Ultra-Processed Foods and Human Health 1

Ultra-processed foods and human health: the main thesis and the evidence

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This first paper in a three-part *Lancet* Series combines narrative and systematic reviews with original analyses and meta-analyses to assess three hypotheses concerning a dietary pattern based on ultra-processed foods. The first hypothesis—that this pattern is globally displacing long-established diets centred on whole foods and their culinary preparation as dishes and meals—is supported by decades of national food intake and purchase surveys, and recent global sales data. The second—that this pattern results in deterioration of diet quality, especially in relation to chronic disease prevention—is confirmed by national food intake surveys, large cohorts, and interventional studies showing gross nutrient imbalances; overeating driven by high energy density, hyper-palatability, soft texture, and disrupted food matrices; reduced intake of health-protective phytochemicals; and increased intake of toxic compounds, endocrine disruptors, and potentially harmful classes and mixtures of food additives. The third and final hypothesis—that this pattern increases the risk of multiple diet-related chronic diseases through various mechanisms—is substantiated by more than 100 prospective studies, meta-analyses, randomised controlled trials, and mechanistic studies, covering adverse outcomes across nearly all organ systems. The totality of the evidence supports the thesis that displacement of long-established dietary patterns by ultra-processed foods is a key driver of the escalating global burden of multiple diet-related chronic diseases. Two companion papers in this Series specify policy actions and wider public health strategies to promote, protect, and support diets based on fresh and minimally processed foods and prevent their displacement by ultra-processed foods.

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This is the first in a **Series** of three papers about ultra-processed foods and human health. All papers in the Series are available at thelancet.com/series/ultra-processed-food

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Introduction

A 2009 commentary[1] and subsequent publications[2–5] proposed that the purpose and extent of industrial food processing had shifted globally in past decades, with harmful—and overlooked—effects on human health, especially diet-related chronic diseases.

Rather than primarily serving to extend the shelf life of whole foods, preserve or enhance sensory properties, or facilitate culinary preparation, industrial food processing has become increasingly aimed at creating substitutes for whole foods and their preparation as dishes and meals. In pursuit of greater profits, especially by transnational corporations, new processing technologies emerged. Unlike long-established methods, such as drying, chilling, freezing, pasteurisation, fermentation, baking, salting, sugaring, bottling, and canning—which largely preserve the natural structure of foods and enhance their durability, palatability, and culinary versatility—these new technologies disrupt food matrices, chemically modify food components, and combine them with additives to produce ready-to-consume, long-lasting, and highly palatable products.[1–5]

This shift, which was common in some high-income countries after World War 2, accelerated in the 1980s with the deregulation of foreign investment and globalisation of the corporate food industry, in parallel with worldwide increases in obesity[2,6] and other diet-related chronic diseases, such as type 2 diabetes,[7] colorectal cancer,[8] and inflammatory bowel disease.[9]

As a result of these new technologies, a new food classification system was introduced that considered the extent and purpose of the industrial processing to which foods are subjected before consumption.[1] This system, later updated and named Nova,[4,5,10] identifies four food groups, with the fourth (and most processed group) termed ultra-processed foods (UPFs). UPFs are branded, commercial formulations made from cheap ingredients, with little or no whole food, designed to compete with the other three Nova groups and their preparation as dishes and meals, and maximise corporate profits.

Among other uses, such as structuring dietary guidelines,[11] Nova enables the measurement of individual-level and population-level exposure to the ultra-processed dietary pattern by calculating the dietary share of UPFs (as a percentage), either by energy or weight.[12] In the aforementioned publications,[1–5] three hypotheses concerning the ultra-processed dietary pattern were proposed. The first hypothesis proposes that the ultra-processed dietary pattern has displaced, and continues to displace, long-established patterns based on the three first Nova groups and their preparation as dishes and meals. The second hypothesis suggests that such a pattern degrades various aspects of dietary quality related to chronic diseases, including—but not limited to—nutrient profiles. The third hypothesis is that exposure to the ultra-processed dietary pattern increases the risk of multiple diet-related chronic diseases through various mechanisms. The thesis arising from these

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See **Online** for appendix

Key messages

- Ultra-processed foods (UPFs), the fourth group in the Nova food classification system, are branded, commercial formulations made from cheap ingredients extracted or derived from whole foods, combined with additives, and mostly containing little to no whole food. UPFs are designed to compete with the other three Nova groups and maximise industry profits.
- A high dietary share of UPFs defines the ultra-processed dietary pattern. This dietary pattern is displacing long-established diets based on the three other Nova groups in most regions worldwide, and further spread is anticipated where the pattern has not yet become the norm.
- Meta-analyses of prospective studies show associations between the ultra-processed dietary pattern and an increased risk of overweight or obesity, abdominal obesity, type 2 diabetes, hypertension, dyslipidaemia, cardiovascular disease or mortality, coronary heart disease or mortality, cerebrovascular disease or mortality, chronic kidney disease, Crohn's disease, depression, and all-cause mortality.
- Pooled risk estimates (high *vs* low UPF intake) were similar—in reverse—to the protective effects of the Mediterranean diet.
- Experimental studies, consisting of clinical and community trials and mechanistic studies, support the association between the ultra-processed dietary pattern and obesity.
- Plausible mechanisms for harm include nutrient imbalances, overeating, reduced consumption of health-protective phytochemicals, toxic contaminants from processing or packaging, harmful additives and mixtures of additives, and subsequent inflammation, dysglycaemia, dyslipidaemia, microbiome dysbiosis, and renal or liver dysfunction.
- The totality of evidence supports the thesis that the displacement of long-established dietary patterns by UPFs is a key driver of the escalating global burden of multiple diet-related chronic diseases.
- Research on the effect of UPFs on human health will continue, but this should not delay public health policies and actions at all levels that are designed to restore, preserve, protect, and promote diets based on whole foods and their preparation as dishes and meals, which are overdue. These actions are set out in the second and third papers in this Series.

hypotheses is that the displacement of long-established dietary patterns by UPFs is a key driver of the escalating global burden of multiple diet-related chronic diseases.

This first paper of a three-part *Lancet* Series on ultra-processed foods and human health combines narrative and systematic reviews with original analyses and meta-analyses to examine the evidence for these hypotheses. Building on this foundation, the second Series paper presents policy actions to reduce the share of UPFs in diets and promote healthier food systems.[13] The third paper in this Series outlines the commercial determinants of ultra-processed diets and strategies for mobilising a global public health response.[14] Together, this Series argues that the rise of UPFs in human diets constitutes a major new challenge for global public health, and that urgent, coordinated public policies and collective actions are needed to address its growing impacts.

The Nova food classification system and levels and distribution of ultra-processed food consumption

Nova identifies industrial food processing as the physical, biological, and chemical methods applied by industry to foods after harvesting and before their culinary preparation and consumption (either at home or elsewhere). These methods include those used to obtain and modify food substances and combine them into final products, and the use of additives. Based on the extent and purpose of industrial processing, Nova classifies all foods and food products, including the individual ingredients of culinary preparations, into four groups: (1) unprocessed or minimally processed foods; (2) processed culinary ingredients; (3) processed foods; and (4) UPFs. We have outlined the definition and characteristics of each Nova group and address the rationale for the three hypotheses examined in this Series paper (panel 1).

