizes of observational studies, even with low UPF identification sensitivity (i.e., true UPF misclassified as not being UPF), make it unlikely that results are biased away from the null by chance [23]. The true magnitude of the association is therefore likely to be larger than what is observed [15]. The evidence supporting health harms of a UPF-dominant diet is consistent in direction across research studies using dietary assessment methods more (FFQ) and less (24-hour recalls, diet records) susceptible to misclassification. Therefore, the limitations of the assessment methods used to estimate exposure to UPF are consistent with those of any other dietary exposure, some of which may be even more imprecisely measured but for which we have reached scientific consensus of health harms (e.g., sodium intake and cardiovascular disease) [24, 25].

Nova and the UPF construct also have utility for policy. To regulate a group of products, policymakers must be able to identify them. This requires rules and thresholds to determine whether individual products in the food supply, and products likely to be introduced in the future, are ultra-processed or not. Several approaches of applying Nova to policy have been proposed, and several others may emerge as science on this topic progresses. For example, UPF can be identified based on the presence of additives, dyes, or ingredients belonging to specific classes (e.g., emulsifiers), catalogued by existing regulatory bodies such as Codex. Alternatively, UPF can be identified by the presence of any ingredient not in Nova groups 1-3 (e.g., ingredients other than minimally processed foods, culinary ingredients, preservatives, vitamins, or minerals). These approaches are currently undergoing validation and reliability testing. Critics argue that they will produce borderline cases - for example, a seltzer with natural flavors or a whole grain bread with soy lecithin may be classified as ultra-processed, despite containing very few additives, none of which have been proven harmful. Borderline cases are inevitable when identifying products for regulation, and the precise threshold at which a product becomes harmful is often unknown. For example, the EU defines an alcoholic beverage as any drink containing at least 1.2% ethanol by volume. This means a kombucha with 1.2% ethanol is regulated as alcohol, while a kombucha with 1.1% alcohol is regulated as food. Similarly, the UK identifies drinks for taxation based on their sugar content, where a drink with over 5g sugar per 100mL is taxed, but a drink with 4.9 g/100mL is untaxed. To address this issue, manufacturers of products close to the threshold often reformulate to avoid regulation, or policymakers use exemptions based on a product's specific formulation or intended use. For example, in the U.S., vanilla extract meets the criteria for an alcoholic beverage but is exempt from regulation because it is intended for use in cooking. Similar strategies could be considered for the regulation of UPF, to complement strategies based on nutritional parameters.

Critique 2. The criteria used to differentiate between ultra-processed food and non-ultra-processed foods are arbitrary, limiting research and policy utility.

Description of critique 2: The criteria used to differentiate UPF from non-UPF do not consider a product's nutrient profile, do not account for the extent of industrial processing techniques but consider purpose. For example, an intensive industrial process used for safety such as pasteurization is not considered ultra-processing but adding synthetic flavor to enhance cosmetic appeal is. Two foods with identical nutrient profiles could fall into different Nova groups if one item is prepared at home and another is purchased premade with similar ingredients. Additionally, UPF are heterogenous, with some UPF containing many more additives than others, and some subgroups contributing health-promoting nutrients to the diet (e.g., fibre-rich ultra-processed whole wheat bread). Grouping such diverse products together as UPF may lead researchers and consumers to incorrectly assume that the health effects of all UPF are equivalent, limiting its utility for research and policy [7, 8, 22, 23].

Our response: The operational criteria to delineate UPF from non-UPF for research relies on the presence of cosmetic additive classes and ingredients of rare culinary use. These operational criteria are consistent with the conceptual definition within the Nova framework and would meet the standard for construct validity. This approach of differentiating UPF from non-UPF is processing-based not nutrient-based, and is therefore agnostic to the nutrition composition of the product. Saying that UPF is not a valid construct because some bread that is high in fibre may be UPF, is like saying high sodium is not a valid construct because most bread high in fibre are also high in sodium. The nutrient composition of a product alone does not and cannot explain physiological responses, health impacts, preferences, or behavioral patterns. As with other aggregated variables in scientific research, UPF represent a composite dietary exposure whose constitutents vary across several dimensions including, but not limited to, nutritional composition. The value of an aggregated construct such as UPF ultimately depends on its capacity to predict meaningful health outcomes. Diets high in UPF have consistently been associated with elevated risk across multiple diet-related diseases, underscoring the construct's utility.

