

**POSTbrief 59**

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# Health impacts of ultra-processed foods



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## Overview

Ultra-processed foods (UPFs) are classified using the Nova system, which categorises foods based on their level of processing. UPFs are typically ready-to-eat, industrially formulated products containing heavily processed ingredients and additives. These foods cannot be made in a domestic culinary setting. Examples include crisps, ice cream, biscuits, baby formula and plant-based meat alternatives. UPFs are primarily composed of substances derived from foods or additives, with minimal or no intact whole foods, and often contain high levels of saturated fat, salt and sugar.

Some food scientists and nutritionists have raised concerns about the Nova classification system. Nova categorises foods based on formulation and processing levels, which can lead to inconsistencies when compared to other classification systems that focus on nutritional profiling. The broad categories used by Nova can sometimes result in negative perceptions of some UPFs that are nutrient-dense, healthy and affordable.

The consumption of UPFs is highest in English-speaking countries with a 'Western' diet, such as the US, UK and Canada. Intake varies significantly across age and socioeconomic status, with the highest consumption seen among children, urban residents, and individuals from lower socioeconomic backgrounds.

Evidence shows that regular or high consumption of UPFs is associated with poor dietary patterns and an increased risk of negative health outcomes, including obesity, type-2 diabetes, cardiovascular disease, poor mental health and various cancers. Emerging research suggests that UPFs may also affect gut health by interacting with the gut microbiome. However, the role of UPFs in human health is not yet fully understood, and experts call for further research to investigate the mechanisms by which UPFs interact with human biological processes.

This briefing discusses the potential impacts of UPFs on health outcomes and public health. It does not explicitly cover potential policy interventions, considerations, or gaps. It is relevant to note that there is a growing discussion on the relationship between UPFs and environmental impacts.

# 1 Background

Ultra-processed foods (UPFs) are ready-to-eat, industrially formulated products. UPFs are most commonly classified using a food system called *Nova*, developed at the University of Sao Paulo, Brazil, in 2009 by Carlos A. Monteiro.<sup>1-3</sup> UPFs are created by the breakdown of whole foods into smaller components such as sugars, starches and proteins. UPFs have multiple industrial ingredients that are extracted from foods or synthesised in laboratories, while containing little to no whole foods. Formulations of ingredients require a series of processes, using equipment and technology not commonly used in domestic kitchens (see subsection 1.1 below).<sup>1,2</sup>

The consumption of UPFs has steadily increased in the UK in the last two decades.<sup>4</sup> Currently, the UK is the second largest consumer of UPF by daily energy intake (~56%), after the United States (58%). Following the UK is Canada (48%) and Australia (42%).<sup>4-7</sup> Amongst countries that record UPF consumption, Italy has the lowest levels of consumption at ~10%.<sup>7</sup>

Several observational studies have found associations between high consumption of UPFs and harmful health outcomes. These include risk of obesity, cancer, risk of cardiometabolic<sup>a</sup> and cardiovascular disease (CVD) and other non-communicable diseases such as depression.<sup>6,8-12</sup>

Despite these associations, generating the evidence to robustly demonstrate direct causality between UPFs and poor health outcomes remains challenging, and evidence remains limited.<sup>13</sup>

Limited evidence and uncertainties can be due to unknown or complex mechanisms and interactions between UPF ingredients and biological processes. Additionally, there can be inaccuracies and limitations in research design and methodology (See section 'Limitations in research evidence').<sup>14</sup> Most research into diet and nutrition tend to be observational studies, with studies on UPFs mostly being retrospective or prospective cohort and case-control designs, rather than experimental. These methodologies can be prone to biases such as confounding factors<sup>b</sup>, publication and selection bias, which present challenges in nutritional epidemiological studies ([PN718](#)).<sup>15,16</sup>

The UK Government have not formally defined or referred to *Nova* processed food groups and do not refer to UPFs in dietary guidelines or

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<sup>a</sup> Cardiometabolic diseases are a group of common but often preventable conditions including heart attack, stroke, diabetes, insulin resistance and non-alcoholic fatty liver disease. There is a global increase in the number of people who experience one or more of these conditions during their lifetime.

