



Ultra-Processed Foods and Metabolic Health: From Food Processing to Gut Microbiome Dysfunction

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Abstract

Ultra-processed foods (UPFs) have become a major component of modern food environments and are increasingly investigated as a potential determinant of metabolic disease. Within the NOVA classification, UPFs are industrial formulations made from food-derived substances and additives and are typically designed for convenience, long shelf life, intense palatability and rapid consumption. High intake is consistently associated in observational research with obesity, type 2 diabetes, cardiovascular disease and other adverse health outcomes, although the magnitude and causality of these associations vary across outcomes and study designs. A controlled inpatient randomized trial demonstrated that participants consumed substantially more energy and gained weight during an ultra-processed diet than during an unprocessed diet despite broadly matched presented macronutrient composition, supporting a plausible causal pathway through eating rate, energy density, palatability and satiety. More recent research has shifted attention toward the gut microbiome as a potential mechanistic bridge between food processing and metabolic dysfunction. UPF-rich dietary patterns can be characterized by low intact dietary fibre and altered food structure, together with exposure to emulsifiers, non-nutritive sweeteners, colours and other additives. These features may modify microbial community structure and function, short-chain fatty-acid production, bile-acid metabolism, intestinal mucus and barrier integrity, microbial-host signalling and low-grade systemic inflammation. However, direct human intervention evidence linking overall UPF exposure to microbiome-mediated metabolic disease remains limited, and effects of individual additives cannot automatically be generalized to all UPFs. This review examines the concept and classification of ultra-processing, nutritional and physicochemical characteristics of UPFs, evidence linking UPF exposure with metabolic health, and emerging mechanisms involving gut microbiome dysfunction, intestinal barrier disruption, inflammation and altered host metabolism. Current limitations, research priorities and practical implications for nutrition and public health are also discussed. The available evidence supports reducing reliance on UPFs while emphasizing minimally processed foods, dietary fibre and overall dietary quality, but it also highlights the need for well-controlled long-term human studies capable of separating processing effects from nutrient composition, energy intake and other correlated dietary factors.

Keywords: Ultra-Processed Foods; NOVA Classification; Metabolic Health; Obesity; Type 2 Diabetes; Insulin Resistance; Gut Microbiome; Dysbiosis; Intestinal Barrier; Inflammation; Short-Chain Fatty Acids; Food Additives

Abbreviation

UPF: Ultra-Processed Food; NOVA: Food Classification System Based on the Nature, Extent and Purpose of Processing; GI: Gastrointestinal; T2D: Type 2 Diabetes; CVD: Cardiovascular Disease; BMI: Body Mass Index; SCFA: Short-Chain Fatty Acid; LPS: Lipopolysaccharide; IBD: Inflammatory Bowel Disease; NAFLD: Non-Alcoholic Fatty Liver Disease; MASLD: Metabolic Dysfunction-Associated Steatotic Liver Disease; ROS: Reactive Oxygen Species; TNF- α : Tumour Necrosis Factor-Alpha; IL: Interleukin; NF- κ B: Nuclear Factor Kappa B; GLP-1: Glucagon-like Peptide-1; PYY: Peptide YY; HDL: High-density Lipoprotein; LDL: Low-density Lipoprotein; RCT: Randomized Controlled Trial; GRADE: Grading of Recommendations Assessment, Development and Evaluation; Source: Author-compiled from terminology used throughout the cited literature.

Introduction

Food processing is an essential part of the food system. Processing can improve safety, preserve foods, increase availability and reduce preparation time. Therefore, the term “processed food” should not be treated as synonymous with unhealthy food. The contemporary discussion focuses increasingly on the nature, extent and purpose of processing and on the distinction between minimally processed foods, processed culinary ingredients, processed foods and ultra-processed foods. The NOVA classification places UPFs in its fourth group and defines them principally by the industrial formulation and purpose of processing rather than by a single nutrient threshold [1,2,12].