A homemade chocolate cookie and an industrially manufactured chocolate cookie may have similar macro- and micro-nutrient compositions but are unlikely to exhibit identical profiles across all their constituent biomolecules. They are also likely to differ in the integrity and organization of their supramolecular and sub molecular structures, reflecting distinct physiochemical architectures that may have divergent digestive, metabolic signalling, and physiological responses, in ways that macro- and micro-nutrient compositions alone cannot capture. These products also demonstrably differ across a range of attributes including availability, time-to-preparation, convenience, price, durability, texture, flavor profile, cosmetic appeal, branding, and marketing. Intake of a UPF cookie means you are less likely to have a non-UPF cookie and in this way UPF displace their non-ultra processed counterparts, altering dietary patterns. These differences in attributes that extend across different scales among seemingly similar products, may have different acute and long-term impacts on preferences, behaviour, physiology and health, and thus represent distinct dietary exposures.

Grouping together UPF of varying nutritional composition and concentration, type, and number of additives (e.g., yogurt with one cosmetic additive like a synthetic fruit flavour and a frozen pizza with four different additive compounds like emulsifiers, modified starch, flavors, coloring agent), also has precedent in nutritional science. All aggregated dietary exposures – from fibre-rich foods, plant-based products, vegan diets, to sugary drinks – similarly combine items that vary in their content and source of the defining ingredient. The category of sugary drinks, for example, groups items with varying amounts and sources of sugars, counting full-sugar soda, flavoured milk, sweetened juice, and lightly sweetened seltzer as part of the same exposure. This pattern is not unique to nutrition; it characterizes all aggregated variables across scientific disciplines and, if conceptualized coherently, serves to improve and not diminish their analytic or predictive utility. What unifies items within a conceptually coherent aggregated construct often has greater explanatory value than the heterogeneity among them. Consistent with this, a large and growing body of evidence demonstrates that a UPF-dominant diet, while heterogeneous, is associated with several adverse health outcomes [4, 5], reinforcing the utility of UPF as a meaningful exposure.

Grouping together UPF yogurt, bread, and soda to represent the ultra-processed diet is not dissimilar from grouping fish, pasta, and red wine because they share characteristics consistent with a Mediterranean eating pattern. The Mediterranean diet includes food categories with divergent nutritional characteristics (e.g., pasta, olive oil), which have been operationalized similarly to the ultra-processed diet for scientific research. Just as a UPF-dominant diet has been shown to be health-harming despite including a variety of foods, the Mediterranean diet has been shown to be health-promoting, even when individual foods that comprise these diets do not confer equivalent health benefits [26-28]. Both diets are informed by observation and theory and have been systematically and extensively tested, adding to our evolving understanding of the links between dietary exposures and disease risk.

Frameworks for regulating a large group of products with varying health risks already exist and could be applied or tailored to UPF. For example, many countries, including the EU and US, regulate tobacco products on a risk continuum. No tobacco product is considered safe for consumption, and these products cannot be sold to youth. However, products belonging to the broad category of “tobacco” are further classified according to risk (e.g., addictiveness, health harms, risk of youth initiation) and regulated accordingly. Combustable tobacco (e.g., cigarettes) is often considered the highest risk category, to which the strictest regulations are applied (e.g., high excise taxes, restrictions on advertising to youth, limits on retail marketing). By contrast, products like nicotine gum or patches, used as cessation aids, are considered lower risk products to which fewer regulations apply. A similar risk-based regulatory structure could be applied to UPF. For example, higher risk UPF like sweetened drinks and meats may be subject to taxes, limits in schools, or marketing restrictions, while lower risk products like unsweetened drinks and whole grain breads may be subject to fewer regulations. Credible and consistent health communication about the UPF construct, as a complementary lens alongside nutrient-based parameters, will be essential across populations and settings.