The analysis of national food intake surveys across 36 countries, all using Nova, shows that the average dietary share of UPFs (as a percentage of total energy intake) ranges from 9% (in Iran) to 60% (in the USA).[15–30] The analysis also reveals that this share correlates with national wealth (r=0·45; 95% CI 0·20–0·70), but is also influenced by cultural and other food systems factors. For instance, the dietary share of UPFs remains below 25% in high-income countries of southern Europe (ie, Italy, Cyprus, Greece, and Portugal) and Asia (ie, Taiwan and South Korea), but exceeds 40% (in Australia and Canada) or 50% (in the UK and USA) in other high-income nations (appendix p 1).

Within countries, the dietary share of UPFs tends to be elevated in groups with high socioeconomic status, where overall UPF intake is low, and in groups with low socioeconomic status, where overall UPF intake is high (appendix p 2).[15–18,24–26,31–35] This pattern mirrors the socioeconomic distribution of obesity,[36] indicating that UPFs, like obesity,[37] first affect wealthier populations before spreading to groups on lower incomes.

The ultra-processed dietary pattern: worldwide time trends

We evaluated the first hypothesis through a narrative review of studies, which applied Nova to three or more

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nationally representative food purchase or intake surveys conducted over decades in the same country. Relevant studies were identified based on the authors' knowledge and longstanding expertise in the field. In addition, we conducted original analyses of Euromonitor International's food sales data from 93 countries.[38]

The energy contribution of UPFs to total household food purchases nearly tripled in Spain[39] over three decades (11·0% to 31·7%), more than doubled in Canada[40] over eight decades (24·4% to 54·9%), and increased from 10% to 23% in Mexico[41] and Brazil[42] over four decades (figure 1). In Argentina, this contribution increased from 19% to 29% over three decades.[43] In China (3·5% to 10·4%),[30] and South Korea (12·9% to 32·6%),[44] the low dietary share of UPFs tripled over three decades. In the USA[20,45] and the UK,[25] where intake was already above 50%, it only increased slightly over two decades, indicating that dietary patterns in these countries are already well established. All studies reported statistically significant increasing trends, except the UK study.

From 2007 to 2022, annual per capita sales of UPFs increased by 60% (20·3 kg to 32·2 kg) in Uganda, the only low-income country assessed by Euromonitor; by 40% (45·3 kg to 63·3 kg) in lower-middle-income countries (n=22); and by nearly 20% (104·0 kg to 121·6 kg) in upper-middle-income countries (n=26; figure 2). All ten UPF subgroups—sweetened carbonated drinks, sweetened non-carbonated drinks, baked goods, sweet snacks, ready meals, savoury snacks, dairy products, sauces and dressings, reconstituted meat products, and other solid foods—increased. Overall sales of UPFs in high-income countries (n=44) remained

***Panel 1:* The Nova food classification system based on the extent and purpose of industrial food processing**

Unprocessed or minimally processed foods (Nova group 1)
This group consists of foods in their natural state or altered by industrial processes that largely preserve their natural structure (matrix), such as removal of inedible or unwanted parts, cutting, drying, crushing, grinding, fractioning, roasting, boiling, pasteurisation, refrigeration, freezing, placing in containers, vacuum packaging, and non-alcoholic fermentation. These processes do not add salt, sugar, oils or fats, or other food substances, to the original food. The shelf life of grains (cereals), legumes (pulses), vegetables (including herbs and spices), fruits, nuts, fungi, milk, meat, poultry, fish, and other whole foods are extended by these processes, enabling the foods to be stored for longer, making their preparation easier or more diverse, and often making them more enjoyable. Many unprocessed or minimally processed foods are often seasoned and cooked with processed culinary ingredients in home kitchens or restaurants and consumed as freshly prepared dishes and meals.

Processed culinary ingredients (Nova group 2)
These substances are obtained directly from group 1 foods or from nature, such as oils, butter, lard, table sugar, honey, and salt, by use of industrial processes such as pressing, centrifuging, refining, evaporating, extracting, or mining. The substances are not consumed alone but are used to season and cook group 1 foods and turn them into freshly prepared dishes and meals.

Processed foods (Nova group 3)
Foods in group 3 are those in group 1 that have been modified by the industry by adding salt, sugar, oil, or other group 2 ingredients, with preparation methods similar to those used in home kitchens or restaurants. These foods include vegetables in brine, fruits in syrup, tinned and cured fish, breads and cheeses, and any commercial food or drink product made from foods in group 1 and ingredients from group 2. The foods can be consumed alone or as part of freshly prepared dishes and meals. The main aim of food processing in this group is to increase the durability of group 1 foods, and to modify or enhance their sensory qualities.

Ultra-processed foods (UPFs; Nova group 4)
UPFs are branded, commercial formulations made from cheap ingredients extracted or derived from whole foods and combined with additives. Most contain little to no whole food, and are designed to compete with the other three Nova groups—and therefore with freshly prepared dishes and meals—and maximise industry profits. UPFs are created through sequential processes, starting with fractioning high-yield crops (eg, soy, maize, wheat, sugarcane, and palm fruits) into starches, fibre, sugars, oils and fats, and proteins. These components are then chemically modified (eg, by hydrolysis, hydrogenation, and interesterification), and combined by use of industrial techniques (eg, extrusion, moulding, and pre-frying). Remnants and scraps of meat are often used in meat products. Flavours, colours, emulsifiers, and other classes of additives with cosmetic functions are used to make the final product look, feel, sound, smell, and taste good, and often hyper-palatable. Attractive packaging often carrying implied or actual health claims, usually made with synthetic materials, concludes the sequence of processes.

Cheap ingredients and processes that add economic value are essential to the main purpose of food ultra-processing: the creation of profitable, branded, uniform substitutes for all other Nova food groups, which can be marketed globally (especially by transnational corporations). The ingredients and processes used in the manufacture of UPFs make them typically durable (ie, with extended sell-by dates), convenient (ready to consume at any time or place), and highly palatable (designed and even advertised as habit forming). These qualities are highly attractive to retailers, caterers, and consumers, and UPFs are therefore often overconsumed.

(Panel continues on next page)

(Panel 1 continued from previous page)

Sugar, fat, or salt (or combinations thereof) are common ingredients of UPFs, typically in higher concentrations than in processed foods. Other common ingredients, also found in processed foods, are preservatives and other classes of additives that prolong their shelf life. But what distinguishes UPFs from processed foods are food substances of exclusive (or almost exclusive) industrial use—such as plant protein isolates, mechanically separated meat, and modified starches and oils—and classes of sensory-related additives, such as colours, flavours, flavour enhancers, non-sugar sweeteners, and emulsifiers. Nova identifies these substances as specific markers of food ultra-processing, and their presence on a product's ingredient list characterises it as being ultra-processed.[4]

UPFs include all carbonated soft drinks; reconstituted fruit juices and fruit drinks; cocoa, other modified dairy drinks, and energy drinks; flavoured yoghurt; confectionery; margarines; cured meat or fish with added nitrites or nitrates; poultry and fish nuggets and sticks, sausages, hot dogs, luncheon meats, and other reconstituted meat products; powdered instant soups, noodles, and desserts; infant formulas and follow-on products; and health-related and slimming-related products, such as meal-replacement shakes and powders. UPFs also include other branded commercial formulations when they contain, as is usually the case, food substances intended for exclusive or predominant industrial use, or additives with cosmetic functions, or both. Examples are mass-produced packaged breads, breakfast cereals, pastries, cakes, ice-creams, cookies and biscuits, sweet or savoury snacks, plant-based meat substitutes, and ready-to-heat, pre-prepared products such as burgers, pies, pasta, and pizza.