<sup>b</sup> Confounding describes the process by which a variable influences both the exposure (independent variable) and the outcome (dependent variable). Confounding can lead to less accurate estimates of the strength and direction of associations and can make exposures appear associated with the outcome, regardless of a causal effect.

recommendations. The UK uses a 'nutrient profiling model', a scoring system developed by the Foods Standards Agency to help stakeholders differentiate between healthy and unhealthy foods, particularly for marketing restrictions. This system does not use the Nova system.<sup>17-21</sup> The UK Government recognise and classify foods high in fat, sugar and salt (HFSS) as 'less healthy' in policy documents, guidelines and food regulation, for example in the Eatwell guide (2016), the Obesity strategy (2020), reformulation programmes or the soft drinks industry levy (2018) ([CBP-7876](#), [PN718](#), [PN686](#)).<sup>17,19,20,22,23</sup>

In 2023, the UK Government's Scientific Advisory Committee on Nutrition (SACN) carried out an evidence-base review, and produced a report evaluating and assessing the evidence on the health impacts of UPFs and the Nova food classification system.<sup>24</sup> The review raised concerns about the impacts of high consumption of UPFs and its links with unhealthy dietary patterns. The report states that there is still limited evidence explaining the relationship and associations between UPFs and the development specific adverse health outcomes.<sup>24</sup>

## 1.1 Classifications

The Nova system categorises foods based on their degree of processing rather than the nutrient composition.<sup>1-3,25</sup> The Nova system classifies foods into four groups:

- Group 1: unprocessed or minimally processed foods (such as fruit)
- Group 2: processed culinary ingredients (such as butter)
- Group 3: processed foods (such as bacon or tinned fish)
- Group 4: ultra-processed foods (such as crisps, see Table 1 for more)

UPFs are heavily processed foods that cannot be produced from non-culinary ingredients in a domestic setting such as a home kitchen, for example a flavoured carbonated 'fizzy' drink.<sup>3</sup>

UPFs capture foods that have been processed and contain additives including modified substances. Processes for making UPFs can include hydrogenation<sup>c</sup>, hydroxylation<sup>d</sup>, extrusion and moulding and pre-processing for frying.<sup>1,2,28,29</sup> The Nova system does not explicitly state which of or how many of these processes make a food a UPF.

In addition to salt, sugar and fats, other additive ingredients may include non-culinary additives such as preservatives, colours, flavours, enhancers,

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<sup>c</sup>Hydrogenation refers to a process where manufacturers add hydrogen to a liquid fat such as palm oil, to turn it into a solid fat at room temperature<sup>26</sup>

<sup>d</sup> Hydroxylation is a chemical process whereby a hydroxyl organic compound group (oxygen and hydrogen) is added to another compound. This is a common process in food additives for example creating and adding food flavouring.<sup>27</sup>

emulsifiers, thickeners and sweeteners. Modified substances can include modified starches, sugar syrups and hydrogenated oils.<sup>1-3,28</sup> These additives are usually added to imitate the sensory qualities of unprocessed foods or minimally processed foods.<sup>1</sup>

The ingredients and processes for UPFs can make them convenient and attractive due to their long shelf-life and ready-to-eat features.<sup>28</sup> UPFs may be more profitable as they can contain low-cost ingredients, for example modified ingredients from high-yield crops such as corn, soy and wheat, which mass manufacturers can produce in bulk and in a shorter period. Some experts argue that it is also helpful for consumers as the preservatives prolong shelf life and therefore reduce food waste and costs.<sup>13</sup>

In addition to ingredients, ultra-processed foods are different in that they require industrial equipment, ingredient handling, sterilization and quality control, specific commercial packaging and a level of consistency and scale of production.<sup>1</sup>

Examples of UPFs include carbonated 'fizzy' drinks, fruit flavoured drinks, sausages, biscuits, ready-to-heat pizza, burgers and instant noodles. UPFs can be further divided into subgroups, shown in Table.1.<sup>28</sup>

<b>Table 1 Ultra-processed Foods</b>	<b>Food or beverages</b>
<b>Snacks and sweets</b>	
Savoury snacks	Crackers; flavoured popcorns (excluding plain air-popped popcorn); chips (potato/vegetable/corn/tortilla/other); pretzels/snack mix
Sweet bakery products	Ready-to-eat or dry-mixed cakes and pies; cookies and brownies; doughnuts, sweet rolls, and pastries
Sweets	Candies, chocolate, chewing gums
Cereal or nutrition bars	Cereal or nutrition bars (cereal/energy/protein/meal replacement bars)
Ice cream and desserts	Ice creams and other frozen dairy desserts; ready-to-eat or dry mixed dairy desserts (such as pudding); fruit desserts; jellies, jams, and preserves; toppings; gelatine desserts
<b>Sugar-sweetened and diet beverages</b>	
Sugar-sweetened and diet soft drinks	Sugar sweetened and diet soft drinks ('fizzy' drinks)
Fruit drinks and other sweetened drinks	Fruit drinks, sport /energy drinks, nutrition drinks
<b>Ready-to-eat/heat mixed dishes</b>	
Ready-to-eat/heat pizza, sandwiches and burgers	Fast food pizza, pizza prepared from frozen, ready-to-eat/heat sandwiches or burgers (cheeseburger, hamburger or chicken burger)

