SACN statement on

processed foods and health

SACN's webpage is available at: www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition

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1 Introduction

1.1 The Scientific Advisory Committee on Nutrition (SACN) considered 'ultra-processed foods (UPF)' at its horizon scanning meeting on 17 June 2022. Members noted that it would be timely to consider this issue since there was increasing discussion and debate regarding the implications of food processing on health. Members agreed that it would be important for SACN to have clarity on these terms to agree a preferred definition for processed foods including UPFs if these were to be used as exposures in future risk assessments.

1.2 In autumn 2022, the Office for Health Improvement and Disparities (OHID) at the Department of Health and Social Care (DHSC) asked that SACN expedite this work. At the November 2022 SACN meeting, SACN members agreed the terms of reference for this work and noted that it should be inclusive of published processed food classifications available in peer reviewed literature. Due to the limited time frame the secretariat agreed to progress this work with support from SACN members outside of a formal Working Group structure.

Terms of reference

1.3 The terms of reference for this position statement were:

   a) Issue a position statement on processed foods and health. To include:

   - Evaluation of existing classifications of processed foods, including ultra-processed foods and the NOVA classification

   - Evaluation of the suitability and methods to apply food processing definition(s) as a dietary exposure

   - Consideration of the availability and quality of evidence associating different forms or levels of food processing with health outcomes

   b) Scope any future work on this issue.

1.4 SACN has not considered wider issues in relation to processing as part of this statement.

1.5 The secretariat progressed this work with advice and support from SACN members as required outside of SACN meetings. The minutes of meetings between the secretariat and SACN members on this topic are provided as an annex to the minutes of SACN meetings held in March and June 2023.

1.6 In this statement, the umbrella term 'processed food' is used to cover the range of classifications available. The terms ultra-processed or UPF are only used in relation to NOVA unless otherwise stated. The majority of evidence in the area of food processing and health refers to the NOVA classification.

2 Background

2.1 There is growing discussion and research literature on food processing and health.

2.2 Food processing has a number of roles including aiming to:

- ensure foods that would otherwise be inedible without processing are edible (for example cooking)

- ensure foods that could otherwise be unsafe to eat are safe (for example pasteurisation)

- increase the shelf life, preservation and retention of nutrients for some foods (for example freezing)

- modify the nutrient composition or bioavailability (for example reformulation for saturated fat, sugar, salt or micronutrient fortification)

- increase palatability (such as through taste and texture)

- increase convenience.

2.3 While there is no universally agreed definition of processed foods, a number of classification systems have been developed globally, which attempt to group foods by their level of processing (Sadler et al, 2021):

- a system developed by the International Agency for Research on Cancer (IARC) (Chajès et al, 2011; Slimani et al, 2009)

- the NOVA system including the ultra-processed foods (UPF) category developed in Brazil (Monteiro et al, 2019; Monteiro et al, 2016; Monteiro et al, 2010) and a variation of the NOVA system (Louzada et al, 2015)

- a system developed by the International Food Information Council (IFIC) (Eicher-Miller et al, 2012; Eicher-Miller et al, 2015)

- a system developed by the International Food Policy Research Institute in Guatemala (IFPRI) (Asfaw, 2011; Moubarac et al, 2014)

- a system developed by the Mexican National Institute of Public Health (MNIPH) (Moubarac et al, 2014)

- the Siga Index (Fardet, 2018)

- a system developed by researchers at the University of North Carolina in 2015 (Poti et al, 2015).

2.4 The purpose of processed food classifications is to categorise foods according to their level of processing. While one classification system has attempted to account for nutritional content and recommended dietary guidelines (Fardet, 2018; Siga, 2017), other classification systems, including NOVA, do not consider the nutrient content of foods.

2.5   Published commentaries (Drewnowski et al, 2020; Fardet, 2016; Forde et al, 2020; Gibney et al, 2017; Gupta et al, 2019; Pulker et al, 2018; Rolls et al, 2020; Srour and Touvier, 2021; Valicente et al, 2023) have proposed a range of hypotheses and potential mechanisms for observed associations between (ultra-) processed foods and adverse health outcomes. This includes:

- higher palatability

- higher energy density

- promotion of a faster eating rate – for example due to softer texture or other changes in the food structure or matrix

- differences in nutrient content – such as higher saturated fat, salt or free sugars content alongside lower fibre content

- effects of high temperature in the production of processed foods

- effects of specific additives, including low or no calorie sweeteners

- contaminants from packaging

- higher consumption due to widespread marketing and lower cost of processed foods

- combined effects of the above.

UK policy and recommendations with respect to food processing

Policy

2.6   In the UK, government dietary policy focuses on making it easier for people to make healthier choices. Actions include progress on the reformulation of foods higher in sugar, salt and calories, the introduction of regulations restricting the placement of food and drink products that are higher in saturated fat, salt or free sugars (HFSS) in key selling locations in store and online (which came into force in October 2022), and the Soft Drinks Industry Levy (SDIL) introduced in 2018.

UK dietary guidelines

2.7   UK government advice on a healthier and more sustainable, balanced diet is encapsulated in the UK's national food guide, The Eatwell Guide. Government dietary advice does not include advice on processed foods specifically, other than the recommendation to limit consumption of processed meat (see paragraph 2.10).

2.8   The Eatwell Guide shows the proportions of the main food groups that form a healthy, balanced diet to help meet nutrient requirements and reduce the risk of chronic disease. Accompanying advice states:

- eat at least 5 portions of a variety of fruit and vegetables every day

- base meals on potatoes, bread, rice, pasta or other starchy carbohydrates; choosing wholegrain versions where possible

- have some dairy or dairy alternatives (such as soya drinks); choosing lower fat and lower sugar options

- eat some beans, pulses, fish, eggs, meat and other proteins (including 2 portions of fish every week, one of which should be oily)

- choose unsaturated oils and spreads and eat in small amounts

- drink 6 to 8 cups or glasses of fluid a day

- if consuming foods and drinks high in fat, salt or free sugars have these less often and in small amounts. These foods are clearly shown outside of the guide and indicated as crisps, biscuits, cakes, chocolate, ice cream, sugary drinks and condiments such as tomato sauce.

SACN risk assessments

2.9 Diets high in processed foods, particularly those defined as UPF, are often high in calories, saturated fat, salt or free sugars and low in fruit and vegetables and fibre (Drewnowski et al, 2020; Fardet, 2016; Forde et al, 2020; Gibney et al, 2017; Gupta et al, 2019; Pulker et al, 2018; Rolls et al, 2020; Srour and Touvier, 2021; Valicente et al, 2023).

2.10 Government dietary advice is based on recommendations from SACN and its predecessor the Committee on Medical Aspects of Food and Nutrition Policy (COMA). The following SACN reports are particularly relevant to the current position statement.

- In its report on 'Salt and Health' in 2003 (SACN, 2003), SACN concluded that reducing the average population salt intake would proportionally lower population average blood pressure levels and confer significant public health benefits by contributing to a reduction in the burden of cardiovascular disease. The UK government recommends that adults should eat no more than 6g salt per day (equivalent to 2.4g per day of sodium) and proportionately lower amounts for children.

- In its report on 'Iron and Health' in 2010 (SACN, 2010), SACN identified an association between red and processed meat and bowel cancer. Based on SACN's conclusions, the UK government advises that adults who regularly consume more than 90g per day of red and processed meat reduce their consumption to no more than the population average of 70g per day of red and processed meat.

- In its report on 'Dietary Reference Values for Energy' in 2011 (SACN, 2011), SACN concluded that sustained energy imbalance will lead to weight gain and that a substantial proportion of the population are overweight and obese.

Obesity increases the risk for a number of diseases (such as type 2 diabetes, certain cancers, hypertensions and coronary heart disease).

- In its report on 'Carbohydrates and Health' in 2015 (SACN, 2015), SACN reported that higher consumption of free sugars increases the risk of tooth decay and consuming excess calories leads to weight gain. The assessment of evidence in adults suggested that higher consumption of sugary drinks showed an association with risk of developing type 2 diabetes. SACN recommended that average population intake of free sugars should not exceed 5% of total dietary energy intake (estimated at 30g for adults). 'Free' sugars are those added to food and drinks, as well as those naturally present in honey, syrups and unsweetened fruit juices, but excluding free sugars naturally present in whole vegetables and fruit and dairy products (Swan et al, 2018).