Nova group 4 is a broad range of products that vary widely in composition, processing, and nutrient profiles. Some UPFs (eg, yoghurts, breakfast cereals, and packaged breads) might be superior than others (eg, soft drinks, cookies, and reconstituted meat products). However, within each category of food, the composition and processing characteristics of ultra-processed versions make them inferior to their non-ultra-processed counterparts. For instance, ultra-processed yoghurts—often made from skimmed milk powder, modified starches, sugar or non-sugar sweeteners, emulsifiers, flavourings, and colourings—are inferior to plain yoghurts with fresh fruits. Ultra-processed breakfast cereals, made from sugar, extruded starches, and additives, are inferior to minimally processed steel-cut oats. Ultra-processed wholewheat breads, made with refined flour, added bran and germ, and emulsifiers, are inferior to processed breads made with wholewheat flour and without emulsifiers. Soft drinks are clearly less healthy than water or pasteurised, 100% fruit juices; cookies less healthy than fruits and nuts; and reconstituted meat products less healthy than freshly prepared meat dishes. Possible exceptions—such as ultra-processed infant formulas compared with minimally processed cow's milk (although not human milk), or ultra-processed plant-based burgers compared with processed meat burgers (though not processed tofu or tempeh)—do not invalidate the general rule that ultra-processed versions of foods are inferior to their non-ultra-processed counterparts. This rule is what supports the hypotheses that the displacement of dietary patterns based on Nova groups 1–3 by the ultra-processed pattern is linked to worsening diet quality and an increased risk of multiple diseases.

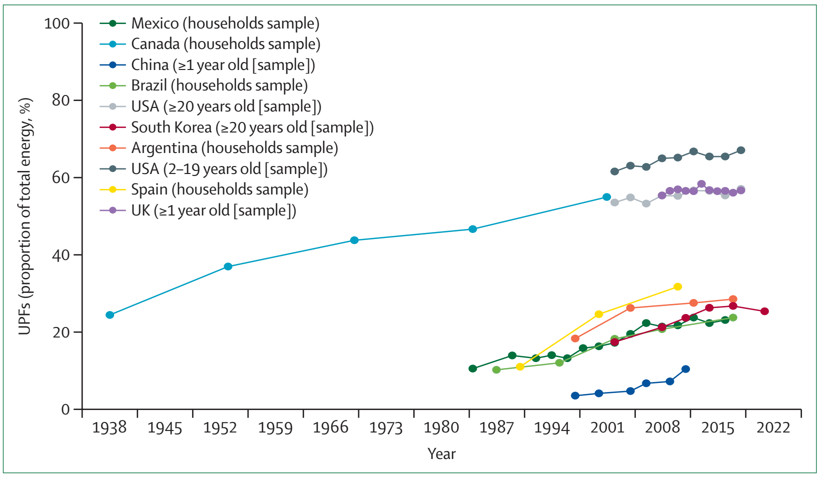

Figure 1: **Time trends in the share of UPFs in nine countries estimated from repeated national food purchase or food intake surveys**
UPFs=ultra-processed foods.

stable at approximately 200 kg per person, as declining sales of sweetened carbonated drinks offset increases in other subgroups.

In the same 2007–22 period, annual per capita overall sales and sales of the ten UPF subgroups increased in south Asia, southeast Asia, and sub-Saharan Africa (starting <100 kg), as well as in central Europe, eastern Europe, Latin America and the Caribbean, central Asia, eastern Asia, north Africa, and the Middle East (starting between 100 kg and 150 kg). UPF sales declined in North America, Australasia, and western Europe, where sales already exceeded 200 kg in 2007, because of declining sweetened carbonated drinks sales and stable or modest increasing sales of other UPF subgroups. In Latin America and the Caribbean, overall UPF sales declined after 2016 due to reduced sweetened drink sales and stable trends in other subgroups (figure 3).

The ultra-processed dietary pattern: effect on diet quality

We evaluated the second hypothesis through a narrative review of observational studies based on national surveys (with 24 h dietary recalls), meta-analyses and pooled analyses of these studies, observational studies of large cohorts (with 24 h dietary recalls or food frequency

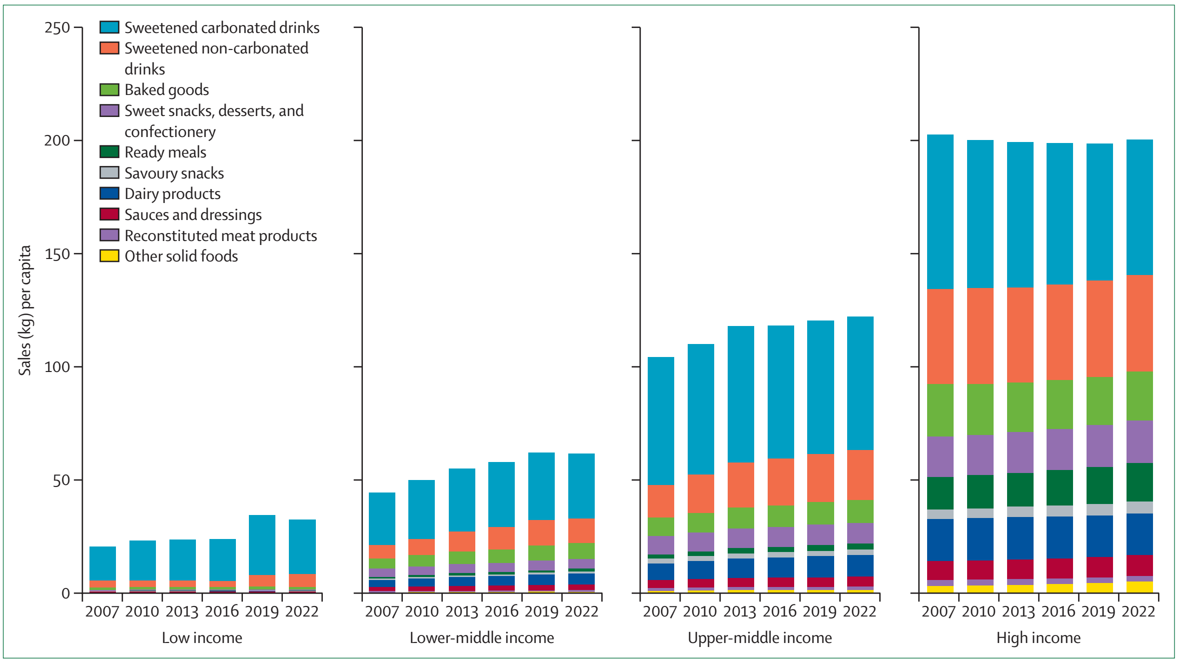

Figure 2: **Time trends in Euromonitor International's food sales data of UPFs (in kg per capita) in 93 countries grouped according to income levels, 2007–22**
The correspondence between the ten grouped categories of UPFs and the original Euromonitor categories is shown in the appendix (p 3). Countries' income groups are based on their gross national income per capita in 2022 and the World Bank's income classification (appendix pp 4–5). The density of drink products is assumed to be 1 kg/L. UPFs=ultra-processed foods.

questionnaires), and, in the case of energy intake, interventional studies as well. Studies, all using Nova, were identified based on the authors' experience and expertise in this area. In addition, we analysed NutriNet–Santé cohort data to assess the association between the dietary share of UPFs and the overall intake of potentially harmful additives and mixtures of additives.