UPFs include many packaged snacks, sugar-sweetened beverages, confectionery, reconstituted meat products, instant noodles, breakfast products and ready-to-eat or ready-to-heat meals. Their formulations commonly combine refined or fractionated ingredients with oils, sugars, starches, proteins, flavourings, colours, sweeteners, emulsifiers, thickeners and other additives. These products are frequently energy dense, convenient and highly palatable and may be consumed rapidly. The NOVA approach therefore raises a question that extends beyond [1,2].

Nutrient composition: whether industrial processing and the resulting food matrix, additives and eating characteristics can influence health independently or synergistically with nutrient quality [1,2,12].

The public-health importance of this question has increased as UPFs have become more prominent in many food environments. Large observational studies and meta-analyses have repeatedly reported associations between higher UPF exposure and obesity, cardiometabolic disease, diabetes and mortality. A 2024 umbrella review of epidemiological meta-analyses synthesized 45 pooled analyses involving 9,888,373 participants and found direct associations between greater UPF exposure and 32 of 45 health outcomes, although the certainty of evidence varied and much of the underlying evidence remained observational [3,11,12].

The mechanistic discussion has also expanded. The gut microbiome is a biologically plausible interface between diet and metabolic health because intestinal microorganisms metabolize dietary components and produce metabolites that influence epithelial integrity, immune function, glucose and lipid metabolism, bile-acid signalling and host energy homeostasis. A diet high in UPFs may alter this ecosystem through reduced fibre and altered food structure as well as through exposure to food additives. However, evidence is heterogeneous, and current human intervention data are insufficient to conclude that microbiome dysfunction is the sole or primary mediator of UPF-associated disease [7,23,24].

This review therefore examines the pathway from food processing to metabolic health, with particular emphasis on the gut microbiome. It integrates nutritional, behavioural, physiological and microbial mechanisms and distinguishes established evidence from emerging hypotheses [3,7,8].

Aim and Scope of the Review

The aim of this review is to critically summarize current evidence on the relationship between ultra-processed food consumption and metabolic health, with specific emphasis on gut microbiome alterations and related mechanisms. The review considers: (i) the definition and classification of UPFs; (ii) nutritional and physicochemical characteristics of UPF-rich diets; (iii) evidence linking UPFs with obesity, insulin resistance, type 2 diabetes, dyslipidaemia, cardiovascular disease and fatty liver disease; (iv) effects on the gut microbiome, microbial metabolites and intestinal barrier; (v) potential roles of food additives and altered food structure; (vi) inflammation and metabolic signalling; and (vii) limitations, research gaps and practical implications [3,7,23].

Literature Search Strategy

This narrative review was updated through 12 September 2026 using PubMed/NCBI-indexed literature, major scientific publisher databases and reference-list screening. The principal coverage period was 2009–September 2026, reflecting the development and subsequent expansion of the NOVA framework and the growth of evidence on ultra-processed foods (UPFs), metabolic health and the gut microbiome. Search concepts included “ultra-processed food”, “NOVA”, “food processing”, “obesity”, “type 2 diabetes”, “insulin resistance”, “metabolic syndrome”, “cardiovascular disease”, “fatty liver”, “gut microbiome”, “dysbiosis”, “intestinal permeability”, “food additives”, “emulsifiers”, “non-nutritive sweeteners”, “short-chain fatty acids”, “controlled feeding”, and “minimally processed diet”. Priority was given to systematic reviews, meta-analyses, umbrella reviews, randomized controlled feeding studies, prospective cohort studies and relevant mechanistic investigations. Studies were considered for inclusion when they directly addressed UPF exposure or a mechanistically relevant component of UPF-rich diets and reported metabolic, microbial, inflammatory or related outcomes. Editorials and commentaries were used only for contextual interpretation, not as primary evidence. Animal and in-vitro studies were retained primarily to explain mechanisms and were explicitly distinguished from human evidence.