- In its report on 'Carbohydrates and Health' in 2015 (SACN, 2015), SACN concluded that there is strong evidence for a lower risk of heart disease, type 2 diabetes and bowel cancer amongst people who eat more fibre in their diet. Noting that most of the evidence for the wide range of health benefits came from studies reporting fibre intake from a variety of foods, including naturally occurring fibre, SACN recommended that fibre intakes should be achieved through a variety of food sources. SACN also recommended that adults should consume 30g of fibre per day, with proportionately lower amounts for children.

- In its report on 'Saturated Fats and Health' in 2019 (SACN, 2019), SACN concluded that eating less saturated fat lowers blood cholesterol and reduces the risk of heart disease. SACN recommended the average contribution of saturated fat to total dietary energy should be no more than about 10% for adults and children aged 5 years and older.

- In its report on 'Feeding Young Children aged 1 to 5 Years' (SACN, 2023a), SACN made several recommendations for this age group in relation to consumption of foods and drinks that would be classified as (ultra-) processed food, as well as endorsing existing recommendations. SACN recommendations included:
  - formula milks (including infant formula, follow-on formula, 'growing-up' or other toddler milks) are not required by children aged 1 to 5 years
  - children aged 1 to 5 years should not be given sugar-sweetened beverages
  - dairy products (such as yoghurts and fromage frais) given to children aged 1 to 5 years should ideally be unsweetened
  - foods (including snacks) that are energy dense and high in saturated fat, salt or free sugars should be limited in children aged 1 to 5 years in line with current UK dietary recommendations
  - commercially manufactured foods and drinks marketed specifically for infants and young children are not needed to meet nutritional requirements.

2.11 Plant-based drinks (such as soya, oat and almond drinks) would be classified as (ultra-) processed food. A joint working group of SACN and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), is conducting a benefit:risk assessment considering both toxicological and nutritional aspects associated with the consumption of plant-based drinks by the UK population. Based on this benefit:risk assessment, the joint committee will provide advice to the UK health departments. The risk assessment is due to be published in 2024.

Food Fortification

2.12 Food fortification, a form of processing, provides an important contribution to nutrient intakes in the UK. The Bread and Flour Regulations 1998 require all flour other than wholemeal flour to be fortified with iron, calcium, thiamin and niacin. In the UK cereal and cereal products, which include fortified breakfast cereals and foods made from fortified wheat flours such as bread and pasta, are the largest source of dietary iron in all age and sex groups (providing on average over a third of intake for adults and around a half for children) and the largest source of calcium for older children (38% of intakes) (Public Health England, 2020) .

2.13 In September 2021, following SACN's 2017 updated recommendations on folic acid (SACN, 2017) and a UK wide public consultation, the UK government and devolved administrations announced their intention to proceed with arrangements to require the mandatory fortification of non-wholemeal wheat flour with folic acid to help prevent neural tube defects.

Food Additives

2.14 The Food Standards Agency (FSA) defines food additives as ingredients that are added to food to carry out particular functions. UK legislation stipulates which food additives can safely be used within foods and drinks sold in the UK following assessment by the FSA. The FSA also ensures the law is strictly enforced and investigates any information that casts reasonable doubt on the safety of an additive.

2.15 COT is responsible for assessing the safety of additives before they can be used in food as well as ensuring that the science on additives is strictly reviewed. In addition, the Advisory Committee on Novel Foods and Processes (ACNFP) reviews the safety of novel foods including novel processes, advising where concerns are raised. Population exposure to additives is not currently monitored and, at the time of writing, there are no plans for future monitoring work.

2.16 SACN members have previously noted the importance of collecting information on trends and intake of low or no calorie sweeteners, due to potential increases in use

resulting from dietary public health policies on reformulation of food and drinks to reduce sugar and calorie intake. In its report on 'Feeding Young Children aged 1 to 5 Years' (SACN, 2023a) SACN made the recommendation for government to monitor intakes of low or no calorie sweeteners in children aged 1 to 5 years.

International policy and recommendations with respect to food processing

2.17 The World Health Organization (WHO) recommends a healthy diet to protect against malnutrition and non-communicable diseases (NCDs) including type 2 diabetes, heart disease, stroke and some cancers. WHO recommends a diet including at least 5 portions of fruit and vegetables a day; legumes, nuts and whole grains; less than 10% of total energy intake from free sugars; less than 30% of total energy intake from fats; less than 10% of total energy intake from saturated fats and less than 5g of salt per day. WHO recommendations on a healthy diet are broadly in line with UK dietary guidelines, discussed above. Although WHO does not mention processed foods in its dietary recommendations it suggests that governments have a central role in creating a healthy food environment and recommends that policy makers should reduce incentives for the foods industry to continue to increase production of processed foods containing high levels of saturated fats, trans fats, salt or sodium and free sugars (World Health Organization, 2020).

2.18 WHO has also recommended against the use of 'non-sugar sweeteners' to control body weight or reduce the risk of noncommunicable diseases (World Health Organization, 2023). In its guideline on use of 'non-sugar sweeteners' published in 2023, WHO recommended that "efforts to reduce free sugars intake should be implemented in the context of achieving and maintaining a healthy diet. Because free sugars are often found in highly processed foods and beverages with undesirable nutritional profiles, simply replacing free sugars with non-sugar sweeteners means that the overall quality of the diet is largely unaffected. Replacing free sugars in the diet with sources of naturally occurring sweetness, such as fruits, as well as minimally processed unsweetened foods and beverages, will help to improve dietary quality, and should be the preferred alternatives to foods and beverages containing free sugars." At its meeting in June 2023, SACN agreed to scrutinise the WHO guideline on use of 'non-sugar sweeteners' and associated systematic review and consider if additional assessment is required.

2.19 A number of countries now make reference to food processing in their national dietary guidelines, not all are easily identified owing to lack of English translations.

2.20 Koios et al (2022) carried out a review of how national dietary guidelines refer to levels of food processing. The analysis identified 105 national dietary guidelines in

total, 91 of which included some level of advice on processing and 45% used terminology such as 'ultra-processed', 'highly processed' or 'processed', to discourage the consumption of certain processed foods.

2.21 Koios et al (2022) identified seven countries that specifically discourage consumption of 'ultra-processing' in their dietary guidelines (Belgium, Brazil, Ecuador, Israel, Maldives, Peru and Uruguay). For example, Ecuador includes advice to 'avoid the consumption of UPFs, fast food and sugar sweetened beverages'. The authors note four of these countries are in South America, which may reflect the origin of the NOVA classification system in Brazil, and that the Brazilian government included advice to avoid UPF in their dietary guidelines in 2014.

2.22 Koios et al (2022) identified five countries (Brazil, Brunei Darussalam, Kenya, Malta, New Zealand) that explicitly recommend consumption of 'minimally processed' or 'unprocessed' foods. For example, Brazil recommends "Make…minimally processed foods the basis of your diet". The authors reflect that the recommendations of some other countries imply a move away from processed foods without explicitly stating this. For example, Qatar recommends "choose fresh, homemade foods".

2.23 Koios et al (2022) state, as a limitation due to data collection methods, that relevant text within some countries' detailed guidelines may not have been identified. Recommendations in the following key guidelines were not identified by Koios et al (2022), and were subsequently identified by the SACN secretariat:

- [Canada's Food Guide](#) recommends "you should limit highly processed foods and drinks because they are not a part of a healthy eating pattern". This advice states that 'highly processed foods are processed or prepared foods and drinks that add excess sodium, sugars or saturated fat to the diets of Canadians'.

- [Food Standards Australia New Zealand](#) recommends "eating a diet with more whole, low or minimally processed foods, and less of the highly processed foods is known to improve overall health".

- [Sante Publique France](#) recommends "to limit sugary drinks, fatty, sugary, salty and ultra-processed foods".

2.24 Colombia will be the first country to introduce fiscal policies stated as being based on ultra-processed food and drink products. Separate taxes on ultra-processed sugar sweetened beverages and industrially ultra-processed food products are expected to come into force on 1 November 2023. UPF are defined as 'edible products formulated from food-derived substances along with additives, that contain added sugars, sodium, and saturated fats'. The tax will be levied on foods which, on the nutrition facts panel, exceed the following values (Global Food Research Program, 2022; UNC GFRP, 2022):

- ≥1mg of sodium per 1 calorie and/or >300mg of sodium per 100g
- ≥10% of total calories from free sugars
- ≥10% of total calories from saturated fats.

The tax rates will be 10% in 2023, 15% in 2024 and 20% in 2025.

2.25 Mexico and Hungary have implemented taxes based on energy density or HFSS. Mexico adopted a tax on 'junk foods' whereby 8% tax on all 'non-essential' foods such as confectionary, prepared cereal products and chocolate containing >275 calories per 100g is applied (Global Food Research Program, 2013). Hungary has adopted a tax on non-essential packaged foods and drinks that contain levels of sugar and salt over a certain threshold in certain product categories, including soft drinks, candy, salty snacks, condiments, and fruit jams. The amount of tax paid is determined by the units of product bought or sold, and units are measured in kilograms or litres (Bíró, 2021).