Multiple nutrient imbalances

A meta-analysis[46] of national surveys from 13 countries (ie, Australia, Brazil, Canada, Chile, Colombia, France, Italy, Mexico, Portugal, South Korea, Taiwan, the UK, and the USA) showed that diets with higher UPF energy shares had higher contents of nutrients directly associated with chronic disease risk (ie, free sugars, total fat, and saturated fat), and lower contents of nutrients inversely associated with chronic disease risk (ie, fibre, protein, potassium, zinc, magnesium, and several vitamins). Further analysis of eight of the 13 countries showed that reducing UPF intake to the lowest quintile would substantially decrease the prevalence of diets with insufficient fibre intake or with excessive energy density, free sugars, or saturated fat, and would reduce the percentage of diets inadequate in all four parameters by 69·4% (in Canada) to 92·1% (in the USA).[47]

National surveys of children and adolescents in Argentina, Australia, Brazil, Chile, Colombia, Mexico, the UK, and the USA showed that the energy share of UPFs correlated positively with energy density and free sugars, and inversely with fibre.[48] Positive associations between the UPF share and nutrient profiles related to chronic diseases were also found in cross-sectional analyses of large cohorts in Europe,[49–52] the USA,[53] and Brazil.[54]

Increased energy intake

The 13-country meta-analysis predicted a 34·7 kcal increase (95% CI 14·7–54·7) in total daily energy intake for each 10% increase in UPF share.[46] This increase aligns with the linear associations shown by the same meta-analysis between the UPF share and dietary nutrient profiles that favour excessive energy intake (ie, high free sugars, total fat, and saturated fat, and low fibre and protein).

A US study at Drexel University (Philadelphia, PA, USA) assessed 14 adults in an 8-week pilot behavioural intervention designed to reduce UPF intake. Three 24 h dietary recalls before and after the intervention were used, and statistically significant reductions in daily energy intake (2561 kcal to 1949 kcal), the number of UPFs consumed (11·5 per day to 6·2 per day), and the energy from UPFs (1944 kcal/day to 993 kcal/day) were reported.[55]

A 2-week, crossover, randomised controlled trial (RCT) by the US National Institutes of Health (NIH) compared 20 weight-stable adult inpatients (BMI 27 ± 1·5 kg/m²) consuming either an ultra-processed diet (~80% of energy from UPFs) or a diet containing no UPFs. The diets were matched for presented calories, energy density, macronutrients, sugar, sodium, and fibre, but differed in

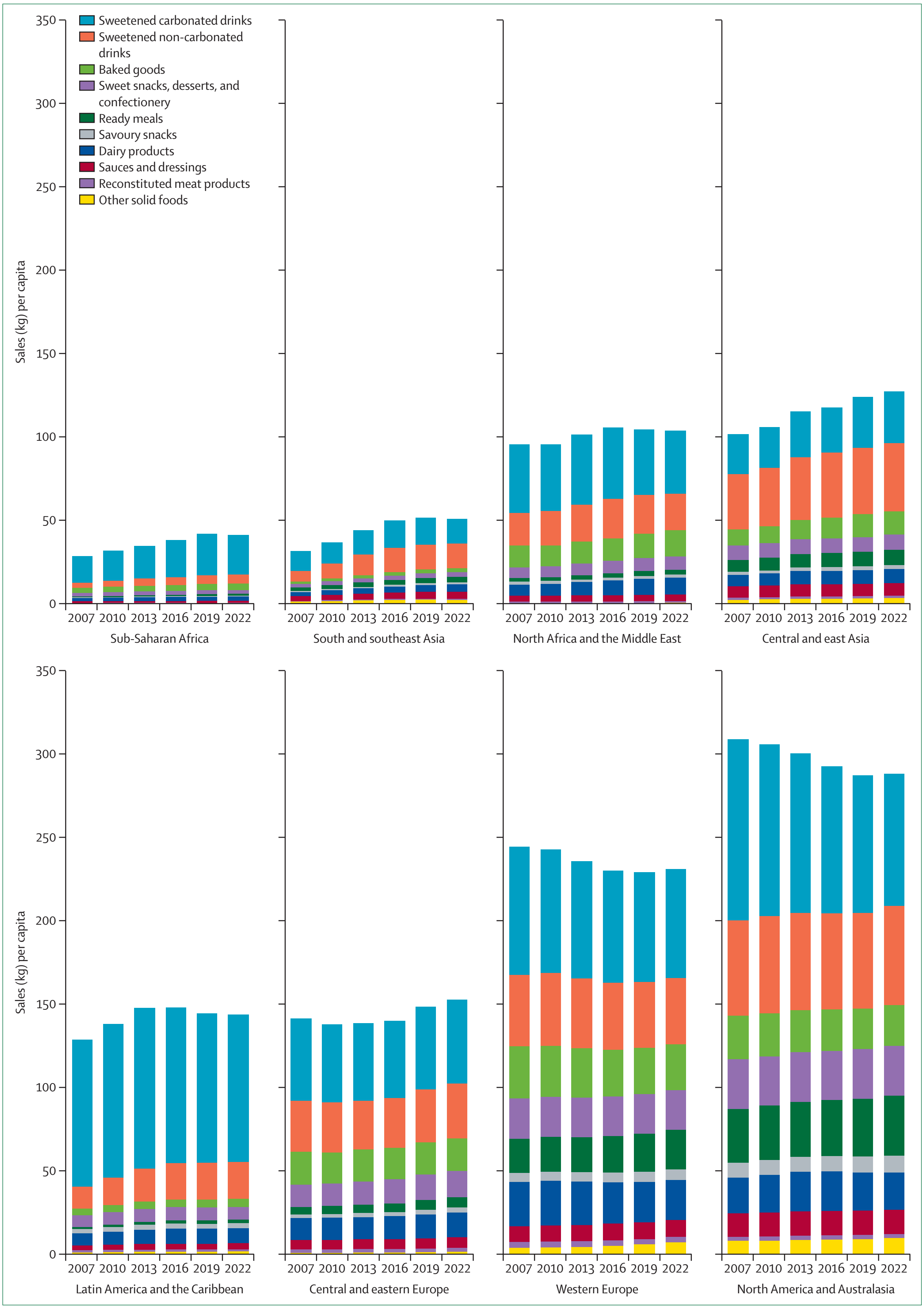

***Figure 3:* Time trends in Euromonitor International's food sales data of UPFs (in kg per capita) in 93 countries grouped according to region, 2007–22**
The correspondence between the ten grouped categories of UPFs and the original Euromonitor categories is shown in appendix p 3. Regions listed as per the Institute for Health Metrics (appendix pp 4–5). The density of drink products is assumed to be 1 kg/L. UPFs=ultra-processed foods.

added versus intrinsic sugar and fibre, and in beverage versus non-beverage energy density. Participants consumed approximately 500 kcal more with the UPF diet and ate faster (with a higher energy intake rate), despite equivalent nutrient profiles.[56] Post-hoc analyses linked these differences to the increased energy density of non-beverages and the greater content of hyper-palatable foods in the ultra-processed diet.[57]

A similar 1-week, crossover RCT[58] at the University of Tokyo Hospital (Tokyo, Japan), involving nine adults with overweight or obesity, compared ad libitum UPF diets (ie, 99·4% of total energy intake from UPFs) with ad libitum non-UPF diets (0% UPFs), matched for presented calories and macronutrients. During the UPF week, participants consumed 813 kcal/day more and had fewer chews per calorie, compared with the non-UPF week.[59–62]