Because this is a narrative review rather than a registered systematic review, no pooled effect estimate was generated and no formal risk-of-bias meta-analysis was undertaken. The evidence was synthesized qualitatively, with particular attention to study design, population size, exposure duration, measured outcomes, consistency of findings and major limitations. This approach is

intended to distinguish established associations from emerging mechanistic hypotheses.

Ultra-processed foods: Definition and classification

The NOVA classification

NOVA classifies foods according to the nature, extent and purpose of processing. Group 1 consists of unprocessed or minimally processed foods, such as fresh or frozen vegetables, fruits, pulses, eggs, milk, meat, fish and whole grains. Group 2 comprises processed culinary ingredients such as oils, fats, salt and sugar. Group 3 contains processed foods produced by adding culinary ingredients to Group 1 foods, for example canned vegetables with added salt, cheeses and traditionally prepared breads. Group 4 consists of UPFs [1,2,17].

Industrial formulations made largely from food-derived substances and additives, generally with little intact whole food remaining [1,2,17].

A practical identifying feature of a UPF is an ingredient list containing substances rarely used in home kitchens or additive classes used to make products more palatable or visually appealing. Examples include hydrolysed proteins, protein isolates, modified starches, hydrogenated or interesterified oils, flavourings, flavour enhancers, colours, sweeteners, emulsifiers, thickeners and glazing agents. The presence of an additive alone, however, should not automatically be interpreted as proof of harm; food safety and physiological effects depend on the specific compound, dose, exposure pattern and food matrix [1,2,17].

NOVA group	General description	Examples	Primary purpose of processing
1. Unprocessed/minimally processed	Foods with minimal alteration of the original food	Fresh/frozen vegetables, fruit, legumes, eggs, milk, whole grains	Preservation, cleaning, drying, chilling or other basic preparation
2. Processed culinary ingredients	Substances obtained from Group 1 foods	Vegetable oils, sugar, salt	Cooking and preparation of meals
3. Processed foods	Whole foods modified mainly by adding Group 2 ingredients	Canned vegetables, cheese, traditional breads	Preservation and sensory modification
4. Ultra-processed foods	Industrial formulations containing food-derived fractions and/or additives, often with little intact whole food	Soft drinks, packaged snacks, confectionery, instant noodles, many ready meals	Convenience, long shelf life, sensory appeal and industrial formulation
Source	Adapted from Monteiro., <i>et al.</i> [1,2,17]		

Table 1: NOVA food classification and principal characteristics [1,2,17].

Why “processing” is not a single exposure

The health effects attributed to UPFs may arise from several overlapping dimensions. These include nutrient composition, energy density, food texture and structure, eating rate, portion size, palatability, replacement of fibre-rich foods, additive exposure, neoformed compounds generated during processing, and packaging-related chemical exposure. Because these dimensions commonly occur together, observational studies cannot always identify which component is responsible for an observed association [3,12,17].

This distinction is important for interpretation. For example, a minimally processed food and an industrial food can have similar calories or macronutrients but differ in physical structure, eating rate, fibre integrity and additive content. Conversely, some processed foods can have favourable nutritional profiles. The term UPF therefore represents a multidimensional exposure rather than a single chemical or nutrient [12,17].

Nutritional and Physicochemical Features of UPF-Rich Diets

Energy density, palatability and eating rate

UPFs are frequently formulated to be highly palatable and easy to consume. Soft textures, liquid calories, refined starches, free sugars and combinations of fat, salt and flavour compounds can reduce the behavioural effort required to eat and may facilitate rapid intake. In the controlled inpatient trial by Hall and colleagues, 20 adults received ultra-processed and unprocessed diets for two weeks each in randomized crossover fashion. The diets were designed to be broadly matched for presented calories, sugar, fat, fibre and macronutrients, yet participants consumed approximately 508 kcal/day more during the ultra-processed diet and gained about 0.9 kg during that period [4]. A subsequent randomized crossover trial by Dicken, *et al.* enrolled 55 adults and provided two 8-week ad libitum diets aligned with UK dietary guidelines: one minimally processed and one ultra-processed. Both diets produced weight loss, but weight loss was significantly greater during the minimally processed diet in the intention-to-treat analysis (50 participants) [25]. Together, these controlled studies support a role for food processing and food structure in energy intake and weight change, while also showing that processing should be interpreted in the context of overall dietary quality.