2.26 In the UK soft drinks companies pay a tax (Soft Drinks Industry Levy, SDIL) for drinks with added sugar and a total sugar content of ≥5g or more per 100ml (approximately 5% sugar content) or a higher levy for drinks that contain ≥8g per 100ml (approximately 8% sugar content). A number of other countries have introduced fiscal policies on sweetened beverages including Barbados, Mexico, Chile, Peru, Columbia and South Africa (Global Food Research Program, no date).

2.27 Israel and Mexico are among a number of countries which have introduced warning labels for foods and drinks containing sweeteners. In Israel, warning labels are specifically related to aspartame being a source of phenylalanine (The Food Foundation, 2023).

3 Methods

3.1 A scoping review was carried out consisting of three components:

- a review of existing classifications of processed foods

- a review of available evidence that uses the UK National Diet and Nutrition Survey (NDNS) dataset to apply the NOVA food processing classification system

- a review of available evidence on the associations between different levels of food processing and health outcomes.

Review of existing classifications of processed foods

3.2 Papers identified by the Committee and secretariat as part of, and subsequent to, the [SACN horizon scanning process](#), were reviewed and a further PubMed search was carried out by the SACN secretariat to identify any other key papers. Reference lists of papers were searched to identify available classification systems on food processing. This included reference lists for: Gibney et al (2017); Moubarac et al (2014); Sadler et al (2021) and British Nutrition Foundation (2023).

3.3 Sadler et al (2021) identified 4 core themes (listed below) with respect to how processing can change foods:

- extent of change (from the natural state)

- nature of change (for example change to food's natural properties, addition of ingredients, or food additives)

- place of change (for example at home, artisanal or industry)

- purpose of change (for example essential, cosmetic, convenience, palatability).

3.4 As agreed by SACN, the classification systems identified in the search outlined in 3.2, were assessed according to whether these 4 core themes had been considered in the development of the system. Details of each classification system identified, the definition of each level of food processing and the type of foods included at each level of food processing within the system were also extracted (see Annex 1).

3.5 A set of initial screening criteria agreed by SACN were then applied to the classification systems identified to understand which systems were practical and applicable for use in the UK and thus would be useful to review further. The criteria included whether:

1. the system could be applied to a UK population

2. there is a clear, "useable definition" of the system (as provided by the studies)

3. the system has been used in peer-reviewed publications by more than one research group

4. there are data available on inter-assessor reliability when applying the system (irrespective of the degree of inter-assessor reliability reported)

5. the classification system has been used to evaluate associations between consumption and health outcomes.

3.6 Eight classification systems were identified (see Annex 1), the results of which are summarised in Chapter 4 with full details presented in Annex 2.

Review of available evidence that uses the UK National Diet and Nutrition Survey (NDNS) dataset to apply the NOVA food processing classification system

3.7 In order to evaluate the suitability of using food processing as a dietary exposure, as outlined in the terms of reference for this work, the scoping review assessed the available evidence that uses the UK National Diet and Nutrition Survey (NDNS) dataset to apply the NOVA food processing classification system. NOVA was identified as the most commonly used classification system for processed foods in the published literature; this was borne out by a further literature search (see Chapter 4).

3.8 The NDNS is the primary and nationally representative tool for monitoring dietary intake in the UK. Any future risk assessment on processed foods and health by SACN would need to, in line with previous risk assessments, consider current levels of consumption of processed foods in the UK (for example estimate the exposure to processed foods) to understand current exposure, using NDNS consumption data.

3.9 The UK Health Security Agency (UKHSA) Knowledge and Library Services (currently providing library support to the Office for Health Improvement and Disparities (OHID) conducted online database searches to identify primary studies that apply the NOVA food processing classification system to foods consumed in the NDNS. The bibliographic databases Embase, Medline (via Ovid), Scopus and PubMed were searched on 11 January 2023 using the terms outlined in Annex 3. No start date for the search was specified.

3.10 After duplicates were removed, 64 records were identified through the online database search. One reviewer considered the references with respect to the application of NOVA to NDNS data, resulting in the exclusion of 52 references. The remaining 12 references were screened by full text. All 12 studies were considered relevant to this scoping review), the results of which are summarised in

Chapter 5 with full details presented in Annex 4. The PRISMA flow diagram in Figure 1 shows each stage of the review process.
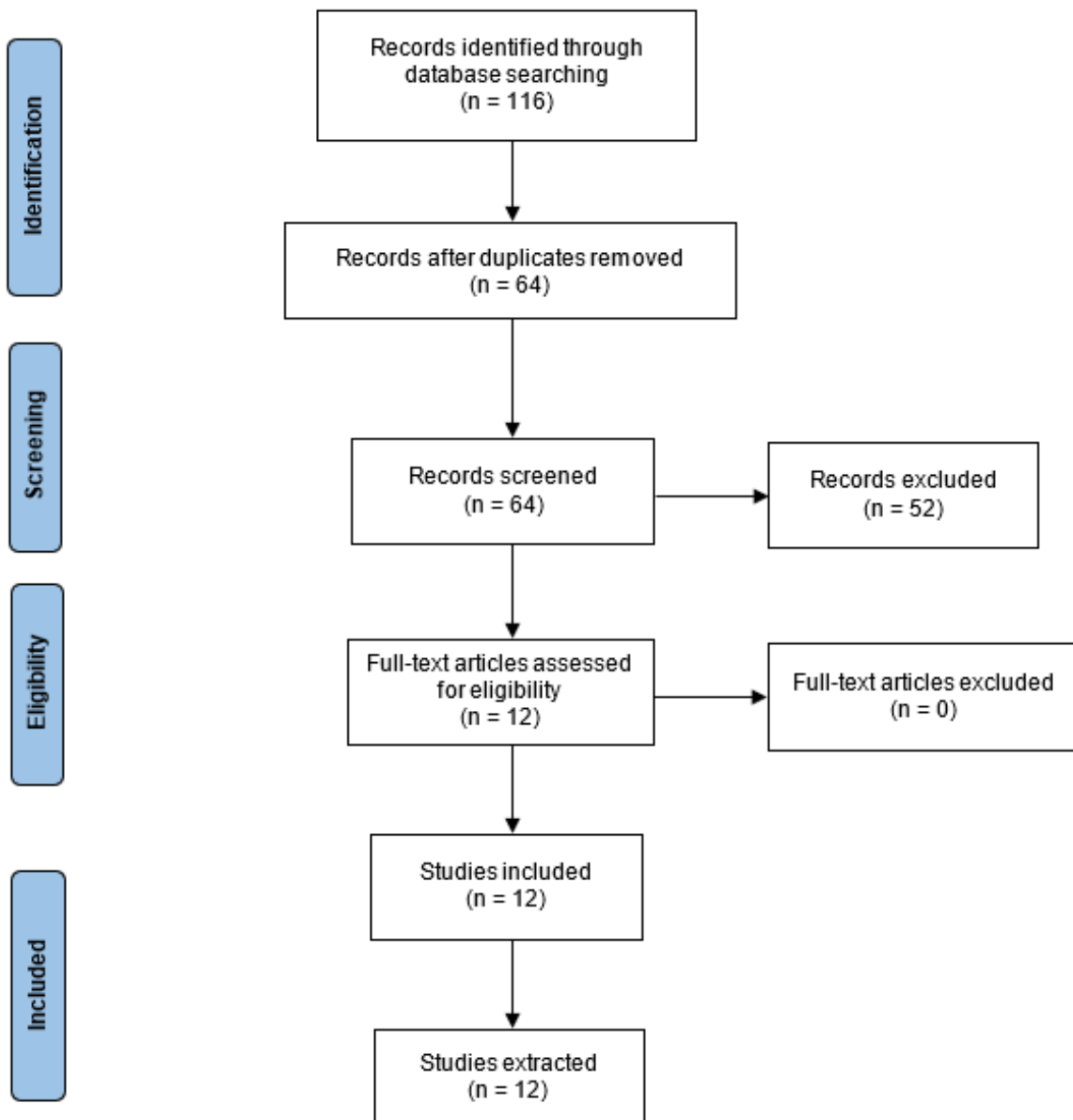
Figure 1. Flow diagram showing the number of studies meeting inclusion criteria for the scoping review to identify available evidence that uses the NDNS dataset to apply the NOVA food processing classification system.