Another plausible mechanism for the increased energy intake associated with ultra-processed diets is the rapid delivery of rewarding, hyper-palatable substances (eg, refined carbohydrates and fats)[63] and additives that enhance their taste, smell, texture, sound, and mouthfeel.[64] Many commonly consumed UPFs are addictive when judged by standards used for tobacco products, including compulsive use and reinforcement.[64] Marketing strategies for UPFs often include explicit encouragements for overconsumption, with phrasing such as "I bet you can't eat just one" and "once you pop you can't stop", and cereal names such as Krave.[65]

Reduced intake of health-protective phytochemicals

The aforementioned 13-country meta-analysis predicted that when UPFs represented 15% of total energy intake, the dietary energy share of fruits, vegetables, and legumes (ie, sources of health-protective phytochemicals) was 12·4%. When UPFs represented 75% of total energy intake, that share dropped to 4%.[46] Cross-sectional analyses of cohort studies found a similar inverse relationship between the share of UPFs and these protective foods.[50–52] Furthermore, nationally representative US studies found linear inverse associations between UPF quintiles and flavonoid intake,[66] and urinary concentrations of phytoestrogens.[67]

Increased intake of xenobiotics (substances foreign to a biological system)

Toxic compounds (eg, furans, heterocyclic amines, polycyclic aromatic hydrocarbons, acrolein, advanced glycation end products, acrylamide, and trans-fatty acids), though not all exclusive to UPFs, are often generated during their manufacture.[68] UPF intake was associated with elevated circulating concentrations of acrylamide biomarkers in the USA[69] and industrial trans-fatty acids in Europe.[70]

Noxious chemicals, such as phthalates, bisphenols, and perfluoroalkyl and polyfluoroalkyl substances (PFAS), which are known endocrine disruptors,[71] can leach from packaging commonly used for UPFs with long shelf lives, or from UPFs consumed directly from packaging.[68] Nationally representative studies from the USA found higher urinary concentrations of PFAS in people with increased UPF intake.[72,73] During pregnancy, an increased UPF intake was associated with greater maternal concentrations of phthalates[74] and umbilical cord PFAS.[75]

Diets with an increased share of UPFs are liable to contain more classes or mixtures of additives that are harmful to health, such as emulsifiers,[76–78] flavour enhancers,[79,80] non-sugar sweeteners,[81–86] colourings,[87–89] and combinations thereof.[90] Within the NutriNet–Santé cohort (n=110 925), participants in the highest UPF dietary share quintile had higher mean daily intakes of emulsifiers (two-fold increase), flavour enhancers (three-fold increase), non-sugar sweeteners (five-fold increase), colourings (15-fold increase), mixtures of emulsifiers and colourings (two-fold increase), and mixtures of emulsifiers, colourings, and non-sugar sweeteners (five-fold increase), than those in the lowest UPF dietary share quintile (appendix p 6).

The ultra-processed dietary pattern: impact on chronic disease risk

Hypothesis 3 has been examined by numerous observational prospective studies and some interventional and mechanistic studies, all using Nova. Here, we present the findings of our systematic review with meta-analyses of the observational studies, along with a narrative review of the interventional and mechanistic studies.

Observational prospective studies

Due to the small number of studies done in children and adolescents—which generally showed prospective associations with short-term and long-term cardiometabolic risk markers, including increases in bodyweight, fat mass, waist circumference, and blood lipid abnormalities[91–94]—our systematic review focused solely on adults. The methods used in the review and meta-analyses are detailed (panel 2). Our review identified 12 831 records; 359 were fully screened, and 104 met the inclusion criteria (appendix p 7).

A full description of the 104 selected studies[42,49–54,100–197] is in the appendix (pp 8–13). All studies were published between 2016 and 2024, and included participants from Europe (n=55), North America (n=23), Latin America (n=12), Asia (n=11), and Oceania (n=1), and two multi-region studies. Three-quarters of these studies included more than 10 000 participants, and a third included more than 100 000. The median and mean follow-up times ranged from 1 to 46 years, but were mostly 5–14 years. Food intake was assessed by food frequency questionnaires (n=63), 24 h recalls (n=29) or records (n=1), and dietary history questionnaires (n=11).

Exposure to the ultra-processed dietary pattern was measured as dietary share by energy (n=22) or by weight (n=36), with mean values ranging from 9·2% to 48·6% (energy) and 4·9% to 41·0% (weight).

Panel 2: Methods used in the systematic review and meta-analyses of prospective studies on the association between ultra-processed food intake and chronic disease outcomes in adults

Search strategy

This systematic review was registered with PROSPERO (CRD42022351111) and conducted following PRISMA[95] and MOOSE[96] guidelines. The following databases were searched from inception to July 4, 2024: PubMed (MEDLINE), Scielo, Latin American and Caribbean Health Sciences Literature, Web of Science, Scopus, and Embase. Additional studies were identified through Google Scholar, grey literature, and reference lists of included articles.

To increase sensitivity, we used only search terms related to exposure (ie, "ultra-processed", "ultraprocessed", "ultraprocessed food", "ultra-processed food", and "ultra processed food") to capture all studies on ultra-processed foods (UPFs) and any health outcome. Search strategies were tailored to each database, targeting terms included in titles, abstracts, or subject headings.

Inclusion criteria

We included prospective studies in adults reporting UPF intake classified by the Nova system.[4] Studies that were focused on non-chronic disease outcomes, conducted during pregnancy, or restricted to specific UPF subgroups were excluded, as were animal studies, in vitro studies, reviews, and systematic reviews. Studies on all-cause mortality were included, as 75% of global deaths result from chronic diseases.[97]

Study selection

Two trained reviewers independently screened titles, abstracts, and full texts, as supervised by MLCL. Disagreements were resolved by MLCL.

Assessment of study quality

MLCL, RBL, LFMR, and GCA evaluated study quality using the Newcastle–Ottawa Scale.[98] Each study was assessed independently by two researchers, with disagreements resolved by consensus among all evaluators.

Statistical analysis

We did random-effect meta-analyses to estimate the relative risk for the highest versus lowest UPF consumption and health outcomes (for all health outcomes with ≥4 studies). Some outcomes were grouped: overweight and obesity, cardiovascular disease incidence and mortality, coronary heart disease incidence and mortality, and cerebrovascular disease incidence and mortality.

Studies reporting odds ratios were converted to relative risk ratios before inclusion in the meta-analyses.[99] When two studies used the same cohort and outcome (eg, UK Biobank cohort),[100,101] we selected the most recent study.[101] For one study reporting relative risk ratios by sex, we pooled results through a fixed-effects model.[53] We contacted authors of four studies[102–105] reporting only continuous associations (eg, relative risk ratios for each 10% increase in UPF) to obtain the relative risk ratio for high versus low UPF intake. Heterogeneity was quantified by I^2.[106] Sensitivity analyses were conducted by excluding studies with Newcastle–Ottawa scores below 7 and studies with fewer than 10 000 participants. For the outcomes with three studies, we presented a narrative review. For outcomes with one or two studies, findings were presented in the appendix (pp 17–28).

Other studies used absolute intake (ie, in grams or servings per day) and adjusted for total food intake. All studies controlled for sociodemographic variables; most adjusted for smoking and physical activity (n=96), BMI (n=79), alcohol (n=57), and potential dietary mediators, including key nutrients (eg, sodium, saturated fat, and added sugar) and food groups (eg, fruits, vegetables, and legumes), or diet quality scores combining these nutrients and food groups (n=54). Only one study stated industry funding.

85 studies were rated as good quality (ie, ≥7 of 9 points on the Newcastle–Ottawa Scale),[98] 18 were rated as fair (5–6 points), and one as poor (<5 points; appendix pp 14–16).