Other ready-to-eat/heat mixed dishes	Frozen or shelf-stable meat/seafood/poultry/egg mixed dishes, grain based mixed dishes (pasta dishes, rice dishes, macaroni, turnovers, and other)
<b>Industrial grain foods</b>	
Breads, rolls and tortillas	Yeast breads (white/whole wheat/wheat/rye/oat/multigrain bread), rolls, buns, bagels, English muffins, tortillas, pita bread, taco shells (baked) that are not homemade or bought from bakery store
Biscuits, muffins and quick breads	Biscuits, cornbread, muffins, and other quick breads that are not homemade or obtained from bakery stores
Pancakes, waffles and French toasts	Pancakes, waffles and French toasts that are not homemade or obtained from bakery stores
Ready-to-eat breakfast cereals	Ready-to-eat cereals
<b>Flavoured dairy foods and dairy substitutes</b>	
Flavoured milk and flavoured yoghurts	Flavoured milk and flavoured yoghurts
Dairy drinks and dairy substitutes	Milkshake and other dairy drinks, dairy substitutes such as almond milk, coconut milk, soy milk
<b>Other</b>	
Fast-food or reconstituted meat, poultry, and fish products	Fast food meat patties/fried chicken/fish sticks, patties, or fillets; chicken nugget; sausages, ham, lunchmeats; meat spreads; beef/port/other meat jerky
Fast food or pre-prepared potato products	Fast food /pre-prepared /frozen French fries, chips, hash browns, potato puffs, stuffed potatoes
Fats, condiments and sauces	Industrial fats, margarine, light or fat free cream /whipped cream, cream substitutes, light or fat free cream cheese, cheese spread; salad dressings, tomato based/soy-based/other condiments; dips, gravies, and other sauces
Other ultra-processed foods	Including soy products such as meatless patties and fish sticks; sweeteners, and all syrups (excluding 100% maple syrup); distilled alcoholic drinks; baby formula

Source: The NOVA classification, Livingston AS, et al. BMJ Nutrition, Prevention & Health 2021<sup>28</sup>

Some experts in nutrition and food science note that various food classification systems are available and that these could be considered in the



context of UK-based epidemiological research (Box 1).<sup>30</sup> However, the SACN evaluation review (2023) screened the use of other classification systems and identified the Nova system as the most consistent and suitable for use in the UK food context.<sup>24</sup> Additionally, the Food and Agriculture Organization of the United Nations use the Nova classification of food processing.<sup>31</sup>

An academic Portuguese study in 2021 compared five internationally recognised food processing classification systems to assess if results are similar or comparable when studies investigate the proportions of 'UPFs' on the overall diet.<sup>30</sup> The contribution of UPFs was calculated as a percentage of the total available grams/kcals of food consumed per day.

### Box 1 Other food classification systems' categorisation of highly processed foods

- **International Agency for Research on Cancer/European Prospective Investigation into Cancer and Nutrition (IARC-EPIC):** a European cohort study that defines foods of the highest processing level as those that have been "industrially prepared and require no or minimal domestic preparation apart from cooking and heating". The study also classifies foods into 3 groups by level of carcinogenic risk of different foods based on food components and nutrients.<sup>30,32</sup>
- **International Food Policy Research Institute (IFPRI),** developed in 2011, in Guatemala, examines the contribution of processed food products to food supplies in lower-income countries. IFPRI consider highly processed foods as those that have "undergone secondary processing into readily edible form, likely to contain high levels of added sugars, fats or salt".<sup>30,33</sup>
- **International Food Information Council (IFIC),** developed in the US in 2012, determines the contribution of processed foods to nutrient intake in the US diet. The highly processed foods include "mixtures of combined ingredients", "ready-to-eat processed foods" and "prepared foods/meals".<sup>30,34</sup>
- **University of North Carolina (UNC) / SIGA Index,** a system developed by researchers in the US adds further subgroups to the NOVA categories. UNC define highly processed foods as "multi-ingredient industrially formulated mixtures processed to the extent that they are no longer recognizable as their original plant or animal source".<sup>35, 30,32,33,36</sup>

Results show that different food classifications categorise some foods as UPFs and some as not, which may confuse attempts to examine and understand any influence of UPFs on health outcomes.<sup>30</sup> Due to the inconsistencies amongst classifications, the study cautioned that careful interpretation of data is required when comparing food processing categories.

## Use of the term 'UPFs'

Some food scientists discuss the issues around food processing classification systems and their complexity in their relationship with health outcomes. UPFs as a category can be broad, as it captures many foods and focuses on the methods of processing including formulation and ease in preparation.