Review of available evidence on the association between processed food consumption and health outcomes

Eligibility criteria and literature searches

3.11 In parallel to the work described in sections 3.2 to 3.10 above, the UKHSA Knowledge and Library Services conducted online database searches for systematic reviews (SRs) with or without meta-analyses (MAs) examining the relationship between two or more levels of food processing and health outcomes. The bibliographic databases Embase, Medline (via Ovid) and PubMed were searched on 12 January 2023 using the terms outlined in Annex 5.

3.12 In line with the [SACN Framework for the Evaluation of Evidence](#) (SACN, 2023b), ideally this position statement would consider primarily evidence provided by SRs and MAs of randomised controlled trials (RCTs) and by prospective cohort studies (PCS). Evidence from other study designs (such as case-control and cross-sectional studies) is not usually considered, because they are subject to greater levels of bias, confounding and/or reverse causality. However, given the nature of the current evidence base on this topic, SACN agreed that for this scoping review data from SRs should be extracted if they included the following:

- RCTs and/or PCS

OR

- mixed study designs if data from RCTs or PCS formed equal to or more than 70% of the total participant weighting.

3.13 Data were not extracted from SRs which included mixed observational study designs that formed greater than 30% of the total weighting. This was to prioritise studies with more robust study design and to be more consistent with SACN's usual approach to observational evidence (SACN, 2023b).

3.14 In addition, eligibility criteria included SRs published in English, in peer-reviewed scientific or medical journals between 2015 to the 12 January 2023. Only SRs published from 2015 onwards were included to ensure that searches captured the updated version of the NOVA classification system (Monteiro et al, 2016). No geographical restrictions were applied. SRs were considered eligible only if they evaluated:

- predominantly healthy populations
- at least two levels of food processing (for example, unprocessed food compared with processed food or high intakes of ultra-processed food (UPF) versus low intakes of UPF)
- 'processed food' was clearly defined by a classification system

3.15　The aim of this scoping review was to assess food processing as a category therefore SRs were not included if they assessed single food groups defined by a level of processing (for example, 'sugar-sweetened beverages' or 'processed meats').

3.16　Full inclusion and exclusion criteria are presented in full in Annex 6.

Registered trials

3.17　[ClinicalTrials.gov](#) was searched on 18 January 2023, and updated on 21 June 2023, to identify ongoing and published RCTs and PCS which may be of relevance to the body of evidence on food processing and associated health outcomes. The search terms used are presented in Annex 7. Eligibility criteria with respect to the population, exposure and outcome (see Annex 6) were applied. The results of which are summarised in Chapter 6.

Selection of studies

3.18　After duplicates were removed, 220 references were identified through the online database search and screened for eligibility based on their title and abstract, resulting in the exclusion of 177 references. The remaining 43 references were screened by full text, resulting in the exclusion of a further 23 references.

3.19　Titles and abstracts were screened by 2 reviewers for eligibility. Thirty-nine papers (18%) were screened in duplicate with 95% agreement. Differences between reviewers were resolved by discussion with a third person.

3.20　Of the 20 SRs that met the scoping review eligibility criteria, 10 were either comprised only of PCS or included mixed observational study designs where data from RCTs or PCS formed equal to or more than 70% of the total participant weighting. As per the eligibility criteria (see Annex 6), data were fully extracted from these 10 papers (see Tables 1 and 2, Annex 8).

3.21　Data were not extracted from the remaining 10 SRs which included mixed observational study designs as their case-control and cross-sectional studies formed greater than 30% of the total participant weighting. These SRs have been listed in Tables 3 and 4, Annex 8. The PRISMA flow diagram in Figure 2 shows the number of articles at each stage of the scoping review process.
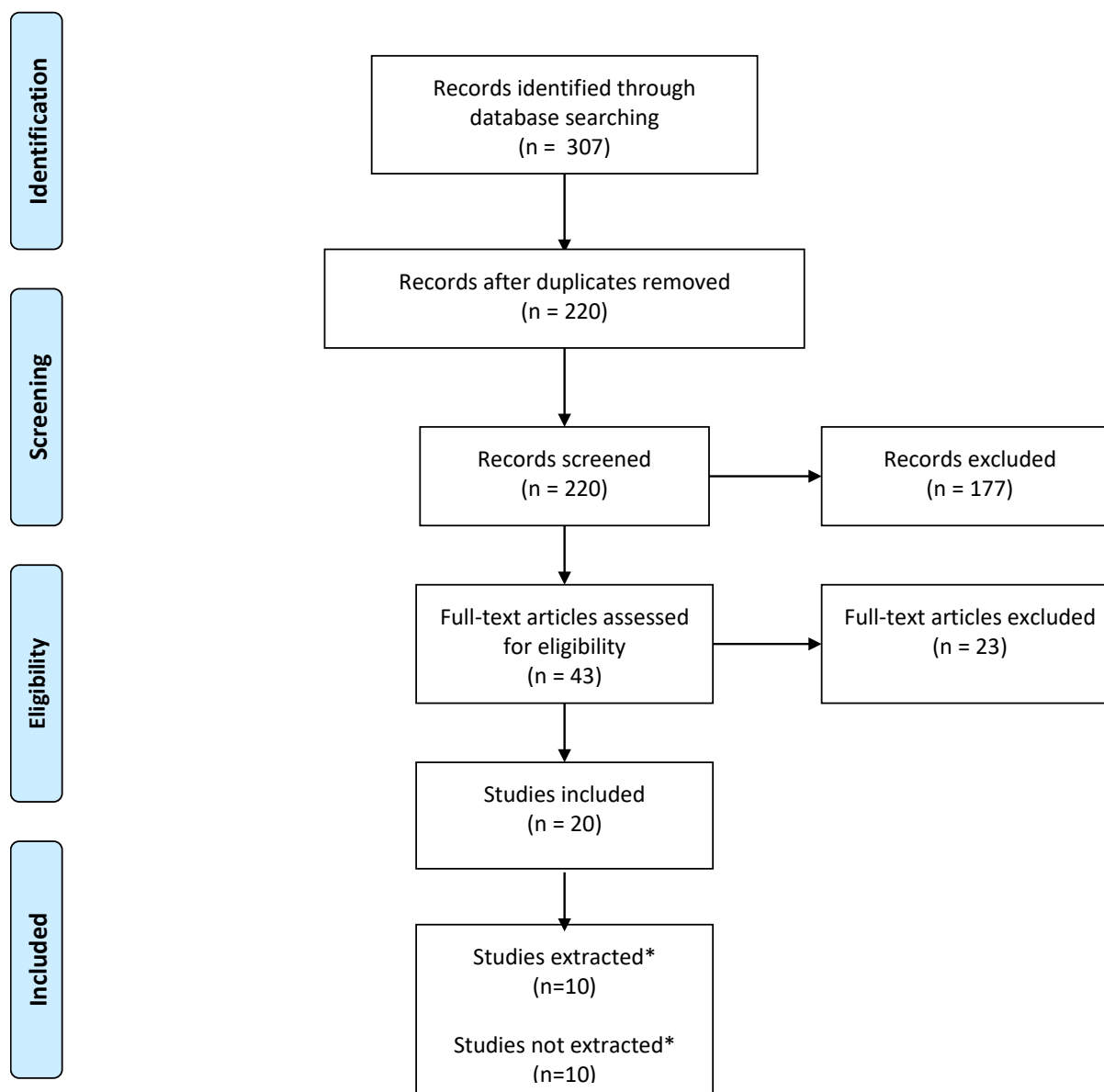
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                  │               │
                  │ Studies not extracted*│
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*Of the 20 SRs that met the scoping review eligibility criteria, 10 were either comprised only of PCS or included mixed observational study designs where data from RCTs or PCS formed equal to or more than 70% of the total participant weighting. As per the eligibility criteria (see Annex 6), data were fully extracted from these 10 papers (see Tables 1 and 2, Annex 8). The remaining 10 SRs included mixed observational study designs that formed equal to or greater than 30% of the total weighting and were therefore not extracted but have been listed (see Table 3 and 4, Annex 8)

Figure 2. Flow diagram showing the number of studies meeting inclusion criteria for the scoping review of available evidence on associations between processed food consumption and health outcomes.

Data extraction

3.22 Relevant data from each of the included SRs were extracted into tables (see Annex 8). Extracted data included the name of the first author, year of publication, research question, selection criteria, statistical analysis, assessment of study quality, total number of participants, mean duration of study, demographics and results. Data on location, dietary assessment methods and the study design of the primary evidence, as reported in the SRs, MAs and pooled analyses, were also extracted. Where data from PCS were reported separately from other observational data, it was extracted alone. Where it was not clear what type of evidence comprised the results (for example data from PCS and other observational study designs were not separated), this was noted and results as described by the SR authors were extracted. Where there was only one PCS for an outcome, data was not extract.