Of the 104 studies, 92 reported associations between exposure to the ultra-processed dietary pattern and increased risk of one or more chronic disease outcomes, including all-cause mortality; cancer-related, cardiovascular-related, or cerebrovascular-related morbidity and mortality; and gastrointestinal, respiratory, kidney, liver, gallbladder, joint, metabolic, and mental illnesses. Of these 92 studies, 78 reported statistically significant linear trend associations (appendix pp 17–24).

Meta-analyses of outcomes with four or more studies (n=72; figure 4, appendix pp 25–26) included 58 studies rated as good quality. The number of studies per outcome ranged from four to 20, and the number of participants ranged from 28 814 to 960 638. In maximally adjusted models, high exposure to the ultra-processed dietary pattern was associated with a greater risk of 12 outcomes: overweight or obesity, abdominal obesity, type 2 diabetes, hypertension, dyslipidaemia, cardiovascular disease or mortality, coronary heart disease or mortality, cerebrovascular disease or mortality, chronic kidney disease, Crohn's disease, depression, and all-cause mortality. Effect sizes ranged from 1·14 (95% CI 1·06–1·23) for cerebrovascular disease or mortality, to 1·90 (1·40–2·59) for Crohn's disease. No associations were found for all-cancer mortality, ulcerative colitis, and colorectal cancer.

Results remained unchanged in a sensitivity analysis excluding low-quality studies, except for Crohn's disease, where the association became statistically non-significant (for two high-quality studies; appendix p 27). No changes occurred after excluding studies with fewer than

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	Number of studies	Total number of participants	Number of cases or events	Risk Ratio (95% CI)	I^2
Crohn's disease	4	960 638	886	1·90 (1·40–2·59)	33%
Abdominal obesity	4	47 589	3492	1·33 (1·24–1·42)	0%
Dyslipidaemia	4	28 814	6619	1·26 (1·12–1·43)	56%
Type 2 diabetes	12	445 133	30 939	1·25 (1·18–1·34)	49%
Depression	6	275 355	13 189	1·23 (1·08–1·39)	84%
Chronic kidney disease	5	272 097	11 831	1·22 (1·09–1·36)	62%
Overweight or obesity	8	541 297	47 143	1·21 (1·15–1·26)	26%
Coronary heart disease or mortality	8	478 968	23 137	1·19 (1·07–1·33)	89%
All-cause mortality	20	859 769	123 877	1·18 (1·12–1·25)	79%
Cardiovascular disease or mortality	19	848 904	51 071	1·18 (1·10–1·26)	81%
Hypertension	6	114 344	15 669	1·17 (1·08–1·26)	21%
Cerebrovascular disease or mortality	7	467 849	9932	1·14 (1·06–1·23)	16%
Colorectal cancer	4	954 765	11 194	1·10 (0·99–1·23)	74%
Ulcerative cancer	4	960 638	1850	1·08 (0·88–1·34)	37%
All-cancer mortality	9	695 822	34 406	1·01 (0·96–1·07)	48%

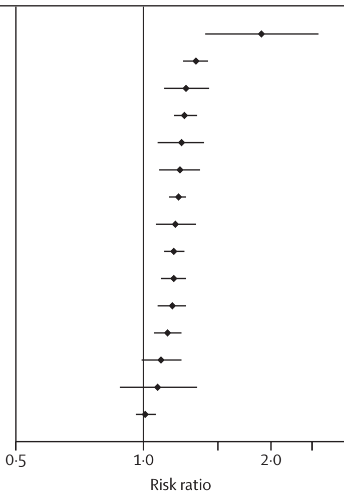

Figure 4: **Results from meta-analyses of prospective studies assessing associations between highest versus lowest exposure to the ultra-processed dietary pattern and risk of chronic disease outcomes**
Error bars are 95% CIs.

10 000 participants, which were more prone to publication bias[198] (appendix p 28).

For outcomes with three studies, the ultra-processed dietary pattern was associated with increased overall cancer incidence in all three and with postmenopausal breast cancer in one. No associations were reported in the three studies on lung, prostate, or premenopausal breast cancers. Findings from outcomes with one or two studies are displayed in the appendix (pp 17–24).

Interventional studies

Long-term RCTs on dietary patterns and chronic diseases are generally not feasible for ethical, financial, or methodological reasons.[199] However, the two crossover RCTs on ad libitum UPF and non-UPF diets matched for presented calories and macronutrients and the pilot behavioural intervention study aforementioned found significant effects of the ultra-processed dietary pattern on weight changes.

In the 2-week US NIH trial with 20 participants, the UPF diet led to a gain of 0·9 kg (95% CI 0·9–1·5) in bodyweight and 0·4 kg (0·2–0·6) in fat mass, while the non-UPF diet led to a reduction of 0·9 kg (0·3–1·5) in bodyweight and 0·3 kg (0·1–0·5) in fat mass.[56]

In the 1-week Tokyo trial with 9 participants, the UPF diet led to a gain of 2·2 kg (1·8–2·6) in bodyweight and 0·7 kg (0·3–1·1) in fat mass, while the non-UPF diet led to a gain of of 1·1 kg (0·5–1·6) in bodyweight and a reduction of 0·4 kg (0·0–0·8) in fat mass.[58]

In the Drexel pilot study with 14 participants, the 8-week behavioural intervention designed to reduce UPF consumption led to a bodyweight reduction of 3·5 kg (1·8–5·2).[55]

Mechanistic studies

A few prospective studies performed mediation analyses to identify mechanisms at the dietary level linking higher UPF consumption and chronic disease outcomes. The Moli-sani study found that 20–33% of associations with all-cause and cardiovascular mortality were mediated by sugar intake, whereas saturated fats and sodium intake had minimal effects.[52] A three-cohort US study found 12% of associations with type 2 diabetes were mediated by dietary factors (eg, intake of fibre, refined starch, added sugar, sodium, minerals, and partially hydrogenated oils).[135]

A systematic review[200] including 37 prospective studies reported that 64 of 66 associations between UPF intake and chronic disease outcomes remained statistically significant after adjusting for diet quality parameters, such as intake of sodium, sugar, and saturated fat; intake of fruits and vegetables; and composite diet quality scores combining nutrients and food groups. This finding aligns with the NIH and Tokyo trials.[56,58]

Altogether, the evidence shows that harm from UPF consumption is not solely due to dietary nutrient profile deterioration. As discussed in hypothesis 2, other plausible factors include hyper-palatability, high non-beverage energy density, disrupted food structures, soft texture, low content of health-protective phytochemicals, toxic contaminants created during processing or released from packaging materials, and potentially harmful classes and mixtures of additives.[57–62,66–89]

With regard to pathophysiological mechanisms linking the ultra-processed dietary pattern to increased disease or mortality risk, a study involving UK and US cohorts showed liver function and inflammation biomarkers explained 20–30% of UPF associations with

Panel 3: Addressing scientific criticisms of the Nova classification and ultra-processed diets, and guiding future research

Low precision in defining ultra-processed foods (UPFs)

Criticism

Nova's criteria for classifying UPFs rely on qualitative descriptors and the presence of specific ingredients and additives, which could introduce subjectivity and classification bias, particularly when dietary datasets lack details.

Response

Assigning some items within Nova groups can be challenging without adequate training and standardised methods,[201] but the use of validated protocols and trained raters reduces inaccuracies.[202] Studies using best practices[203] have found food frequency questionnaires to be acceptably valid and reliable in classifying foods using Nova.[204–207] Furthermore, misclassification of poorly detailed food items (eg, bread) does not appear to affect study conclusions.[49] Several 24 h dietary recalls and food frequency questionnaires specifically designed to assess consumption of Nova food groups have been developed[202,206,208–211] and could be used in future research.