UPFs as a definition does not include nutritional composition, which may result in difficulties when intending to create appropriate dietary guidelines from research analysis.<sup>13,36</sup>

The level of processing and nutritional content of food are not necessarily related and both can influence an individual's health. For example, plant-based processed food or wholemeal bread are categorised as a UPF while also having a nutritional value that may be considered healthier than other UPFs.<sup>37</sup>

In 2023 a large prospective study (266,666 participants) investigated the risk associated between UPFs and cancer and cardiometabolic disease. It found that within the category of UPFs, subgroups had different related adverse health outcomes. For example, plant-based alternatives, breads and cereals were not associated with risk, while higher consumption of other UPFs was found to increase the risk of cancer and cardiometabolic disease (see more details in section 4).<sup>38</sup>

The functionality of the Nova system has also been queried by some experts. For example, an industry research study in 2022 demonstrated inconsistencies amongst different individual evaluators when assigning foods based on ingredients into categories according to the Nova system.<sup>39</sup>

The UK's current food policy on front of package labelling (FOPL) intends to inform consumers of the nutrient content of food. It uses the 'traffic light system' of red, yellow and green. The Food Standard Agency guidelines state that if a food has been processed in some way, it must be included in the title, for example 'smoked bacon', but this does not consider or include the level of food processing like the Nova categories.<sup>19,40,41</sup>

A 2024 study investigated the food and drink in the UK National Diet and Nutrition Survey (NDNS) to evaluate the extent in which the current dietary recommendations for HFSS foods cover processed foods particularly UPFs using the Nova system. The study found that UPFs were more likely to have a red FOPL as they contained greater energy, fat, saturated fat, total sugars and salt than minimally processed foods.<sup>42</sup>

Stakeholders have highlighted the importance for policy makers, academics and other relevant professions to combat misinformation on UPFs and equip the public with accurate explanations on the associations between processed foods and risks of poor health outcomes.<sup>37,43</sup> This will enable individuals to make more informed decisions on food consumption and improve dietary patterns.<sup>37</sup>

## 2

# Patterns of consumption

There have been dietary studies investigating the relationship between the intake of ultra-processed foods, their dietary profile and risk of poor health outcomes. In the adult UK population, it has been found that an increased share of UPFs in someone's diet was associated with increased sugar, saturated fat, processed meats, sodium, and/or lower in fruit, vegetables, fibre and protein.<sup>29,38,44</sup>

A 2019 national representative cross-sectional study, using data from the UK National Dietary Survey<sup>e</sup> between 2008 to 2014, investigated the NOVA food classification across a 4-day food diary. It found that in the UK diet, UPFs account for approximately 57% of the average total energy intake (TEI) and 65% of total free sugars.<sup>6,29</sup> This study found that the trend of excessive free sugar intake increased as the consumption of UPFs increased for all age groups except the elderly. Additionally, removing some UPFs such as sugar-sweetened beverages, from the diet could potentially reduce the prevalence of excessive sugar intake by 47%.<sup>29</sup>

A 2023 study investigating trends in processed food consumption over 11 years (2008-2019) using NDNS data showed that there were no major changes in UPF consumption over time. However, over the period culinary ingredients (Nova Group 2) slightly increased and UPFs slightly decreased.<sup>7</sup> There were noteworthy changes in some subgroups, such as a reduction in the energy share of red meat, sausages and other reconstituted meat products as well as the increase of fruits, ready meals, breakfast cereals, cookies, pastries, buns and cakes.<sup>7</sup>

A 2020 study, using NDNS data between 2008-2016, showed that an increased consumption of UPFs was associated with greater accumulation of body fat than lean mass (adiposity) and Body Mass Index (BMI) in the UK adult population.<sup>46</sup> The study also concluded that high consumption of UPFs increase the risk of obesity, and obesity is the leading most preventable risk-factor in developing diseases such as cancer and heart disease.<sup>16,33,46,47</sup>

## 2.1

### Demographic factors

In the UK, children and young people consume the most UPFs as a proportion of their energy intake.<sup>29,44,48</sup> As of 2018/19 a representative cross-sectional study of adolescents found that in 11-18 year olds, UPF consumption accounted for 66% of TEI of their diet, compared to adults (above 18 years) and children (below 11 years). This was a 3% decrease

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<sup>e</sup> The National Diet and Nutrition Survey assesses the diet, nutrient intake and nutritional status of the general population of the UK.<sup>45</sup>

from figures taken in 2008/09.<sup>48</sup> Though it is important to note that certain foods for younger children such as infant formula are categorised as a Nova group 4 UPF, this categorisation has been a topic of concern for some academics and clinical practitioners.<sup>49,50</sup>

Other demographic factors among adolescents that were associated with having a higher %TEI from UPFs included:

- adolescents with lower socioeconomic status (with parents in an intermediate or routine and manual occupation) have a higher consumption of UPFs compared to those with a high socioeconomic status (62% vs 69% respectively)
- from a white ethnicity background
- living in the North of England
- male adolescents
- living with obesity<sup>48</sup>

An older study characterising UK diet according to the degree of processing also investigated the associations between socio-demographic factors and processed food in adults (2008-2012).<sup>44</sup> The study found that in an adult's diet, approximately 53% of energy was derived from UPFs. Though there were no major differences in trends across socio-demographic factors, it was evident that those living in households of the lowest occupational social class consumed less minimally processed foods (Nova Group 1), but no significant differences were seen in UPF consumption.<sup>44</sup>

## Box 2 International comparisons

- In the United States (US), analysis of the National Health and Nutrition examination Survey (2007-2012) showed that in individuals aged two and above almost 60% of calories consumed came from UPFs.<sup>51</sup> Consumption decreased with an increase in age and income level. Consumption increased in non-Hispanic White and non-Hispanic Black people compared to all other ethnicity groups. Contributions of UPFs in consumption increased every cycle (yearly cohort), and was higher for males, adolescents and those with high school education.<sup>51</sup>
- In France, data from the national study Étude Nationale Nutrition Santé (ENNS), show that those with the highest consumption of UPFs are young individuals and those living in urban areas.<sup>52</sup>
- In Belgium, the national Food Consumption Survey cohort studies (2004 and 2014-15) showed that children (33.3%) had a higher dietary share (daily energy intake) of UPFs than adults (29.6%) and adolescents (29.2%).<sup>53</sup>
- In Australia, data from the Australian Health Survey (2011 – 2013) showed that the consumption of UPFs was higher among young adults (19-30 years), those experiencing greatest area-level disadvantage, lower educational attainment and the second lowest household income quintile.<sup>54</sup>
- In Brazil, data taken from the 2019 cohort of the 'National surveillance system for risk and protective factors for chronic diseases by telephone survey' found that the frequency of high consumption of UPFs was 18.2%. Consumption is higher in the adult population of Brazil for males, younger adults and those with less education than university level.<sup>55</sup>

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### 3

## UPFs and human health outcomes

Evidence suggests that UPFs increase the risk of harmful health outcomes such as developing chronic diseases and death.<sup>10</sup>

Academics and epidemiologists strongly suggest that more evidence is required to understand and investigate the causal relationship between UPFs and adverse health outcome. Further evidence is required because the biological processes and interactions between UPFs and the human body are still not comprehensively understood.<sup>8,42,56,57</sup> Though as mentioned in the sections above, it is helpful to interpret the data with caution as observational research studies identifying an association between UPF consumption and risk of disease can be biased and appear to show confounding results.<sup>56</sup>

There are several harmful health outcomes directly related to increased consumption or exposure to UPFs. These include mortality (death), cancer, respiratory, cardiovascular, gastrointestinal, mental and metabolic health outcomes.<sup>9,10,58</sup> Evidence has indicated that reducing UPFs from the diet may improve the quality of food consumption and could contribute to the prevention of developing diet-related non-communicable diseases.<sup>6</sup> This is not uniform for all UPFs, for example, a multinational 2023 study found that there was no association between consumption of ultra-processed plant-based alternative foods (vegan foods) and risk of developing cancer or cardiometabolic disease.<sup>38</sup>

Emerging evidence has shown that UPFs could affect and/or alter an individual's intestinal ('gut') health through an imbalance in the gut microbiome, increasing inflammation.<sup>57,59-61</sup> This recent research has led to the understanding that the microbiome<sup>f</sup> has the potential to influence food digestion and therefore human health outcomes.<sup>60</sup>

Previous research on the functionality of microbiome showed that bacteria can interact with sugars and other additives, both of which are core ingredients in UPFs.<sup>57</sup> Emerging research suggests that the gut microbiome could also potentially impact brain function and cognitive processes as food additives from UPFs can interact with microbiota and the "gut-brain axis".<sup>60</sup> Experts have suggested that further research focusing on the mechanisms by which UPFs interact with the microbiome and metabolome will be essential in understanding how exactly UPFs impact human health.<sup>61</sup>

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<sup>f</sup> A microbiome is the community of microorganisms that can usually be found living together in any given habitat.

## 3.1 Non-communicable diseases

The most recent comprehensive study on the consumption of ultra-processed foods (UPFs) and their relationship with adverse health outcomes and disease risks is an umbrella review of epidemiological meta-analyses published in February 2024. The quality of the selected studies was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) framework. The credibility of the evidence was evaluated using the authors' statistical analysis methods and categorized into classes I to IV, with 'class I' (convincing) being the strongest and 'class IV' (weak) being the weakest. The study also investigated the differences between dose-related and non-dose-related risks.<sup>9</sup> The risk of developing specific adverse health outcomes was weighted based on their association with the credibility and quality of evidence (see Figure 1).