Methods for reviewing evidence

3.23 Chapters of the draft position statement were initially compiled by the SACN secretariat. These chapters provided the basis for discussions with SACN, with the final text, conclusions and recommendations, discussed and agreed by SACN.

Evaluation of the quality of identified evidence

3.24 Evidence was prioritised according to study design as outlined by the SACN Framework for the Evaluation of Evidence (SACN, 2023b). SACN did not formally quality assess or grade the evidence considered, as a full risk assessment was not undertaken.

Alcohol

3.25 Consideration of issues related to alcohol are only within SACN's remit in relation to its energy contribution; other aspects are outside SACN's remit. Distilled alcoholic beverages (for example whisky and vodka) are considered UPF according to NOVA (NOVA 4). Fermented alcoholic beverages (for example beer and wine) are considered 'processed' (NOVA 3) (see Chapter 4 for description of NOVA classifications). Estimates of energy intake from UPF should theoretically include any contribution from alcohol, however none of the papers included in this scoping review made specific mention of alcoholic drinks. This scoping review has not considered SRs assessing relationships with individual food or drink items, such as alcoholic drinks.

4 Review of existing food processing classification systems

4.1 The methods used to identify and assess classification systems on food processing are outlined in Chapter 3, paragraphs 3.1 to 3.5.

4.2 Eight systems were identified (see Annex 1). The initial screening criteria, as agreed by SACN members, were applied to these classification systems, the results of which are summarised in Table 1 below with full details presented in Annex 2.

Table 1: Summary of classification system initial screening criteria

Classification	Applicable to UK?	Useable definition?	Published by >1 group?	Data on inter-assessor reliability?	Health outcomes evaluated?
NOVA	Yes	Yes	Yes	Yes	Yes
International Agency for Research on Cancer (IARC)	Yes	Yes	No	No	No
The Siga Index	Yes	No	No	No	No
International Food Information Council (IFIC)	Yes	Yes	No	No	No
da Costa Louzada	Yes	No	No	No	No
International Food Policy Research Institute in Guatemala (IFPRI)	No	No	No	No	No
Poti et al (2015)	Yes	Yes	No	No	No
Mexican National Institute of Public Health (MNIPH)	No	No	No	No	No

4.3 Two systems, one developed by IFPRI in Guatemala (Asfaw, 2011; Moubarac et al, 2014) and one by MNIPH in Mexico (Moubarac et al, 2014) did not meet any of the initial screening criteria.

4.4 Two systems, the Siga Index (Fardet, 2018; Siga, 2017) and a variation of the NOVA system (Louzada et al, 2015; Sadler et al, 2021) met one criterion: potential to be able to be applied to a UK population:

- the Siga Index (Fardet, 2018; Siga, 2017), reported being based on European regulatory guidelines, following advice on risk assessment of ingredients and additives from the WHO, European Food Safety Authority (EFSA) and The French Agency for Food, Environmental and Occupational Health & Safety (ANSES). The Siga Index was also reported to follow 'nutritional thresholds' set by the FSA UK

- the system by Louzada et al (2015), was based on an early iteration of the NOVA system and included food items that are recognisable within the UK diet

- both systems provided limited information on a useable definition and no evidence was identified on whether the systems had been published by more than one research group, on inter-assessor reliability when applying the systems or whether the systems had been used to evaluate health outcomes.

4.5 Three systems, one developed by IFIC (Eicher-Miller et al, 2012; Eicher-Miller et al, 2015), one developed by IARC (Chajès et al, 2011; Slimani et al, 2009) and one developed by Poti et al (2015) met 2 of the initial screening criteria: a clear useable definition and potential to be able to be applied to a UK population:

- each system provided sufficient information to define each level of food processing and which foods fall within levels

- each system also reported being based on data collected from large longitudinal studies from Europe, including the UK, (IARC (Chajès et al, 2011; Slimani et al, 2009)) or the US (IFIC (Eicher-Miller et al, 2012; Eicher-Miller et al, 2015) and Poti et al (Poti et al, 2015)), and were therefore deemed applicable to the UK population

- no evidence was identified on whether the systems had been used in publications from more than one research group, on inter-assessor reliability when applying the systems or whether the systems had been used to evaluate health outcomes.

4.6   NOVA was the only system (Monteiro et al, 2019; Monteiro et al, 2016) that met all 5 of the initial screening criteria:

- NOVA is considered potentially applicable to a UK population. Although it was developed in Brazil, foods described in each level of food processing are recognisable within the UK diet

- a definition is set out by authors including 4 distinct groups defining each level of food processing and provides a list of some foods that fall within each group, although there may be some ambiguity around how some foods would be classified

- research using NOVA has been published by numerous research groups

- information on inter-assessor reliability has been published. SACN however, noted that the literature on inter-assessor reliability may be unclear or inconsistent:

  o one study was identified through the literature search; Braesco et al (2022) evaluated whether the NOVA classification system leads to consistent assignment to processing level by food and nutrition specialists. Authors concluded that "overall consistency among evaluators was low, even when ingredient information was available. These results suggest current NOVA criteria do not allow for robust and functional food assignments". Mean Fleiss' κ (range: 0 to 1, where 1 = 100% agreement) was calculated as 0.32 and 0.34 for 'marketed foods' and 'generic foods' respectively, indicating that assessors agreed on the classification of approximately one third of foods

  o a number of other studies, identified after the literature search, have reported higher inter-assessor reliability. One study (Sneed et al, 2023) evaluating inter-assessor reliability between pairs of trained coders assigning NOVA categories to individual foods collected via 24 hour dietary recalls found inter-assessor agreement of 88.3% (overall κ coefficient, 0.75; 95% CI [0.73, 0.77]). Another study (Khandpur et al, 2021), evaluating inter-assessor reliability between three researchers assigning NOVA categories to individual foods collected via food frequency questionnaires from 3 large cohorts, found inter-assessor agreement of 70.2%

- systematic reviews assessing the association of NOVA classification with health outcomes were identified (see Chapter 6).

4.7   As NOVA was the only classification system to meet the initial screening criteria and is the most commonly identified in the research literature this system was the focus of further consideration in this scoping review.

Description of the NOVA classification system of processed foods

4.8 The NOVA classification started with 3 categories in 2010 (Monteiro et al, 2010) and was later adjusted and redefined to 4 categories in 2016 (Monteiro et al, 2016).

4.9 NOVA places foods and food ingredients into 4 categories:

1) unprocessed/minimally processed foods

2) processed culinary ingredients

3) processed foods and

4) ultra-processed food (UPF).

4.10 Publications produced by the Monteiro et al group to support the application of the NOVA classification system (Monteiro et al, 2019; Monteiro et al, 2018) provide a broad narrative description on the characteristics of the UPF category. The authors describe UPF (NOVA group 4) as follows (Monteiro et al, 2016):

- "industrial formulations typically with five or more and usually many ingredients"

- "ingredients only found in [UPF] include substances not commonly used in culinary preparations, and additives whose purpose is to imitate sensory qualities …or disguise undesirable sensory qualities of the final product"

- "substances only found in ultra-processed products include some directly extracted from foods, such as casein, lactose, whey, and gluten, and some derived from further processing of food constituents, such as hydrogenated or interesterified oils, hydrolysed proteins, soy protein isolate, maltodextrin, invert sugar and high fructose corn syrup"

- "classes of additive only found in ultra-processed products include dyes and other colours, colour stabilisers, flavours, flavour enhancers, non-sugar sweeteners, and processing aids such as carbonating, firming, bulking and anti-bulking, de-foaming, anti-caking and glazing agents, emulsifiers, sequestrants and humectants"

- "common attributes of ultra-processed products are hyper-palatability, sophisticated and attractive packaging, multi-media and other aggressive marketing to children and adolescents, health claims, high profitability, and branding and ownership by transnational corporations."

4.11 UPF are classified by their level of processing and not by their energy or nutrient content, however many products that are energy dense and high in saturated fat, salt and free sugars, and low in fruit and vegetables and fibre would be categorised as UPF (Dicken et al, 2023; Drewnowski et al, 2020; Gupta et al, 2019; Rolls et al, 2020).

4.12   The UPF category captures a wide range of foods, including many which other
        approaches to dietary assessment also typically classify as less 'healthy', such as
        soft drinks, sweet and savoury packaged snacks, confectionery, mass-produced
        and/or packaged bakery items and pre-prepared meals. However, the UPF
        category also captures products that other approaches to dietary assessment may
        classify as 'healthier' such as fortified foods, low fat yogurts, vegetable sauces and
        higher fibre breakfast cereals. For countries where research has been carried out
        into UPF (NOVA group 4), descriptions are generally supported by lists of example
        products. These lists are not necessarily applicable to the UK market.