Few randomised controlled trials (RCTs)

Criticism

Most existing evidence on the adverse health effects of UPFs is observational and cannot definitively establish causality. More research is needed, especially from RCTs.

Response

Short-term RCTs (eg, those by the US NIH[56] and Tokyo Hospital[58]) have shown consistent and biologically plausible effects of ultra-processed diets on precursors of obesity, including excessive total energy intake and increases in bodyweight and fat mass. These experiments support the plausibility of associations with the incidence of obesity observed in long-term prospective cohorts. Additional well designed trials assessing other short-term physiological responses are needed. Short-term trials are invaluable for testing biological plausibility, whereas well designed prospective cohort studies with sufficient follow-up and robust confounding control provide key evidence in population-level nutrition research. Both study types are important and have complementary roles. As previously stated, large-scale RCTs on dietary patterns and long-term outcomes are rarely feasible.

Unknown mechanisms of UPFs on health

Criticism

The biological pathways through which UPFs contribute to adverse outcomes are not fully established, and it is therefore premature to include UPF reduction in dietary guidelines or to implement regulatory policies targeting UPFs.

Response

The breadth of health outcomes linked to ultra-processed diets suggests multiple interacting mechanisms, which will likely take decades of research to fully elucidate. Strong evidence already supports the plausibility of several mechanisms acting alone or in combination: gross nutrient imbalances;[46–52] overeating[46,55,56,58] driven by UPFs with high energy densities and hyper-palatability,[57] as well as degraded food matrices and soft textures;[58–62] reduced intake of healthy phytochemicals;[66,67] and increased exposure to toxic compounds,[69,70] endocrine disruptors,[72–75] and harmful classes and mixtures of various additives.[76–90] Although further studies on these mechanisms, including new RCTs, are scientifically important and could also support the targeted regulation of particular UPF subgroups or ingredients, existing evidence is consistent with the current biological and epidemiological knowledge of how UPFs contribute to disease risk. This evidence is more than sufficient to justify recommending UPF reduction in dietary guidelines and implementing UPF regulatory policies.

Tobacco smoking involves exposure to thousands of chemical compounds, many of which are toxic or carcinogenic.[212] Public health recommendations and actions have been made without knowledge of the specific effects of almost all of these components, either singly or in combination.[213] Furthermore, the Mediterranean diet is widely promoted with incomplete knowledge of the specific mechanisms underlying its protective effects,[214] and John Snow's landmark study[215] linking cholera outbreaks to contaminated water, and his action to block the source, preceded the discovery of *Vibrio cholerae*. These examples illustrate that effective public health action can—and should—be guided by epidemiological evidence, even in the absence of complete mechanistic understanding.

Within-group nutrient profile heterogeneity

Criticism

UPFs vary in nutritional composition, so Nova might overlook health-relevant distinctions and misclassify certain foods as being unhealthy.

Response

Although Nova does not stratify UPFs by nutrient content, exploring the health effects of UPF subgroups based on their nutrient profile might be relevant for regulatory purposes—especially where UPFs dominate the food supply (eg, in the USA and the UK) and subgroups-specific policies are considered.

A few prospective cohort studies that have found direct associations between exposure to the ultra-processed dietary pattern and an increased risk of chronic disease outcomes have attempted to isolate the health effects of UPF subgroups, with mixed results depending on the subgroup, outcome, and cohort. For instance, in the Harvard cohorts, ultra-processed yoghurts and dairy desserts were associated with all-cause mortality,[118] frailty,[177] and features of prodromal Parkinson's disease;[216] had no association with cardiovascular mortality;[118] and were inversely associated with type 2 diabetes[137] and cardiovascular diseases.[217] In a Brazilian cohort study,[218] six UPF subgroups—savoury snacks, sweet snacks, meat products, mixed dishes, sweetened drinks, and distilled alcoholic

(Continues on next page)

(Panel 3 continued from previous page)

beverages—were positively associated with at least one chronic disease outcome. Packaged bread was positively associated with anxiety disorders and inversely associated with metabolic syndrome; yoghurts and dairy desserts were inversely associated with type 2 diabetes; and spreads had no association with chronic diseases. However, these studies all compare UPF subgroups to the overall non-UPF diet, hindering the isolation of specific effects of ultra-processing within food categories and conflating processing effects with those of the food type.[219]

Future studies should directly compare UPFs to their minimally processed or processed counterparts, such as flavoured versus plain yoghurts or extruded versus wholegrain cereals, to better isolate the effects of ultra-processing itself. However, analyses of the health effects of individual UPF subgroups, rather than the overall ultra-processed dietary pattern, face methodological challenges. These include confounding by other food components (both UPFs and non-UPFs), multicollinearity between UPF subgroups and total UPF intake, low consumption and little variability within specific subgroups, and uncorrected multiple model testing. These challenges are all liable to compromise the validity and precision of estimates.[220,221]

all-cause and cardiovascular mortality.[131] In the UK Biobank cohort, dysglycaemia, dyslipidaemia, and inflammation explained 1–10% of the associations with chronic pulmonary obstructive disease.[182] In the Moli-sani cohort, renal biomarkers explained 8–20% of associations with all-cause and cardiovascular mortality.[52]

Scientific criticisms and future research

Valid scientific criticisms of both the Nova classification system and evidence for the harmful effects of UPFs have been raised and are welcome. These criticisms and possible responses are summarised (panel 3) and could be used as frameworks for future research. Attempts by corporations, their front groups, and others (usually with conflicted interests) to discredit Nova and the mass of evidence linking ultra-processed diets to ill health, are addressed in the third paper of this Series.

Advancing the study of UPFs and their effects on health requires a multi-pronged research agenda. Beyond studies using tools specifically designed to measure Nova group intakes—which are increasingly available[202,206,208–211]—research priorities include mechanisms linking ultra-processed diets to multi-system harm; RCTs on short-term health outcomes; and comparing the health effects of UPF subgroups with their non-UPF counterparts (panel 3). Further research efforts are needed in areas such as cancer, mental disorders, and gastrointestinal, respiratory, and liver diseases; UPF sales and consumption trends in low-income countries; UPF-related addiction, UPF health effects in children and during pregnancy; and UPF health impacts through sociocultural, commercial, economic, and environmental pathways.

Conclusion

Here, we summarise how the accumulated evidence supports or refutes the three hypotheses, which, if upheld, justify the thesis that the displacement of long-established dietary patterns by UPFs is a key driver of the escalating global burden of multiple diet-related chronic diseases.

Hypothesis 1: global displacement of long-established dietary patterns

The share of UPFs in total energy intake increased over the past three to four decades in eight of nine middle-income and high-income countries with repeated intake or purchase surveys using Nova. Increases were greater in countries with initially low UPF shares (ie, <20%) and smaller where the share was already high (ie, 50%). From 2007 to 2022, annual UPF sales (initially <150 kg/person) rose in low-income, lower-middle-income, and upper-middle-income countries, and across all lower income regions. This increase was also apparent in all ten Euromonitor UPF subgroups, indicating a uniform global spread of UPFs. UPF sales in high-income countries and higher income regions (≥200 kg/person in 2007) declined slightly after sales of sweetened carbonated drinks dropped, which is likely due to an increase in regulatory policies targeting these products.[13] However, all other UPF subgroups showed stable or increasing sales, highlighting the persistence of the ultra-processed dietary pattern once established.