Critique 3. The biological mechanisms underpinning the health impacts of the ultra-processed diet are unclear and what is known is not unique, raising questions about construct utility.

<u>*Description of critique 3*</u>: People who consume an ultra-processed diet are exposed to a wide range of additives and processing techniques. It is not yet clear how each of the additives, processes, and their interactions alter biological mechanisms underpinning health. Therefore, researchers cannot definitively say that “ultra-processing”, per se, causes poor health outcomes. Rather, it could be other properties common to UPF, such as the nutrient profile, texture, or rate of absorption, that are driving the relationships between the ultra-processed diet and disease [7, 8, 29, 30]. This raises

questions about the additional utility of the UPF construct, beyond what is already known in the field.

Our response: Mechanistic uncertainty is common across the health sciences, and the absence of fully specified biological pathways does not diminish the validity or the analytical and predictive utility of a coherent scientific construct. Smoking was epidemiologically linked to cancer well before biological mechanisms were understood. In the case of the ultra-processed diet, multiple dietary components, both nutrient-based and non-nutritive, that are excessive or insufficient in the ultra-processed diet relative to a minimally processed diet have been hypothesized to impact health, through several plausible biological pathways, acting simultaneously. Some of the changes in dietary components and their biological mechanisms are known. Others warrant investigation. Lack of mechanistic clarity does not undermine the validity of the UPF concept, nor does it invalidate the consistency of the epidemiological findings.

Food contains thousands of unique substances, the health implications of many of which are unknown or incompletely characterized [31-33]. The processing of food alters several dietary components and nutritive and non-nutritive properties, modifying biomolecular composition and structural integrity. These altered dietary components and properties differ between UPFs and non-UPFs. The ultra-processed diet triggers a cascade of biological responses that is likely to be different compared to that from a minimally processed diet. The health effects of diets arise from the simultaneous and chronic influence of multiple biological responses rather than a single causal pathway. Elucidating the biological pathways for industrial additives and processing techniques will be one of the frontiers of this science.

The imbalanced nutritional composition of an ultra-processed diet has been demonstrated in nationally representative samples across several low-, middle- and high-income contexts [38]. Increased UPF intake has been shown to strongly correlate with an increase in free sugars, total fat, and saturated fat, as well as a decrease in fibre, protein, potassium, zinc, magnesium, and several vitamins [38]. The content and type of phytochemicals and bioactive compounds, like glucosinolates, flavonoids, proanthocyanidins, isoflavones, that likely have a protective role in human health [39], also warrant further study. Given that UPF are characterized by the destruction of the original plant-matrix, inter- and intra-cellular water, and the displacement of fresh, whole foods (vegetables and fruit), it is likely that phytochemicals from these sources are lower in the ultra-processed diet compared to a minimally processed diet, although this warrants confirmation.

Another dietary component that is likely to underpin UPF-related health impacts is the increased intake of xenobiotics - compounds not normally found in or metabolized by the human body. Compared to a non-ultra-processed diet, the ultra-processed diet is associated with higher intakes of food additives including non-nutritive sweeteners and emulsifiers, as well as processing- and packaging-related contaminants like acrylamide, phthalates, bisphenols, advanced glycation end-products, microplastics, and per- and polyfluoroalkyl substances (PFAS) [40, 41]. While our understanding of the biological mechanisms and health impacts of this group of compounds continues to evolve, there is emerging evidence to suggest undesirable alterations to the metabolome and microbiome, and inflammatory potential [42, 43]. Newer technologies like targeted metabolomics may help characterize the xenobiotic signature of a UPF-dominant diet and clarify its influence on metabolism and health [43].