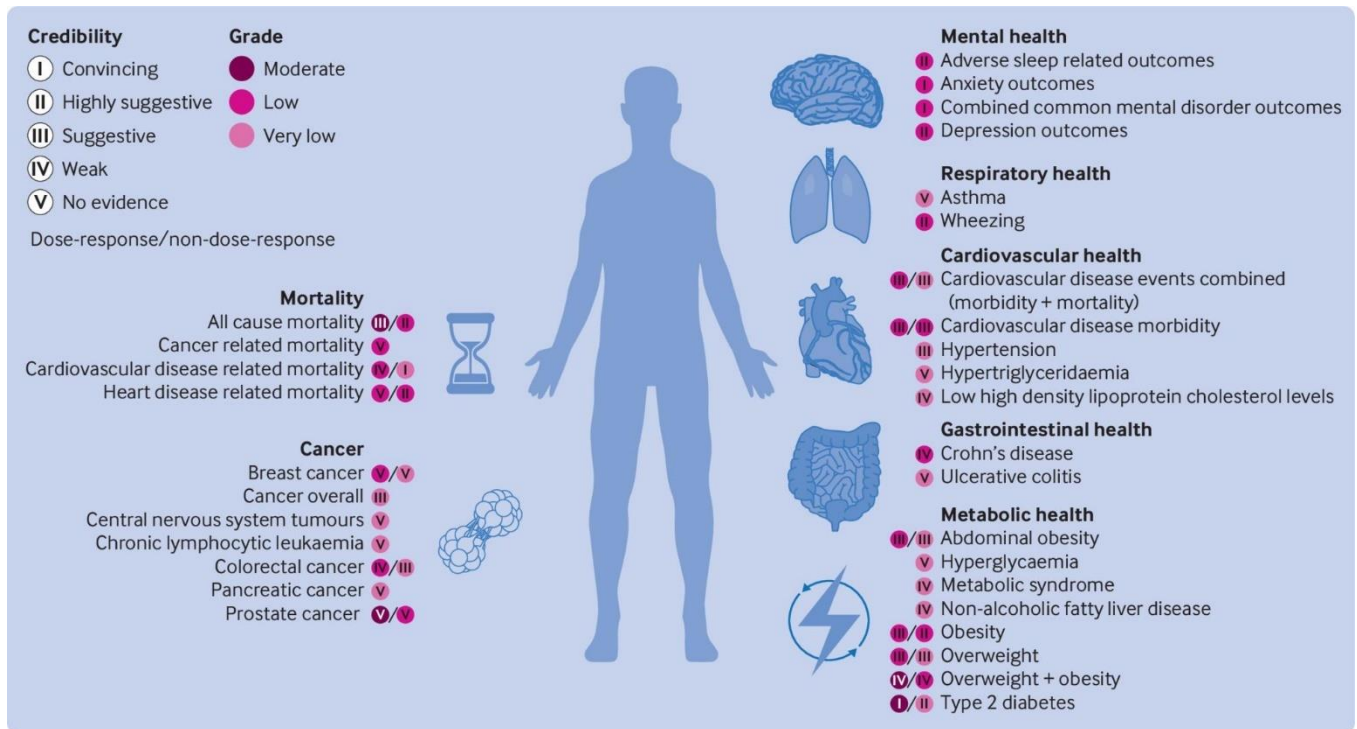
The review analysed 45 studies and found that 32 (71%) of them reported adverse health outcomes associated with higher exposure to UPFs. These outcomes included all-cause mortality (death from any cause), cancer, and various mental, cardiovascular, gastrointestinal, respiratory, and metabolic health issues. Based on the criteria explained above, the most significant associations were:

1. **Convincing Evidence:** The highest risks directly associated with greater exposure to UPFs were CVD, type 2 diabetes, prevalence of anxiety and combined common mental disorder outcomes.
2. **Highly Suggestive Evidence:** results indicated that greater exposure to UPFs was directly associated with a higher risk of heart disease-related death, type 2 diabetes (non-dose-response), depressive outcomes, adverse sleep-related outcomes, wheezing and obesity.<sup>10</sup>

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<sup>9</sup> Dose-related risks refer to the adverse effects or risks that are directly related to the amount of substance administered/consumed. Non-dose-related risks are the adverse effects or risks that not directly correlated with the amount of substance taken, it occurs unpredictably.

**Figure 1 Credibility and GRADE ratings for associations between greater exposure to ultra-processed foods and risks of each adverse health outcome**



Melissa Lane et al. 2024, British Medical Journal <sup>10</sup>

Numerous observational research, including prospective cohort studies and meta-analyses, have investigated the associations between ultra-processed food (UPF) consumption and human health outcomes. A summary of some of the most recent studies of statistical significance<sup>h</sup> have been selected and presented in Table 2 below.