These trials do not prove that all UPFs cause overeating or that processing alone is responsible for every observed difference.

Potential contributors include eating rate, food texture, energy density, protein content, fibre structure, palatability and satiety signalling [4,25].

Dietary fibre and food structure

Many UPFs contain refined starches and isolated ingredients rather than intact plant structures. This can reduce the quantity and diversity of fermentable substrates reaching the colon. Intact plant cell walls and naturally occurring fibre influence chewing, gastric emptying, intestinal transit and microbial fermentation. Loss of food structure during milling, extrusion and other processes may therefore alter postprandial physiology even when labelled macronutrient content is similar [17,20,21].

Low dietary fibre is relevant to the microbiome because fermentable carbohydrates are substrates for microbial production of SCFAs such as acetate, propionate and butyrate. These metabolites participate in epithelial nutrition, immune regulation and host metabolic signalling. Thus, reduced fibre may represent one pathway through which a UPF-rich dietary pattern indirectly affects metabolic health [20,23].

Additives and industrial ingredients

Food additives used in UPFs include emulsifiers, stabilizers, thickeners, colours, sweeteners and flavour enhancers. Preclinical evidence indicates that some additives can alter microbial composition, intestinal mucus, epithelial interactions or inflammatory signalling. Human evidence is more limited and additive-specific. A 2024 Nature Reviews Gastroenterology and Hepatology review concluded that evidence for UPF-associated gut disease is largely observational, while evidence concerning individual additives is often derived from in-vitro or animal studies [7,13,14].

Accordingly, the scientifically appropriate interpretation is not that all additives are harmful, but that selected additives and additive mixtures warrant mechanistic and long-term human evaluation [7,13,14].

Ultra-processed foods and metabolic health

Obesity and weight gain

Obesity is the metabolic outcome for which a behavioural and experimental mechanism is particularly plausible. Higher UPF

consumption is repeatedly associated with higher body mass index and obesity in cohort and cross-sectional studies. The controlled feeding trial by Hall, *et al.* provides complementary evidence that an ultra-processed diet can increase spontaneous energy intake and body weight under inpatient conditions [3,4,9,25].

Potential mechanisms include greater energy density, faster eating rate, reduced satiety, liquid or soft textures, hyper-palatability, larger portion sizes and altered protein-to-energy ratios. UPFs may also displace minimally processed foods that are naturally rich in fibre and have lower energy density. Importantly, weight gain should not [4,25].

Be attributed to a single additive or processing step; it likely reflects the combined effect of food formulation, eating behaviour and dietary displacement [4,25].

Insulin resistance and type 2 diabetes

Prospective cohort studies have reported positive associations between UPF intake and incident type 2 diabetes. In the NutriNet-Santé cohort, greater UPF exposure was associated with increased type 2 diabetes risk after adjustment for multiple dietary and lifestyle factors. The 2024 BMJ umbrella review classified the dose-response association between greater UPF exposure and type 2 diabetes as convincing, with a moderate GRADE rating, although the authors emphasized the observational nature of the evidence [6].

Several pathways may contribute. High UPF intake may increase total energy intake and adiposity, which can promote insulin resistance. Refined carbohydrates and free sugars can increase postprandial glucose and insulin excursions, while low fibre intake may reduce beneficial microbial fermentation. Altered bile-acid signalling, inflammation and microbial metabolites are additional candidate pathways. Because adiposity, dietary quality and UPF exposure are closely correlated, causality should be interpreted cautiously [6,21,22].