We have growing evidence for several hypothesized pathways, consistent with epidemiologic research. First, UPF meals have been shown to increase energy intake through potentially more efficient oral processing and altered neurobiological processing. In randomized controlled trials, people tend to consume more calories through carbohydrates and fats when offered UPF meals (versus minimally processed meals) [34]. They consume more calories when UPF meals are higher in energy density and softer in texture [35]. A combination of refined carbohydrates, fats, and additives found in UPF strongly activate brain reward systems, as seen in neuroimaging studies [36, 37], and may cause symptoms consistent with other substance use disorders (e.g., excessive intake despite negative consequences).

The evolution of our understanding of the differences in dietary components between UPF- and non-UPF diets and their mechanistic underpinning, raises an important question about where the burden of proof should lie: whether public health researchers must continually evaluate the long-term health effects of newly introduced ingredients and processing technologies, or whether food manufacturers should be required to demonstrate, with convincing evidence, that these ingredients and processes - individually and in combination as they are consumed – indeed promote and are safe for long-term health. This tension reflects a broader regulatory challenge in which the pace of innovation in UPF formulation outstrips the generation of independent data, creating an asymmetry between the introduction of novel exposures and the evidence needed to determine their long-term health impact.

Critique 4. The evidence of health harms from observational studies is inconclusive, limiting the utility of the ultra-processed food construct to infer causality.

Description of critique 4: Conclusions about the health effects of the ultra-processed diet are based on observational research. Therefore, it is not possible to make causal determinations about the health harms of this diet [6,7]. This constraint inevitably raises questions about the utility of the UPF construct to infer causality or guide causal interpretations.

Our response: The reliability, validity and utility of a scientific construct are not determined by the limitations of observational evidence. Observational studies can provide strong evidence when associations are consistent across population samples, study designs, data collection instruments, contexts, and are temporally ordered, biologically plausible, and robust to confounding and sensitivity analysis – all of which have been demonstrated by the UPF construct in characterizing the ultra-processed diet exposure.

Every study design, including randomized controlled trials, are limited in their ability to establish causal impacts of long-term dietary patterns in free living individuals, with recruitment, retention, adherance, compliance, baseline diet, being well-known challenges of trials [44]. Imporantly, randomized trials manipulate UPF meals to vary on one or more dimensions under study (ex. texture, eating rate, or emulsifier-load), rather than replicating the complex, self-selected, free-living food choices that characterize the ultra-processed diet in observational studies. Observational data, therefore remains essential for evaluating the long-term health effects of free-living, habitual eating behaviour that cannot be realistically captured by randomized trials. While these data alone cannot establish causality, the association between the ultra-processed diet and adverse health outcomes has been replicated across diverse populations with different dietary patterns and demographic and socio-economic profiles, persists after adjustment for possible confounders, and demonstrates dose-response relationships. The totality of evidence, including some randomized controlled trials, underscores the consistency of the epidemiological findings linking UPF-dominent diets to poorer health.

Alongside triangulation across studies, applying the Bradford Hill criteria of consistency of association, strength, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy [45], can help to gauge the quality of the epidemiological evidence. A recent application of these criteria support the thesis that the ultra-processed diet increases weight gain and elevates risk for several chronic diseases in adults [4]. Besides overweight and obesity, high UPF intake was associated with an increased risk of type 2 diabetes, cardiovascular disease, chronic kidney disease, Crohn’s disease, and all-cause mortality. The consistency in the increased risk across different regions, study designs and data collection instruments; the strength of the increase in risk; the temporality of the association; the dose-response seen; the biological plausibility, coherence with what is currently known about disease pathophysiology, and experimental evidence seen with body weight and fat mass gains, met seven of the nine criteria mentioned [4].

Dietary recommendations are grounded in the highest quality of available evidence, relying heavily on well-designed prospective cohort studies where both associations and potential mediating pathways are studied, and on controlled feeding studies and mechanistic studies that help underpin biological plausibility. This triangulated approach underpins the recommendations promoting the Mediterranean and the Dietary Approaches to Stop Hypertension diets and limiting sugary drink intake, for chronic disease prevention. For instance, the 2025 Dietary Guidelines for Americans’ recommendation on sugary drink intake is based on 58 prospective cohort studies and only eight randomized trials [46]. The burden of proof for the health impacts of a UPF-dominant diet should be held to the same standard applied to other dietary exposures, relying on the convergence of high-quality observational, experimental, and mechanistic evidence.