4.13   In summary, based on the initial screening of classification systems identified,
        NOVA is the only classification that warrants further investigation in this scoping
        review. The NOVA classification met all of the initial screening criteria agreed by
        SACN and is the most commonly identified classification system in the literature.
        The NOVA classification groups food and food ingredients into 4 categories based
        on their level of processing and not their energy or nutrient content. Foods typically
        considered 'unhealthy' are commonly classified as UPF (NOVA group 4), however,
        some foods typically considered 'healthier' may also fall within the UPF group.

5 Review of available evidence that uses the UK National Diet and Nutrition Survey (NDNS) dataset to apply the NOVA food processing classification system

5.1 The methods for reviewing available evidence that applied NOVA to NDNS data are outlined in chapter 3 paragraphs 3.7 to 3.10.

Applying NOVA to UK consumption data

5.2 The UK NDNS rolling programme was established in 2008 to collect continuous data on the diet and nutritional status of the UK population. Dietary assessment for the first 11 years of the programme (2008 to 2019) was based on a paper food diary kept for 4 consecutive days and coded centrally. Population intakes of nutrients were calculated from these consumption records, underpinned by a nutrient databank (NDB) containing more than 5,000 individual food and drink codes. This dataset has been used in research to estimate the contribution of NOVA groups, particularly UPF (NOVA group 4), to UK dietary energy intakes.

5.3 In Year 12 (2019 to 2020) of the NDNS rolling programme, the dietary assessment method for NDNS changed to an automated 24-hour recall using a self-completion web-based tool, Intake24 (Bradley et al, 2016; Public Health England, 2021). This requires the participant to select the foods most appropriate to their consumption from a pre-set list of items. In order to make the food lists more manageable for participants the number of food codes has been reduced and new generic codes have been created for items such as sandwiches and salads which were previously coded as multiple individual components. The impact of these changes on the ability to allocate foods to specific NOVA categories has not been assessed.

5.4 The NDNS NDB is designed to capture the nutrient content of foods and drinks that are most commonly consumed by the UK population. Each food, composite dish or drink code has assigned values per 100g for energy and over 50 macro- and micronutrients. For packaged or ready-made food and drink products sold in supermarkets, nutrient data per 100g are obtained directly from product labels. Data for similar retail products are combined to calculate a median value for each nutrient and this generic product profile is allocated a code in the NDB. For foods recorded as homemade (for example beef lasagne), a standard recipe food code is allocated, which includes the weighted contribution of individual ingredients (for example white pasta, minced beef, onions, tinned tomatoes) to the total dish.

5.5   The NDB has been updated annually since the rolling programme began in 2008 to reflect the nutrient composition of the food supply for each NDNS data collection year. Updates focus on those food groups where changes in nutrient content are known to have occurred as a result of reformulation or changes in fortification practices. Naming conventions for food codes have evolved over time, are not fully systematic and vary in detail. They reflect key components that are important to capture the nutritional content of a food or drink consumed.

Applying NOVA to the UK NDNS NDB

5.6   The NDNS food grouping system was set up with a view to categorising foods according to their main constituents and nutritional attributes. Food codes are organised into food types and food groups. For example, the food type 'cereals and cereal products' includes food groups for bread, pasta, rice, breakfast cereals, cakes, biscuits and puddings. Therefore a range of assumptions have to be made in order to apply NOVA to the NDNS data.

5.7   Where NOVA clearly defines specific food groups, such as milk, it is straightforward to apply this to the NDB. In the NDNS many main food groups are sub-divided into subsidiary groups and some of these distinguish between manufactured or retail products and homemade dishes (for example the food group 'beef, veal and dishes' is sub-divided into two groups: 'Manufactured beef products including ready meals' and 'other beef and veal including homemade dishes'). The grouping of codes identified as 'manufactured products and ready meals' or 'purchased' to some extent aligns with NOVA group 3 (processed foods) or 4 (UPF). However, this distinction between manufactured and homemade is not made for all food groups. The NDB also does not have many specific codes for foods consumed out of home, such as in restaurants and takeaways.

5.8   The NDB does not allow separate identification of homemade dishes that include some UPF ingredients, or conversely manufactured food products that contain only unprocessed ingredients and no additives. Researchers coding dietary consumption data from food diaries or 24-hour recalls will need to make assumptions when determining whether the entire dish or just a proportion of the dish is categorised as UPF.

5.9   The NDB does not systematically capture non-nutritive contents, such as additives (for example low or no calorie sweeteners, emulsifiers, thickening agents or preservatives) although to some extent the likely presence of additives can be inferred from the food description. It does not systematically distinguish between added or intrinsic micronutrients including sodium. In addition, the NDB does not capture the origin of ingredients or method of processing or packaging unless there is a nutritional implication.

5.10 The NDB does not capture wider aspects of food processing that may affect the properties of foods. It is noted that innovations in food technology are developing rapidly and there is often limited information on the precise processing method applied to individual food products.

5.11 All NOVA group definitions include non-nutritive characteristics, including packaging and preservation methods ("in bulk or packaged" (NOVA 1 - unprocessed); "with added antioxidants" (NOVA 2 - processed culinary ingredients); canned or bottled (NOVA 3 - processed foods); "packaged" (NOVA 4 - UPF). NOVA also categorises foods based on their origin, "starches extracted from corn and other plants", "salt mined or from seawater" or "honey extracted from combs". This information is not captured within the NDB.

5.12 Taking bread as an example, the NDB categorises breads by flour type as this is the key characteristic that determines its nutrient content, for example, 'white bread', 'wholemeal bread' and 'brown, granary and wheatgerm bread'. Bread is not coded according to how it is manufactured. By contrast in the NOVA classification system 'freshly baked' breads are assigned to NOVA 3 (processed foods) and 'mass-produced' breads are assigned to NOVA 4 (UPF), based on the presence of additives in mass produced breads. While most of the bread consumed in the UK is likely to be bought from a retailer (some of which will be freshly baked in store), the existing NDB food codes for bread do not make this distinction and more precise definitions would be needed to collect information from participants to allow accurate classification.

5.13 Collecting accurate population food consumption and nutrient intake data relies on the ability and willingness of NDNS participants to use the 24-hour recall tool. There is a balance to be achieved between the detail collected and the need to ensure the tool remains manageable for participants to use, maximising participant engagement, response and data quality. Including additional subcategories for participants to choose from in order to record the level of processing, presence of additives and type of packaging as well as the type of food consumed would add substantial additional participant burden which may have a detrimental impact on data quality. Intake24, the automated 24-hour recall web-based tool used in the NDNS, does not currently include technology such as the facility to photograph a food or meal or scan a product bar code. While these could potentially assist in the collection of data on levels of processing, the impact on participant engagement and data collection is unclear (Eldridge et al, 2019; Gazan et al, 2021).

5.14 Further information about the NDB is included within the 2021 NDNS methodology evaluation report (Public Health England, 2021).

5.15   In order to undertake further assessment of processed food intakes using NDNS, consideration would need to be given to:

- what assumptions would need to be made in order to code the current NDB against NOVA categories without further adjustments to NDNS methodology, what error or bias might this introduce and how this would impact on interpretation of findings

- whether adjustments are required to the NDNS methodology and the potential impact of these on resource, participant burden and response rates.

Available evidence on dietary intakes of processed foods in the UK

5.16   Twelve studies were identified as relevant to this scoping review (Aceves-Martins et al, 2022; Adams and White, 2015; Lam and Adams, 2017; Madruga et al, 2022; Martines et al, 2019; Onita et al, 2021; Parnham et al, 2022; Rauber et al, 2018; Rauber et al, 2019; Rauber et al, 2022; Rauber et al, 2020; Souza et al, 2022). These applied the NOVA classification to dietary consumption data collected through the various NDNS datasets published from 2008 to 2019 (see Annex 4).

5.17   Of the 12 studies identified, 9 share a common author (Rauber, University of São Paulo, Brazil, credited with developing the NOVA classification) (Madruga et al, 2022; Martines et al, 2019; Onita et al, 2021; Parnham et al, 2022; Rauber et al, 2018; Rauber et al, 2019; Rauber et al, 2022; Rauber et al, 2020; Souza et al, 2022). Of the remaining 3 studies, 2 share a common author (Adams, University of Cambridge, UK) (Adams and White, 2015; Lam and Adams, 2017).