Cardiovascular health and dyslipidaemia

Higher UPF exposure has been associated with cardiovascular disease events and cardiovascular mortality in several observational datasets. Possible explanations include greater sodium, free sugar and saturated-fat exposure in some UPFs, lower

dietary fibre and micronutrient density, excess energy intake and metabolic consequences of adiposity. The BMJ umbrella review found convincing evidence for an association between greater UPF exposure and cardiovascular disease-related mortality, although the certainty of evidence for this outcome was rated very low using GRADE [3,11].

The classification therefore identifies a population-level dietary pattern associated with risk rather than proving that processing itself independently causes cardiovascular disease. Future studies need to disentangle processing from sodium, sugar, fat quality, fibre, energy density and overall dietary pattern [3,11,12].

Metabolic syndrome and hypertension

Metabolic syndrome is characterized by a cluster of abdominal obesity, dysglycaemia, elevated blood pressure and adverse lipid profiles. UPF-rich diets may contribute to several components simultaneously through excess energy intake, high sodium and free sugar exposure, low fibre, and reduced dietary quality. Epidemiological evidence supports associations with several intermediate metabolic outcomes, but heterogeneity between cohorts and classifications remains substantial [3,17].

Fatty liver and metabolic dysfunction-associated steatotic liver disease

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed NAFLD, is closely linked to obesity, insulin resistance and excess energy intake. UPFs may contribute indirectly through weight gain, high free-sugar intake and adverse dietary patterns. Emerging literature also suggests that intestinal barrier dysfunction, microbial metabolites and inflammatory signalling may influence hepatic fat accumulation [3,7,21].

Through the gut-liver axis. However, direct causal evidence specifically linking UPF exposure, microbiome changes and MASLD in humans remains insufficient [7,21,22].

Gut Microbiome: A potential link between UPFs and metabolic dysfunction

The gut microbiome and metabolic homeostasis

The gut microbiome comprises a complex microbial ecosystem that interacts continuously with dietary substrates and host tissues. Microbial metabolism produces SCFAs, modifies bile acids, transforms amino acids and generates [21,22].

Numerous other metabolites. These products can influence intestinal epithelial cells, immune pathways, appetite signalling, glucose homeostasis and lipid metabolism [21,23].

Microbial diversity and community structure are influenced by diet, age, medications, geography, lifestyle and host genetics. Consequently, there is no single “healthy” microbiome profile that applies to every individual. The most defensible interpretation is that dietary patterns can shift microbial functions and ecological interactions in ways that may be beneficial or detrimental depending on context [21].

UPF-associated dysbiosis

A growing body of literature proposes that diets high in UPFs may be associated with lower microbial diversity or altered abundance of taxa involved in fibre fermentation and mucosal homeostasis. A 2024 narrative review specifically examining UPFs and the human gut microbiome concluded that available studies frequently report associations between UPF exposure and changes in microbial composition, but also emphasized methodological differences in NOVA classification and the need for mechanistic research [7,8].

Importantly, taxonomic changes alone do not establish dysfunction. Functional outputs such as SCFA production, bile-acid transformation, microbial gene expression, intestinal permeability and inflammatory markers may be more informative than relative abundance of individual taxa. Future studies should therefore combine metagenomics or metatranscriptomics with metabolomics and clinical metabolic phenotyping [7,8,21].

Reduced fibre fermentation and short-chain fatty acids

SCFAs, particularly acetate, propionate and butyrate, are major products of microbial fermentation of dietary fibre. Butyrate is an important energy substrate for colonocytes and can support epithelial barrier function. SCFAs also interact with host receptors and influence immune and metabolic pathways. A diet low in fermentable fibre may reduce substrate availability for SCFA production and thereby weaken some beneficial microbiota-host interactions [20,23].

This mechanism is biologically plausible but should not be oversimplified. SCFA concentrations in stool do not directly represent total production or host utilization, and the effects of

individual SCFAs can differ by tissue and physiological context [20,23].