<sup>h</sup> Results are statistically significant when they are unlikely to have been caused by chance. Researchers set a level of probability (p-value) at which they consider a result statistically significant.



**Table 2 Studies investigating the associations between UPFs and risks of adverse health outcomes, 2018-2024**

1 <sup>st</sup> Author	Year	Country	Sample size	Study population	Health outcome and statistical measures <sup>i</sup>
Cordova	2023	Denmark, Germany, Italy, Spain, Sweden, the Netherlands and UK	266,666	Adults (EPIC study)	Multimorbidity cancer and cardiometabolic disease. ( <u>Statistically significant</u> Hazard Ratio)
Chang	2023	UK	197,426	Adults (UK Biobank)	Overall cancer, ovarian cancer, breast cancer and cancer-related mortality ( <u>Statistically significant</u> Hazard Ratio)
Morales-Berstein	2023	Denmark, France, Germany, Italy, Spain, Sweden, the Netherlands, Norway and UK	450,111	Adults (EPIC study)	Head, neck and oesophageal cancer (Statistically significant Hazard Ratio)
Kliemann	2023	Denmark, France, Germany, Italy, Spain, Sweden, the Netherlands, Norway and UK	450,111	Adults (EPIC study)	Head, neck, oesophageal, colon and liver cancer (Statistically significant Hazard Ratio)
Chang	2021	England	9025	Children (Avon Longitudinal Study of	Increased Weight trajectories average of BMI and waist

<sup>i</sup> **Hazard ratio (HR)**, **relative risk (RR)**, and **odds ratio (OR)** are different measures used in statistical analysis

- **Hazard ratio (HR)** represents instantaneous risk over a study time period.
- **Relative risk (RR)** is cumulative over an entire study, using a defined endpoint.
- **Odds ratio (OR)** is the ratio of the odds of an event in one group compared to another group.

				Parents and Children (ALSPAC))	circumference measures)
Banoccio	2021	Italy	22,475	Adults	All-cause mortality and CVD mortality (Statistically significant Hazard Ratio)
Romero Ferreiro	2021	Spain	4,679	General population (DRECE cohort)	All-cause mortality (Statistically significant Hazard Ratio)
Du	2021	US	13,548	Adults (Atherosclerosis Risk in Communities)	Coronary Artery Disease (Statistically significant Hazard Ratio)
Lo	2021	US	24,511	Adults (NHS II & HPF)	Crohn's disease and ulcerative colitis (Statistically significant Hazard Ratio)
Gomes-Donoso	2021	Spain	14,907	Adults (SUN cohort)	Depression (Statistically significant Hazard Ratio)
Adjibade	2021	France	26,730	Adults (NutriNet-Santé cohort)	Depressive symptoms (Statistically significant Hazard Ratio)
Donat-Vargas	2021	Spain	1082	Older Adults	Dyslipidaemia <sup>j</sup> (Statistically significant Odds Ratio)
Leone	2021	Spain	3730	Pregnant women	Gestational Diabetes (Statistically significant Odds Ratio)

<sup>j</sup> Dyslipidemia refers to abnormal levels of lipids in the bloodstream, which poses a significant risk factor for cardiovascular (CV) diseases. Dysregulation in these lipid levels, whether due to genetic predispositions or lifestyle factors, can lead to atherosclerosis and other CV complications.<sup>62</sup>

Scaranni	2021	Brazil	8754	Adults (ELSA-Brazil)	Hypertension (Statistically significant Odds Ratio)
Narula	2021	20 countries	116087	Adults (PURE cohort)	Inflammatory Bowel Disease (Statistically significant Hazard Ratio)
Zhang	2021	China	16,168	Adults (TCLSIH cohort)	Non-alcoholic fatty liver disease (Statistically significant Hazard Ratio)
De Melo	2021	Brazil	196	Breastfed infants	Overweight associated with maternal consumption of UPF while breastfeeding (Statistically significant Hazard Ratio)
Li	2021	China	12,451	Adults (China Nutrition and Health Survey)	Overweight/Obesity (Statistically significant Odds Ratio)
Beslay & Srour	2021	France	110,260	Adults (NutriNet-Santé cohort)	Overweight/Obesity (Statistically significant Hazard Ratio)
Cordova	2021	9 European Countries	348,748	Adults EPIC study)	Overweight/Obesity (Statistically significant Hazard Ratio)
Rey-García	2021	Spain	1312	Older Adults	Renal function decline (Statistically significant Odds Ratio)
Llavero-Valero	2021	Spain	20,060	Adults (SUN cohort)	Type 2 diabetes (Statistically significant Hazard Ratio)