Conclusion

In this perspective, we argue that the UPF construct, as articulated within the Nova framework, demonstrates coherance, reliability, validity, and scientific utility. UPF represent the aggregate of ready-to-heat/eat products manufactured by the industrial food system, and the conceptual definition of this construct is clear. Epidemiology frequently relies on such conceptual exposure categories to characterize dietary patterns and to elucidate diet-disease relationships. The Nova framework is based on a processing perspective but is similar in its conceptualization and operationalization, further highlighting the complementarity with established nutrient-based parameters. The operational criteria used to identify UPF for research are processing-based and rely on the presence of cosmetic additive classes and of ingredients of rare culinary use. They are aligned with the underlying conceptual definition and are likely to satisfy standard criteria for construct validity.

The application of these operational criteria to distinguish between UPF and non-UPF for research has demonstrated good reliability, with repeated assessments showing agreement across raters, contexts and datasets. Validation studies indicate that these criteria tend to underestimate true UPF intake. Such misclassification errors typically biases diet-disease associations toward the null, implying that observed effect sizes are likely conservative relative to the true magnitude of risk. UPF, like other aggregated constructs in scientific research, represent a composite dietary exposure whose constituent products vary across multiple dimensions, including but not limited to, nutritional composition, ingredient profiles, processing techniques, and additive loads, but which does not diminish its analytic or predictive utility. This multidimensionality is characteristic of many exposure constructs in epidemiology.

The grouping of nutritionally diverse products within the UPF construct, and the operationalization of the UPF exposure in epidemiological research, aligns with established approaches used to classify other complex nutritional exposures and has been shown to reliably characterize dietary patterns. The heterogeneity observed between nutritionally similar UPF and non-UPF items is likely to arise from both microscopic differences - including distinct physical and chemical architectures - and macroscopic distinctions related to convenience, price, durability, and sensory properties. These multidimensional differences make UPFs and non-UPF meaningfully distinct exposure categories, capable of shaping preferences, eating behaviours, and health outcomes in divergent ways that can be scientifically tested.

The reliability of the UPF construct is further reflected in the consistent direction and magnitude of associations observed between the UPF-dominant diet and adverse health outcomes. This consistency has been demonstrated across multiple regions, diverse population samples, different dietary assessment instruments, and varied epidemiologic study designs, indicating a stable and reproducible exposure-outcome relationship. The central issue is therefore not the presence of mechanistic uncertainty - an inherent feature of many areas of nutrition science - but whether such uncertainty meaningfully limits the utility of the UPF construct. Scientific constructs frequently operate under partial mechanistic understanding; their value lies in their capacity to delineate a coherent exposure and to predict health outcomes reliably. The UPF construct functions in this manner: despite internal heterogeneity and ongoing investigation into specific biological pathways, it consistently identifies a pattern of dietary exposure associated with elevated risk of multiple adverse outcomes. In this context, the construct's utility is empirically demonstrated, even as mechanistic research continues to mature.

When held to the same standard as other nutritional exposures and examined in totality, the evidence on the health harms of the ultra-processed diet very much aligns with the evidence on the health impacts of other diets, food groups and nutrients, providing sufficient grounds for precautionary public health guidance, as with other dietary risks. The debate about the health harms of the ultra-processed diet also raises a broader question about the appropriate allocation of the burden of proof: whether public-health researchers should be expected to continually assess the long-term effects of food innovations, or whether food manufacturers should be required to demonstrate that these products, individually and in combination as consumed, are safe for chronic intake. This debate also invites scrutiny on how responsibility for health and risk of diseases is allocated. If UPF as a category are associated with substantially elevated risk of disease, as current evidence suggests, then responsibility cannot rest solely with individual consumers. UPF-related manufacturers, retailers, and governments, should accept shared responsibility to reduce these risks. How this responsibility is allocated is a matter for societal discussion.