Intestinal barrier dysfunction and microbial translocation

The intestinal barrier consists of epithelial cells, tight junctions, mucus, antimicrobial factors and immune components. Disruption of this barrier can increase exposure of host tissues to microbial products. Lipopolysaccharide from Gram-negative bacteria is frequently discussed in relation to metabolic endotoxaemia, in which microbial products may contribute to systemic inflammatory signalling [7,21,22].

Experimental studies of selected emulsifiers have shown effects on mucus properties, microbial composition and inflammatory responses. However, evidence that typical human dietary exposure to UPFs causes clinically meaningful barrier disruption is still developing. Human intervention studies that directly measure permeability, microbial function and metabolic outcomes are therefore a major research priority [7,13].

Food additives and microbial ecology

Emulsifiers are used to stabilize mixtures of water and fat and to improve texture and shelf life. Preclinical studies have raised concerns that some emulsifiers may modify microbial ecology and host-microbe interactions. Non-nutritive sweeteners have also been investigated for potential effects on microbiota and glucose tolerance; experimental human and animal findings have been mixed, and responses may be highly individual [7,13,14].

The correct scientific conclusion is that selected additives are plausible biological modulators, not that all additives universally cause dysbiosis. Dose, exposure duration, food matrix, microbial baseline and host characteristics must be considered [7,13,14].

The gut–liver and gut–metabolic axes

Microbial metabolites and barrier integrity provide routes through which intestinal events can influence distant organs. Altered bile-acid metabolism can affect receptors such as FXR and TGR5, which participate in glucose and lipid regulation. Microbial products can influence innate immune signalling, while SCFAs can modulate energy metabolism and appetite-related pathways. These interactions form a gut–metabolic axis that may connect dietary patterns with systemic metabolic disease [21–23].

The gut–liver axis is especially relevant to MASLD because portal circulation delivers microbial metabolites and microbial products directly to the liver. Nevertheless, mechanistic evidence should be interpreted as supportive rather than definitive until long-term human intervention studies establish temporal and causal relationships [21,22].

Inflammation, oxidative stress and metabolic signalling

Chronic low-grade inflammation is a common feature of obesity and insulin resistance. UPF-rich diets may promote inflammatory signalling indirectly through excess energy intake, adiposity, high intake of refined carbohydrates and saturated fats in some products, low fibre, and altered gut microbial interactions. Candidate

pathways include activation of NF-κB and other inflammatory signalling networks, cytokine production and oxidative stress [7,18,21].

Oxidative stress can further affect mitochondrial function and insulin signalling. Conversely, diets rich in vegetables, fruits, legumes, whole grains, nuts and other minimally processed foods supply fibre and antioxidant compounds that may support microbial and host redox homeostasis. The relationship is therefore likely to reflect overall dietary pattern rather than one isolated food component [18,21].