5.18   Ten of the 12 studies estimated the contribution of UPF (NOVA group 4) to total dietary energy intakes (Aceves-Martins et al, 2022; Madruga et al, 2022; Martines et al, 2019; Onita et al, 2021; Parnham et al, 2022; Rauber et al, 2018; Rauber et al, 2019; Rauber et al, 2022; Rauber et al, 2020; Souza et al, 2022). The contribution of UPF to total dietary energy intakes varied by age group:

- 63.5% (children aged 1.5 to 11 years)

- 68% (adolescents aged 12 to 18 years)

- 51% (adults aged over 19 years)

- 57% (all children and adults).

5.19   Two studies (Adams and White, 2015; Rauber et al, 2020) provided measures of energy intake from UPF separately for adult males and females (53.3% and 55.9% for males and 52.8% and 52.8% for females, respectively). Both studies also reported an income gradient in relation to total dietary energy intake from UPF. Authors found UPF (NOVA group 4) contributed a higher proportion of total energy

intake for lower-income occupational and social classes (routine and manual, 54.7% and 57.3% respectively) than for higher-income classes (managerial and professional, 52% and 50.3% respectively).

5.20   Based on the detail provided in the papers, researchers appear to have used similar approaches to applying the NOVA classification system to the food codes within the NDB. Studies identified in this scoping review allocated 'manufactured' subsidiary groups to NOVA 3 (processed foods) or NOVA 4 (UPF).

5.21   There was however a difference in the treatment of the NDNS 'homemade' subsidiary groups. Eleven studies interpreted codes identified in the 'homemade' subsidiary group individually, disaggregated the ingredients and then attributed a classification to each ingredient for 'accuracy' (Adams and White, 2015; Lam and Adams, 2017; Madruga et al, 2022; Martines et al, 2019; Onita et al, 2021; Parnham et al, 2022; Rauber et al, 2018; Rauber et al, 2019; Rauber et al, 2022; Rauber et al, 2020; Souza et al, 2022). However, Aceves-Martins et al (2022) describe a limitation of the NDNS recipe codes noting that there is insufficient information to disaggregate them, so attributed all homemade codes to processed foods (NOVA group 3). Aceves-Martins et al (2022) did not present dietary energy intakes for any NOVA or population groups and instead estimated the proportion of food groups and codes in the NDNS year 11 NDB related to each NOVA group.

5.22   Supplemental files illustrating how subsidiary food codes in the NDNS NDB were assigned to NOVA classifications were provided in 2 publications (Adams and White, 2015; Madruga et al, 2022). At the time of publication, of Adams, in 2015, the NOVA classification did not include the current NOVA 3 category, 'processed food'. Comparison of the supplemental files detailing NOVA group classification for each NDNS NDB subsidiary group shows a high level of concordance in identifying main and subsidiary food groups as UPF (NOVA group 4) or unprocessed/minimally processed (NOVA group 1). However, it is not possible to compare concordance in classification of processed culinary ingredients (NOVA group 2) or processed foods (NOVA group 3) primarily due to the evolution in the NOVA definition.

5.23   Two studies (Adams and White, 2015; Lam and Adams, 2017) used the early NOVA classification with 3 groups (Monteiro et al, 2010) and 10 studies (Aceves-Martins et al, 2022; Madruga et al, 2022; Martines et al, 2019; Onita et al, 2021; Parnham et al, 2022; Rauber et al, 2018; Rauber et al, 2019; Rauber et al, 2022; Rauber et al, 2020; Souza et al, 2022) used the redefined NOVA classification with 4 groups (Monteiro et al, 2016) in their assessment. Additionally, 3 studies (Onita et al, 2021; Rauber et al, 2018; Rauber et al, 2019) used NDNS datasets spanning the same years (years 1 to 6 [2008 to 2014] from the NDNS rolling programme). All other studies evaluated data sets across different time periods from the NDNS rolling programme. Although these studies all assessed the NDNS database,

because the NOVA classification changed over this period and different population year groups were assessed this complicates the drawing of conclusions.

5.24 SACN is also aware of one further study, in pre-print (Dicken et al, 2023) identified by the secretariat after the date of the scoping review search. Dicken et al (2023) performed an analysis of food and drink items from the UK NDNS based on nutrient content, the NOVA classification, and front of pack 'traffic light' labelling (FOPL).

5.25 Ahead of completion of peer-review authors concluded that:

- there is some overlap between the NOVA classification and nutrient content of food and drink items available in the UK

- UPFs tended to have an 'unhealthier' nutritional profile according to the FOPL with more red FOPL traffic lights, and fewer green FOPL traffic lights, and were more energy dense compared to minimally processed foods

- UPFs tended to have a similar nutritional profile to processed foods, but were still more energy dense, however, many UPFs did not contain any red FOPL traffic lights and did contain multiple green FOPL traffic lights, which have an improved nutritional profile equivalent to many minimally processed foods

- 'healthy' UPFs (defined as products with no red FOPL traffic lights) still tended to contain more fat, saturated fat, total sugar and salt than minimally processed foods with an equivalent FOPL traffic light score, were more energy dense and more likely to be hyper-palatable

- these results have important implications for understanding how consumers may interpret the relative healthiness of minimally processed foods and UPFs, and for updating UK food and drink labelling.

5.26 A number of limitations in applying the NOVA classification to the NDNS were identified. These are summarized in Chapter 7.

International perspective

United States

5.27 It was not possible within the time frame of this scoping review to carry out a systematic search of international assessments of UPF consumption. However, it was noted that a similar process has been undertaken in the US using nationally representative data from the National Health and Nutrition Examination Survey (NHANES) (Steele et al, 2023). Steele et al (2023) applied the NOVA classification system to years 2001 to 2018 of What We Eat in America data (WWEIA), the dietary intake component of the NHANES, using the 'reference approach' which was developed by the creators of NOVA and has been used in most previous

studies reported by the NOVA research group. In determining the reference approach, 3 variables from the NHANES recall databases were used to determine the NOVA group: 'main food description', 'additional food description' which qualitatively describes food codes, and 'standard reference description' which qualitatively describes each of the underlying standard reference codes. Full details of the 'reference approach' is provided in Annex 9a.

5.28 Data were also used to estimate the percentage energy from NOVA groups 1 to 4 for WWEIA, NHANES years 2017 to 2018 in individuals aged one year or more using the reference approach. Four sensitivity analyses were then conducted comparing potential alternative approaches (for example, opting for more versus less degree of processing for ambiguous items) to the reference approach, to assess how the percentage of energy from NOVA groups differed between approaches. Detail of the sensitivity analyses are included in Annex 9b.

5.29 Results from the primary analysis of years 2017 to 2018 (using the reference approach, see Annex 9) estimated an average of 58.2% plus or minus 0.9% UPF contribution to total dietary energy intake. Unprocessed/minimally processed foods (NOVA group 1) contributed 27.6% of total energy intake, processed culinary ingredients (NOVA group 2) contributed 5.2% and processed foods (NOVA group 3) contributed 9%.

5.30 Results from the 4 sensitivity analyses comparing potential alternative approaches provided estimates of the contribution of energy from UPF (NOVA group 4), ranging from approximately 53 to 60% total dietary energy.

5.31 The 'reference approach' used to assign NOVA food groups to NHANES WWEIA data was developed by the creators of NOVA. All identified studies that adopted the 'reference approach' have been authored by the NOVA research group, although a systematic search of the literature was not conducted to confirm this.

5.32 The authors reported that a range of assumptions were required (see Annex 9c). It is unclear how the impact of these assumptions affects inter-assessor reliability.

France

5.33 An analysis has also been undertaken in France, where the contribution of UPF in adult diets was estimated using nationally representative data from the French NutriNet-Santé study (Beslay et al, 2020; Julia et al, 2018). Participant data from 2009 (baseline) until 2014 were included in the analysis. Each food item was categorised in the food composition table of the NutriNet-Santé study (containing over 3000 foods and beverages) to NOVA groups 1 to 4 (unprocessed/minimally processed foods, processed culinary ingredients, processed foods and UPFs) using the 2016 NOVA classification. Julia et al (2018) estimated UPF consumption as 35.9% total dietary energy intake.

5.34 In summary, estimated average UPF consumption in the US (58.2% ± 0.9%) is comparable to estimates conducted for the UK (53.3% for males and 52.8% for females (Adams and White, 2015); and (55.9% for males and 52.8% for females) (Rauber et al, 2020)). Estimated average UPF consumption in France (35.9%) is somewhat lower than estimates in the UK. However, it is unclear if this is due to differences in dietary patterns, data collection methods, the methods used to estimate UPF consumption, or a combination of some, or all of these issues.