*****

References

1. Monteiro, C. A., Cannon, G., Levy, R. B., Moubarac, J. C., Louzada, M. L., Rauber, F., ... & Jaime, P. C. (2019). Ultra-processed foods: what they are and how to identify them. Public health nutrition, 22(5), 936-941.
2. Martinez-Steele, E., Khandpur, N., Batis, C., Bes-Rastrollo, M., Bonaccio, M., Cediel, G., ... & Monteiro, C. A. (2023). Best practices for applying the Nova food classification system. Nature Food, 4(6), 445-448.
3. Baker, P., Machado, P., Santos, T., Sievert, K., Backholer, K., Hadjikakou, M., ... & Lawrence, M. (2020). Ultra-processed foods and the nutrition transition: Global, regional and national trends, food systems transformations and political economy drivers. Obesity Reviews, 21(12), e13126.
4. Monteiro, C. A., Louzada, M. L., Steele-Martinez, E., Cannon, G., Andrade, G. C., Baker, P., ... & Touvier, M. (2025). Ultra-processed foods and human health: the main thesis and the evidence. The Lancet, 406(10520), 2667-2684.
5. Lane, M. M., Gamage, E., Du, S., Ashtree, D. N., McGuinness, A. J., Gauci, S., ... & Marx, W. (2024). Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. bmj, 384.
6. USDA (2025). Scientific Report of the 2025 Dietary Guidelines Advisory Committee. Accessed from https://www.dietaryguidelines.gov/sites/default/files/2024-12/Scientific_Report_of_the_2025_Dietary_Guidelines_Advisory_Committee_508c.pdf, November 2025
7. Astrup, A., & Monteiro, C. A. (2022). Does the concept of "ultra-processed foods" help inform dietary guidelines, beyond conventional classification systems? NO. The American Journal of Clinical Nutrition, 116(6), 1482-1488.