Srouf	2020	France	104,707	Adults (NutriNet-Santé cohort)	Type 2 diabetes (Statistically significant Hazard Ratio)
Levy	2020	UK	21,730	Adults (UK Biobank)	Type 2 diabetes (Statistically significant Hazard Ratio)
Melo	2018	Brazil	109,104	Adolescents (National Survey of School Health)	Asthma (Statistically significant Odds Ratio)
Fiolet & Srouf	2018	France	104,980	Adults (NutriNet-Santé cohort)	Cancer (overall cancer and by site) (Statistically significant Hazard Ratio)

Source: Srouf et al. 2022, Cordova et al. 2023, Morales-Beirstein et al. 2023, Kliemann et al. 2023 and Chang et al. 2023.<sup>11,38,57,63</sup> This list of research studies is not exhaustive and has been adapted from Srouf et al. 2022. Studies are ordered according to year.

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## 4

# Challenges and innovations in research

Nutritional epidemiology, particularly in the context of UPF consumption, presents specific research challenges (PN718). These challenges stem from the complexity of dietary patterns and the multifaceted nature of their health impacts.<sup>64–66</sup> While case-control, cross-sectional, retrospective or prospective cohort studies, have been the basis of research in this field, they come with inherent limitations.

The European Prospective Investigation into Cancer and Nutrition (EPIC) study is a large-scale prospective cohort of approximately 500,000 participants. The EPIC study aims to report the relationships between diet, nutrition and cancer as well as other chronic diseases.<sup>67</sup> However, even comprehensive studies such as EPIC face challenges in establishing causal relationships between UPF consumption and health outcomes.

Key challenges in UPF consumption research can include:

- **Exposure quantification:** accurately measuring individual exposure to UPFs is complex due to variations in dietary habits, food composition, and consumption patterns.<sup>68</sup>
- **Confounding factors<sup>k</sup>:** socioeconomic status, lifestyle choices, and genetic predispositions can significantly influence both UPF consumption and health outcomes, making it difficult to isolate the specific effects of UPFs.
- **Bias mitigation:** Selection, recall and publication bias<sup>l</sup> can skew research findings. Recall bias can be particularly challenging in retrospective dietary studies.
- **Temporal considerations:** the long latency period between UPF exposure and the manifestation of health outcomes complicates the establishment of clear causal links.<sup>69</sup>

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<sup>k</sup> Confounding describes the process by which a variable influences both the exposure (independent variable) and the outcome (dependent variable). Confounding can lead to less accurate estimates of the strength and direction of associations and can make exposures appear associated with the outcome, regardless of a causal effect.

<sup>l</sup> Selection bias occurs when individuals or groups in a study differ systematically from the population of interest leading to a systematic error in an association or outcome.

Publication bias refers to the publication of study results dependent on their strength or direction, hindering the accurate evaluation and review of evidence.

- Mechanistic understanding: explaining the biological mechanisms through which UPFs impact health requires sophisticated research methodologies.

To address these challenges, experts advocate for enhanced high-quality research methodologies that leverage innovative technologies, large-scale diverse prospective cohort studies, and interdisciplinary approaches.<sup>14,24,70,71</sup> For example:

- Digital food diaries: user-friendly, digital food logging tools can capture real-time consumption data, reducing recall bias and providing more accurate exposure measurements.<sup>72</sup>
- Nutriomics<sup>m</sup> integration: the application of nutriomics – the study of nutrition on gene expression – can offer deeper insights into the biological mechanisms underlying the health effects of UPFs.<sup>74–76</sup>
- Biomarker development: identifying and validating biomarkers specific to UPF consumption could offer objective measures of exposure and potential health impacts.<sup>75,77</sup>
- Machine learning and AI: advanced analytical techniques can help process and interpret the vast amounts of data generated by these studies, potentially uncovering patterns and associations not readily apparent through traditional methods.<sup>78</sup>
- Interdisciplinary Collaboration: combining expertise from nutrition, epidemiology, genetics, and data science can provide a more holistic understanding of UPF impacts on health.

By adopting these innovative approaches, researchers can generate high-quality epidemiological and mechanistic insights necessary for accurately assessing the health impacts of UPF consumption.<sup>72,79</sup> This enhanced understanding could be imperative in informing evidence-based public health policies and dietary recommendations in the context of increasing UPF consumption.

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<sup>m</sup> Nutriomics refer to using genomics, proteomics, metabolomics, epigenomics and transcriptomics as tools for nutritional research.<sup>73</sup> It aims to enhance scientific evidence base and effectiveness of nutritional guidelines through 'omics' technologies (using technology to study several types of biological molecules). Nutriomics offer personalised approaches towards improved nutritional guidance and wellbeing.

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