Evidence from human and experimental studies

Study/evidence	Sample size/ population	Exposure and duration	Key measured outcomes	Main finding	Key limitation	Source
Hall., <i>et al.</i> (2019), random- ized crossover feeding trial	20 adults; weight-stable inpatient partici- pants	Ultra-processed vs unprocessed diets; 14 days each, crossover	Ad libitum energy intake, body weight, mac- ronutrients	~508 kcal/day higher intake and ~0.9 kg weight gain during the ultra-processed diet	Small sample and short duration; not primarily designed for microbiome outcomes	[4]
Srour., <i>et al.</i> (2020), prospec- tive cohort	104,707 French adults	UPF exposure by NOVA; median follow-up about 6 years	Incident type 2 diabetes	A 10-percentage- point increment in UPF intake was associated with higher T2D risk	Observational design, residual confounding and dietary measure- ment error	[6]
Srour., <i>et al.</i> (2019), prospec- tive cohort	105,159 French adults	UPF exposure; median follow-up 5.2 years	Cardiovascu- lar, coronary and cere- brovascular disease	Higher UPF expo- sure was associ- ated with higher cardiovascular disease risk	Observational design and possible residual confounding	[11]
Lane., <i>et al.</i> (2024), umbrella review	9,888,373 participants across 45 pooled analyses	Systematic synthesis of meta-analyses; literature through June 2023	Mortal- ity, cancer, mental, respiratory, cardiovascu- lar, gastroin- testinal and metabolic outcomes	Direct asso- ciations were reported for 32 of 45 pooled health parameters; evi- dence certainty varied	Most underlying evi- dence observational; heterogeneity and GRADE limitations	[3]
Chassaing., <i>et al.</i> (2022), con- trolled-feeding study	16 healthy adults (9 con- trol; 7 CMC)	15 g/day carboxy- methylcellulose vs control; 11 days	Gut micro- biota, fecal metabolome, abdominal symptoms	CMC altered microbiota and metabolome and modestly in- creased abdomi- nal discomfort	Small sample, short duration and additive- specific exposure	[13]

Dicken., <i>et al.</i> (2025), randomized crossover feeding trial	55 adults randomized; 50 in intention-to-treat analysis	Minimally processed vs ultra-processed diets; 8 weeks each, UK Eatwell Guide	Weight change and cardio-metabolic outcomes	Both diets produced weight loss; minimally processed diet produced greater weight loss	Short duration; crossover design; findings concern specific guideline-based diets and should not be generalized to all UPFs	[25]
Chassaing., <i>et al.</i> (2015), animal mechanistic study	Mouse models; exact group sizes vary by experiment	Carboxymethylcellulose or polysorbate-80; up to 12 weeks	Microbiota composition, mucus, inflammation and metabolic phenotype	Selected emulsifiers altered microbiota and promoted inflammatory/metabolic changes in mice	Animal model and exposure conditions limit direct extrapolation to typical human intake	[24]
Source note	Study details are summarized from the cited primary studies and reviews; sample size, duration and outcomes are reported only where verified.					

Table 2: Selected human and experimental evidence on UPFs, metabolic health and gut-related mechanisms [3,4,6,7,13,25].

Proposed mechanistic pathway

A useful conceptual model is: high UPF exposure → increased palatability/energy density and reduced food structure → increased energy intake and adiposity; simultaneously, low fibre and altered food matrix → reduced or altered microbial fermentation; additive exposure and dietary displacement → changes in microbial ecology and intestinal barrier interactions; these changes → altered microbial metabolites, bile-acid signalling and inflammatory pathways; the combined effects → insulin resistance, dyslipidaemia, adiposity and other metabolic abnormalities [4,6,7,13,21,25].

This pathway is best viewed as a network rather than a linear chain. Different UPFs may act through different routes, and the same product can influence several pathways at once. Host factors, baseline microbiota, physical activity, sleep, medications and socioeconomic context can modify the response [7,21].

Challenges and limitations of current evidence

First, UPF exposure is difficult to measure. Dietary assessment tools may not consistently capture the degree of processing, and

NOVA classification can require subjective decisions for mixed dishes and reformulated products. Second, UPF consumption is strongly correlated with other dietary and social factors, including lower fibre intake, higher energy density, socioeconomic conditions and lifestyle behaviours. Statistical adjustment can reduce but not eliminate residual confounding [3,7,8,12].

Third, most long-term evidence is observational. The controlled feeding evidence is persuasive for increased energy intake and short-term weight gain, but there are comparatively few long-duration trials examining disease outcomes or the gut microbiome. Fourth, additive-specific evidence is often derived from animal or in-vitro experiments and should not be extrapolated directly to human disease [3,4,25].

Finally, the microbiome is highly individualized. A shift in the abundance of one bacterial taxon cannot automatically be labelled as dysbiosis, and microbial composition does not necessarily reflect microbial function. Future studies should therefore use

standardized UPF definitions, controlled diets, longitudinal sampling, metagenomics/meta transcriptomics, metabolomics and clinically relevant metabolic outcomes [7,8,21].