8. Lockyer, S., Spiro, A., Berry, S., He, J., Loth, S., Martinez-Inchausti, A., ... & Stanner, S. (2023). How do we differentiate not demonise–Is there a role for healthier processed foods in an age of food insecurity? Proceedings of a roundtable event. Nutrition bulletin, 48(2), 278-295.
9. Braesco, V., Souchon, I., Sauvant, P., Haurogné, T., Maillot, M., Féart, C., & Darmon, N. (2022). Ultra-processed foods: how functional is the NOVA system?. European Journal of Clinical Nutrition, 76(9), 1245-1253.
10. Khandpur, N., Rossato, S., Drouin-Chartier, J. P., Du, M., Steele, E. M., Sampson, L., ... & Sun, Q. (2021). Categorising ultra-processed foods in large-scale cohort studies: evidence from the Nurses' Health Studies, the Health Professionals Follow-up Study, and the Growing Up Today Study. Journal of Nutritional Science, 10, e77.
11. Du, M., Mozaffarian, D., Wong, J. B., Pomeranz, J. L., Wilde, P., & Zhang, F. F. (2022). Whole-grain food intake among US adults, based on different definitions of whole-grain foods, NHANES 2003–2018. The American journal of clinical nutrition, 116(6), 1704-1714.
12. Franz, M., & Sampson, L. (2006). Challenges in developing a whole grain database: Definitions, methods and quantification. Journal of Food Composition and Analysis, 19, S38-S44.
13. Trichopoulou, A., Martínez-González, M. A., Tong, T. Y., Forouhi, N. G., Khandelwal, S., Prabhakaran, D., ... & de Lorgeril, M. (2014). Definitions and potential health benefits of the Mediterranean diet: views from experts around the world. BMC medicine, 12, 1-16.
14. Sweeting, H. N. (2007). Measurement and definitions of obesity in childhood and adolescence: a field guide for the uninitiated. Nutrition journal, 6(1), 32.
15. Loftfield, E., Zhang, P., O'Connell, C. P., Kahle, L. L., Herrick, K., Abar, L., ... & Hong, H. G. (2025). Performance of a food frequency questionnaire for estimating ultra-processed food intake according to the Nova classification system in the US NIH-AARP Diet and Health Study. The Journal of Nutrition.
16. Willett, W. C. L. E. (1998). Reproducibility and validity of food-frequency questionnaires. Nutritional epidemiology.
17. Saravia, L., Moliterno, P., Skapino, E., & Moreno, L. A. (2022). Food diary, food frequency questionnaire, and 24-hour dietary recall. In Basic Protocols in Foods and Nutrition (pp. 223-247). Springer US.
18. Fangupo, L. J., Haszard, J. J., Leong, C., Heath, A. L. M., Fleming, E. A., & Taylor, R. W. (2019). Relative validity and reproducibility of a food frequency questionnaire to assess energy intake from minimally processed and ultra-processed foods in young children. Nutrients, 11(6), 1290.
19. Jung, S., Park, S., & Kim, J. Y. (2022). Comparison of dietary share of ultra-processed foods assessed with a FFQ against a 24-h dietary recall in adults: results from KNHANES 2016. Public Health Nutrition, 25(5), 1166-1175.
20. Sneed, N. M., Ukwuani, S., Sommer, E. C., Samuels, L. R., Truesdale, K. P., Matheson, D., ... & Heerman, W. J. (2023). Reliability and validity of assigning ultraprocessed food categories to 24-h dietary recall data. The American journal of clinical nutrition, 117(1), 182-190.
21. Jurek, A. M., Greenland, S., Maldonado, G., & Church, T. R. (2005). Proper interpretation of non-differential misclassification effects: expectations vs observations. International journal of epidemiology, 34(3), 680-687.
22. Willett, W. (1989). An overview of issues related to the correction of non-differential exposure measurement error in epidemiologic studies. Statistics in Medicine, 8(9), 1031-1040.
23. Yland, J. J., Wesselink, A. K., Lash, T. L., & Fox, M. P. (2022). Misconceptions about the direction of bias from nondifferential misclassification. American journal of epidemiology, 191(8), 1485-1495.
24. Cobb, L. K., Anderson, C. A., Elliott, P., Hu, F. B., Liu, K., Neaton, J. D., ... & Appel, L. J. (2014). Methodological issues in cohort studies that relate sodium intake to cardiovascular disease outcomes: a science advisory from the American Heart Association. Circulation, 129(10), 1173-1186.
25. Whelton, P. K., Appel, L. J., Sacco, R. L., Anderson, C. A., Antman, E. M., Campbell, N., ... & Van Horn, L. V. (2012). Sodium, blood pressure, and cardiovascular disease: further evidence supporting the American Heart Association sodium reduction recommendations. Circulation, 126(24), 2880-2889.