Together, despite scarce data from low-income countries, the converging trends in consumption, purchase, and sales make evident the global displacement of long-established dietary patterns by UPFs and indicate further rapid spread in regions where UPFs are not yet dominant.

Hypothesis 2: extensive deterioration of diet quality

National surveys, large cohorts, and three interventional studies consistently show that exposure to the ultra-processed dietary pattern broadly degrades diet quality. Harmful consequences include major nutrient imbalances; multiple features that promote overeating; reduced intake of health-protective phytochemicals; and increased intake of toxic compounds, endocrine disruptors, and potentially harmful classes and mixtures of food additives.

Despite the paucity of studies in low-income countries and emerging research on phytochemicals and xenobiotics, the breadth and consistency of the evidence

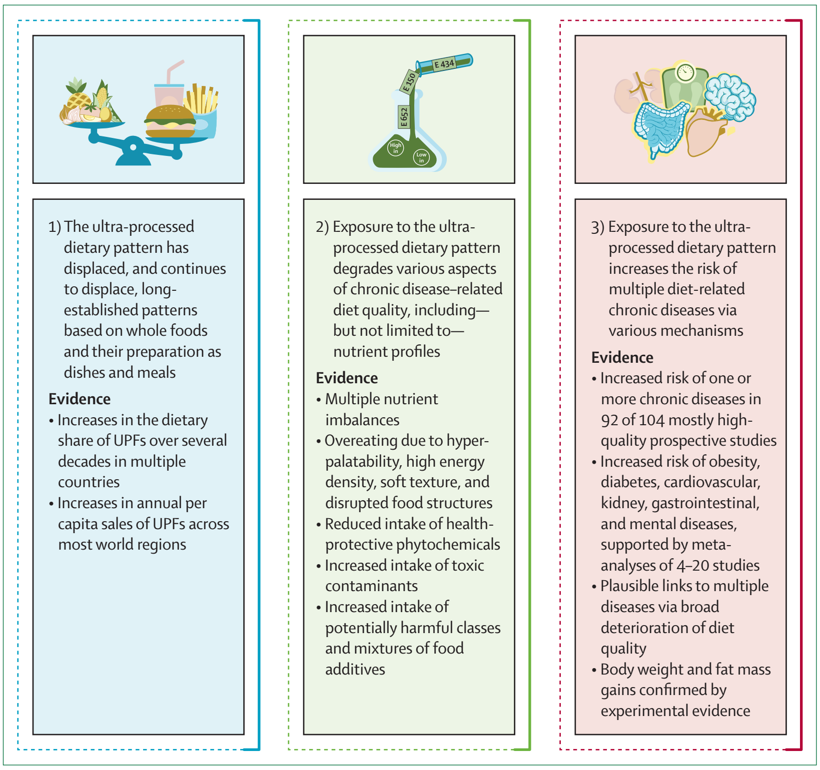

***Figure 5:* Three hypotheses underlying the thesis that the displacement of long-established dietary patterns by UPFs is a key driver of the escalating global burden of multiple diet-related chronic diseases**
UPFs=ultra-processed foods.

strongly support the conclusion that exposure to the ultra-processed dietary pattern broadly degrades diet quality.

Hypothesis 3: high risk of chronic diseases

Our systematic review of 104 prospective studies found 92 showing an association between the ultra-processed dietary pattern and increased risk of chronic disease outcomes. Meta-analyses of 15 outcomes (with ≥4 studies) found statistically significant associations for 12, including: overweight or obesity; type 2 diabetes and other cardiometabolic risk factors; cardiovascular, kidney, and gastrointestinal diseases; depression; and all-cause mortality. Pooled estimates, based on maximally adjusted models (often conservative due to adjustment for potential mediators) were similar in magnitude (in reverse) to the protective effects of the Mediterranean dietary pattern.[222] After the initial submission of this Series paper, similar associations between UPF consumption and adverse health outcomes were reported in three umbrella reviews of meta-analyses.[223–225] Additionally, a study across eight countries with varying levels of UPF consumption estimated that UPFs account for 4% (in Colombia) to 14% (in the USA and the UK) of premature all-cause mortality.[226] As noted earlier, two crossover RCTs on disease precursors confirmed the association with obesity, which was further reinforced by two similar trials published shortly before this Series paper was accepted.[227,228] Triangulation of evidence[229]—drawing on four trials, mediation analyses, comparisons with and without nutrient and food-group adjustments, and findings related to hypothesis 2—shows that the harmful effects of ultra-processed diets result from deteriorated nutrient profiles and other dietary characteristics, such as hyper-palatability, high energy densities, soft textures, disrupted food structures, low contents of phytochemicals, toxic contaminants, endocrine disruptors, and harmful additives. Mediation analyses also identified biomarkers of inflammation and of liver and renal dysfunctions as pathophysiological pathways linking the ultra-processed dietary pattern to increased disease and mortality risk.

Despite limitations of observational studies (eg, residual confounding and non-differential misclassification of the exposure), associations were consistent across large, high-quality cohorts, and some trials. Together, the evidence fulfils seven of the nine Bradford Hill criteria to infer causality.[230] These criteria are consistency (ie, increased risk repeatedly observed in many countries and settings by different researchers using different methods and research designs); strength (risk equivalent to the protection conferred by the Mediterranean dietary pattern); temporality (exposure precedes the outcome); biological gradient (the higher the dietary share of UPFs, the higher the risk of diseases); plausibility (consistent with broad deterioration of diet quality and multiple potential pathophysiological mechanisms); coherence (no conflict with the known facts of the natural history and biology of the identified diseases); and experiment (bodyweight and fat mass increases). The specificity and analogy criteria do not apply due to the multiplicity of outcomes and the absence of equivalent exposures.

Therefore, the accumulated evidence on the three hypotheses supports the thesis that the displacement of long-established dietary patterns by UPFs is a key driver of the escalating global burden of multiple diet-related chronic diseases (figure 5).

Although more research is clearly warranted, the need for further evidence should not delay public health action. Policies that promote and protect dietary patterns based on a variety of whole foods and their preparation as dishes and meals, and that discourage the production and consumption of UPFs, cannot be postponed. These policies are particularly urgent in countries where the ultra-processed dietary pattern does not yet prevail. These strategies should complement—not replace—existing policies and actions designed to reduce consumption of products high in added fats, sugar, or salt, and excessive red meat intake, as such consumption is harmful regardless of the level of processing. These strategies are discussed in the second[13] and third[14] papers of this Series.

Contributors
CAM developed the first draft of the manuscript with contributions from MLCL, ES-M, and GC. CAM was responsible for funding acquisition,

administration of the commissioned studies, and co-leadership of the *Lancet* Series on ultra-processed foods and human health. CAM and MLCL were responsible for the systematic review and meta-analyses. MLCL, RBL, LFMR, and GCA assessed the quality of the studies included in the systematic review using the Newcastle–Ottawa Scale. All authors contributed to the design of the manuscript, and to the revision and writing of several drafts, including the final draft.

Declaration of interests

CAM, MLCL, GC, J-CM, and RBL integrated the team that developed the Nova food classification system. The body of work informing this study, and the *Lancet* Series on ultra-processed foods and human health, was supported by funding from Bloomberg Philanthropies. The study funder had no role in the design or conduct of the work, nor in determining the content of the final manuscript. The findings reported in this manuscript reflect the viewpoints and findings of the authors only, and do not necessarily represent the views, decisions, or policies of the study funder, nor the institutions with which the authors are affiliated. All other authors declare no competing interests.

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