Future research directions

Future research should prioritize long-term randomized controlled feeding studies comparing diets matched for energy, macronutrients, fibre and food quality while differing in degree of processing. Such studies should measure energy intake, body weight, insulin sensitivity, lipid profiles, blood pressure, inflammatory markers, intestinal permeability and comprehensive microbiome/metabolome outcomes [3,4,7,8,25].

Research should also distinguish the effects of the overall UPF dietary pattern from individual components such as emulsifiers, sweeteners, colourants, refined starches and packaging-related chemicals. Dose-response studies reflecting real-world exposure are particularly important. Standardized definitions and validated dietary assessment instruments would improve comparability across cohorts [7,13,14,25].

The most informative future trials will likely combine dietary intervention with multi-omics approaches, including metagenomics, meta transcriptomics, metabolomics and bile-acid profiling. Stratification by baseline microbiome, metabolic phenotype, age and medication use may help identify responders and non-responders [7,8,21,25].

Practical and public health implications

The current evidence supports a practical dietary approach that emphasizes minimally processed foods and freshly prepared meals rather than focusing only on isolated nutrients. Increasing vegetables, fruits, legumes, whole grains, nuts and seeds and choosing water instead of sugar-sweetened beverages can improve dietary quality while reducing reliance on many UPFs [3,17].

At the population level, strategies should consider food affordability, accessibility, time constraints, food environments and product reformulation. Messages that simply label all processed foods as harmful may be inaccurate and can undermine practical nutrition guidance. A more useful approach is to distinguish necessary and beneficial processing from industrial formulations that are frequently energy dense, highly palatable and nutrient-poor [3,12,16,17].

Conclusion

Ultra-processed foods represent a complex dietary exposure that intersects food formulation, food structure, eating behaviour, nutrient composition and the intestinal ecosystem. Higher UPF consumption is consistently associated with several adverse metabolic outcomes, particularly obesity, type 2 diabetes and cardiovascular disease-related outcomes [3,6,11]. Controlled feeding evidence demonstrates that an ultra-processed diet can increase spontaneous energy intake and short-term weight gain [4], while newer controlled evidence indicates that both minimally processed and ultra-processed diets can support weight loss under guideline-based conditions, with greater loss on the minimally processed diet [25]. These findings strengthen the case for considering processing alongside overall dietary quality rather than treating processing as an isolated exposure.

The gut microbiome provides an important and biologically plausible bridge between dietary patterns and metabolic dysfunction. Reduced fibre and altered food structure may modify microbial fermentation, while selected additives may influence microbial ecology, mucus and barrier function [7,13,14,21]. Changes in SCFAs, bile-acid metabolism and inflammatory signalling may then affect systemic metabolism [21-23]. Nevertheless, direct human evidence proving that microbiome dysfunction mediates the relationship between UPFs and metabolic disease remains limited. Current findings should therefore be interpreted as a converging evidence base rather than proof of a single causal pathway.

Future research should move from association toward mechanism by using standardized UPF classification, well-controlled long-term human interventions and integrated microbiome-metabolome measurements [3,7,8,25]. In the meantime, reducing dependence on UPFs and increasing the proportion of minimally processed, fibre-rich foods represents a reasonable public-health strategy consistent with the current evidence [3,15,17].

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Conflict of Interest

The authors declare that they have no competing interests related to this manuscript.

Author Contributions

Bansari Upadhyay: conceptualization, literature search, manuscript preparation and revision. Debabrata Sarkar: literature review, scientific interpretation and critical revision. Ronak Chhaya: literature review, scientific interpretation and critical revision. All authors reviewed and approved the final manuscript.

Ethics Approval

Not applicable because this is a literature review and contains no new human or animal participant data.

Data Availability

Not applicable. No new dataset was generated for this review.

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