26. Eleftheriou, D., Benetou, V., Trichopoulou, A., La Vecchia, C., & Bamia, C. (2018). Mediterranean diet and its components in relation to all-cause mortality: Meta-analysis. British Journal of Nutrition, 120(10), 1081-1097.
27. Tapsell, L. C., Neale, E. P., & Probst, Y. (2019). Dietary patterns and cardiovascular disease: insights and challenges for considering food groups and nutrient sources. Current atherosclerosis reports, 21, 1-8.
28. Grosso, G., Marventano, S., Yang, J., Micek, A., Pajak, A., Scalfi, L., ... & Kales, S. N. (2017). A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: are individual components equal?. Critical reviews in food science and nutrition, 57(15), 3218-3232.
29. Scientific Advisory Committee on Nutrition (2025). Processed foods and health: SACN's rapid evidence update summary. Accessed from https://www.gov.uk/government/publications/processed-foods-and-health-sacns-rapid-evidence-update/processed-foods-and-health-sacns-rapid-evidence-update-summary, November 2025.
30. Valicente, V. M., Peng, C. H., Pacheco, K. N., Lin, L., Kielb, E. I., Dawoodani, E., ... & Mattes, R. D. (2023). Ultraprocessed foods and obesity risk: a critical review of reported mechanisms. *Advances in nutrition*, *14*(4), 718-738.
31. Bland, J. S. (2019). The dark matter of nutrition: dietary signals beyond traditional nutrients. Integrative Medicine: A Clinician's Journal, 18(2), 12.
32. Mozaffarian, D. (2021). Nutrition's dark matter of polyphenols and health. Nature Food, 2(3), 139-140.
33. Menichetti, G., Barabási, A. L., & Loscalzo, J. (2025). Chemical Complexity of Food and Implications for Therapeutics. New England Journal of Medicine, 392(18), 1836-1845.
34. Hall, K. D., Ayuketah, A., Brychta, R., Cai, H., Cassimatis, T., Chen, K. Y., ... & Zhou, M. (2019). Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. Cell metabolism, 30(1), 67-77.
35. Lasschuijt, M. P., Heuven, L. A., Gonzalez-Estanol, K., Siebelink, E., Chen, Y., & Forde, C. G. (2025). The effect of energy density and eating rate on ad libitum energy intake in healthy adults—a randomized controlled study. The Journal of nutrition, 155(8), 2602-2610.
36. DiFeliceantonio, A. G., Coppin, G., Rigoux, L., Thanarajah, S. E., Dagher, A., Tittgemeyer, M., & Small, D. M. (2018). Supra-additive effects of combining fat and carbohydrate on food reward. Cell metabolism, 28(1), 33-44.
37. Morys, F., Kanyamibwa, A., Fängström, D., Tweedale, M., Pastor-Bernier, A., Azizi, H., ... & Dagher, A. (2025). Ultra-processed food consumption affects structural integrity of feeding-related brain regions independent of and via adiposity. Metabolic Health and Disease, 3(1), 13.
38. Martini, D., Godos, J., Bonaccio, M., Vitaglione, P., & Grosso, G. (2021). Ultra-processed foods and nutritional dietary profile: a meta-analysis of nationally representative samples. Nutrients, 13(10), 3390.
39. Fahey, J. W., & Kensler, T. W. (2021). Phytochemicals: Do they belong on our plate for sustaining healthspan?. Food Frontiers, 2(3), 235-239.
40. Martínez Steele, E., Khandpur, N., da Costa Louzada, M. L., & Monteiro, C. A. (2020). Association between dietary contribution of ultra-processed foods and urinary concentrations of phthalates and bisphenol in a nationally representative sample of the US population aged 6 years and older. PloS one, 15(7), e0236738.
41. Yates, J., Kadiyala, S., Deeney, M., Carriedo, A., Gillespie, S., Heindel, J. J., ... & Muncke, J. (2024). A toxic relationship: ultra-processed foods & plastics. Globalization and health, 20(1), 74.
42. Chassaing, B., Compher, C., Bonhomme, B., Liu, Q., Tian, Y., Walters, W., ... & Lewis, J. D. (2022). Randomized controlled-feeding study of dietary emulsifier carboxymethylcellulose reveals detrimental impacts on the gut microbiota and metabolome. Gastroenterology, 162(3), 743-756.
43. Muli, S., Blumenthal, A., Conzen, C. A., Benz, M. E., Alexy, U., Schmid, M., ... & Nöthlings, U. (2024). Association of Ultraprocessed Foods Intake with Untargeted Metabolomics Profiles in Adolescents and Young Adults in the DONALD Cohort Study. The Journal of Nutrition, 154(11), 3255-3265.
44. Crichton, G. E., Howe, P. R., Buckley, J. D., Coates, A. M., Murphy, K. J., & Bryan, J. (2012). Long-term dietary intervention trials: critical issues and challenges. Trials, *13*(1), 111.

45. Fedak, K. M., Bernal, A., Capshaw, Z. A., & Gross, S. (2015). Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology. Emerging themes in epidemiology, 12, 1-9.
46. USDA. (2025). Dietary Guidelines Advisory Committee Systematic Reviews. What is the relationship between sugar-sweetened beverage consumption and growth, body composition, and risk of obesity? Accessed from https://nesr.usda.gov/2025-dietary-guidelines-advisory-committee-systematic-reviews/sugar-sweetened-beverages_growth-obesity, November 2025.