6 Results of the review of the available evidence on associations between processed food consumption and health outcomes

Evidence from systematic reviews

6.1 Of the 20 systematic reviews (SRs) that met the scoping review inclusion criteria:

- ten were either comprised only of prospective cohort studies (PCS) or randomised controlled trials (RCTs) or included mixed observational study designs with more than 70% of the total participant weighting from PCS or RCT evidence. These papers have been fully extracted (see Tables 1 and 2, Annex 8). A summary of these studies is presented in Table 2.

- ten included mixed observational study designs that formed greater than 30% of the total participant weighting. These were not extracted but have been listed in two groups (a) SRs that considered two different levels of food processing (see Table 3, Annex 8) and (b) SRs that considered high versus low consumption of ultra-processed food (UPF) and health outcomes (see Table 4, Annex 8).

6.2 The 10 SRs which were fully extracted considered associations between UPF intake and:

- overweight and obesity (2 SRs)

- chronic non-communicable diseases including type 2 diabetes, hypertension, cardiovascular disease (CVD), cerebrovascular disease and gastrointestinal tract disease (6 SRs)

- depression (2 SRs)

- mortality risk including all-cause mortality, CVD-cause mortality, heart-cause mortality and cancer-cause mortality (4 SRs)

- maternal and child health outcomes including gestational weight gain, gestational diabetes, hypertension during pregnancy, pre-eclampsia, low-birth weight, large-for-gestational age, preterm birth and child adiposity (2 SRs).

See Tables 1 and 2, Annex 8 for full data extraction tables.

Barbosa et al (2022)

6.3 Barbosa et al (2022) is a SR without meta-analysis (MA) of PCS (78% participant weighting) and case-control studies. It considered the relationship between UPF (NOVA group 4) and blood pressure (BP) or arterial hypertension (AH) in adults

and older people. As data from different study types were not reported separately, data from both PCS and cross-sectional studies were extracted (see Table 2, Annex 8) and included.

6.4   The review identified 9 studies (114,849 participants, aged 20 years old and over), conducted in Brazil (3 studies), USA (2 studies), Spain (2 studies), Canada (one study), and Mexico (one study). Authors reported a positive association between UPF intakes and BP or AH in 7 of 9 included studies. No association was found in the remaining 2 studies.

6.5   Tertiles and quintiles of UPF intake were mentioned as the exposure in some studies, but details of measures used to quantify exposure to UPF were not provided for each study. Specific values for what was considered high UPF intake in primary studies were not provided in the SR.

6.6   Details of adjustments were not listed for each primary study. SR authors report that 8 of the 9 studies included diverse covariables in the multivariate analysis. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Delpino et al (2022)

6.7   Delpino et al (2022) is a SR with MA of PCS which considered the relationship between UPF and risk of type 2 diabetes. Only 3 of the 18 included studies used a defined classification (NOVA). The other 15 studies evaluated single UPF foods (for example, sugar-sweetened beverages and processed meats) and have therefore not been extracted or included.

6.8   The review identified 3 studies (146,497 participants aged 18 to 90 years) which used a defined classification system (NOVA), conducted in the UK (one study), France (one study) and Spain (one study). A MA of studies which used a defined classification system (NOVA) assessed the associations for moderate UPF consumption (3 studies, 146,497 participants) or high consumption (2 studies, 41,790 participants). No association was found between moderate UPF consumption and risk of type 2 diabetes (RR 1.10 [95% CI 0.99, 1.23]) and high UPF consumption was associated with an increased risk of type 2 diabetes (RR 1.48 [95% CI 1.48, 1.89]).

6.9   The measures used to quantify exposure to UPF were increments of 10%, quartiles and tertiles. Specific estimates of what was considered moderate or high UPF intake in primary studies were not provided in the SR.

6.10   A list of covariates was provided for each included study. Adjustment across primary studies appears inconsistent overall. SR authors report that their MA included results from fully adjusted models. Sensitivity of SR pooled estimates to

adjustments for different covariates in primary studies not reported for MA of interest. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Jardim et al (2021)

6.11 Jardim et al (2021) is a SR without MA of PCS (88.4% participant weighting), cross-sectional studies and case-control studies. It considered the relationship between UPF (NOVA group 4) and chronic disease risks (including obesity, hypertension, diabetes, cardiovascular disease, gastrointestinal tract disease). As data from PCS were reported separately from cross-sectional and case-control studies, for the purpose of this scoping review only data from PCS were extracted (see Table 2, Annex 8) and included.

6.12 The review identified 19 PCS (762,947 participants, all age groups), conducted in countries including Brazil, Europe, the UK, the US, and South America. Authors reported that higher UPF consumption was positively associated with obesity (5 studies) hypertension (7 studies), type 2 diabetes (3 studies), CVD (2 studies) and gastrointestinal tract disease (2 studies). Further SR details are shown in Table 2, Annex 8.

6.13 A wide range of measures were used to quantify intakes, including percent of energy, quartiles (in weight and grams per day), quintiles (servings per day), tertiles (percentage of total daily energy intake), total daily percent of kcal and proportion of each NOVA category (continuous data). Specific estimates of what was considered high UPF intake in primary studies were not provided in the SR.

6.14 Details of covariables adjusted for in each study were not provided. SR authors state that adjusted risk estimates and confidence intervals were extracted from each study and that when a multivariate model was reported, risk estimates with the greatest control for potential confounding effects were extracted. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Lane et al (2021)

6.15 Lane et al (2021) is a SR with MA of PCS (MA of PCS conducted separately to other study designs, 100% participant weighting), cross-sectional and case-control studies which considered the relationship between UPF (NOVA group 4) and chronic non-communicable diseases. As data from PCS were reported separately from cross-sectional and case-control studies, for the purpose of this scoping review only data from PCS were extracted (see Table 2, Annex 8) and included.

6.16 The review identified 19 PCS (624,671 participants in all age groups) and conducted two meta-analyses of PCS only. Studies were conducted in countries

including Brazil, Europe, the US, the UK, Canada, Lebanon and Malaysia. A MA of 4 studies (including 88,247 participants) found a positive association between higher consumption of UPF (ranging from >35.7% to >36.0% of calories or from 5.2 to <29.8 times per day) and increased risk of all-cause mortality compared with lower consumption (ranging from 14.1% to <21.6% of calories or <2.6 times per day) in adults (HR 1.28 [95% CI 1.11, 1.48]; $P = 0.001$; $I^2 = 45\%$). A second MA of 2 studies (including 41,637 participants) found that higher consumption of UPF (ranging from between 19.0% and 76.0% to >33.0% of calories) was associated with an increased risk of depression compared to lower consumption adults (ranging from ≤10.0% to <15.0% of calories) in adults (HR 1.22 [95% CI 1.16, 1.28]; $P < 0.001$; $I^2 = 0\%$).

6.17   A wide range of measures were used to quantify exposure to UPF, including 10 or 15% increase in consumption, percentage calories and absolute calories, quintiles and quartiles.

6.18   A list of covariates adjusted for are provided for each included study. Adjustment across primary studies appears inconsistent overall. SR authors report that many of the studies reported results from several analyses (for example, main statistical models versus sensitivity testing and unadjusted versus adjusted results) and that those results reported in the studies' abstracts were considered as the main statistical models for extraction unless otherwise indicated by the original primary study authors. Sensitivity of SR pooled estimates to adjustments for different covariates in primary studies not reported.

6.19   SR authors note that "while the majority of studies in the present review adjusted for potential covariates, residual confounding remains possible" and that "it remains to be established if more consistent associations would have been found had a principled confounder selection framework been utilized. In order to address the possible presence of confounding factors, future studies are encouraged to use appropriate analytical approaches, including adjusted models".

de Oliveira et al (2022)

6.20   de Oliveira et al (2022) is a SR without MA of PCS (84% participant weighting) and cross-sectional studies which considered the relationship between UPF consumption (NOVA group 4) and a range of health outcomes in pregnant women and children. As data from PCS were reported separately from cross-sectional studies, for the purpose of this scoping review only data from PCS were extracted (see Table 2, Annex 8) and included.

6.21   The review identified 8 PCS (89,922 participants, pregnant women of any age, neonates, infants and children under 10 years old). Studies were conducted in countries including Brazil, Europe, the US, the UK and Chile. Authors reported positive associations between high maternal UPF consumption and third trimester

gestational weight gain (3 studies) and also child adiposity measures ((body mass index (BMI), weight, fat mass index, waist circumference)) (2 studies) (see Table 2, Annex 8).

6.22   A range of measures were used to quantify exposure to UPF, including percentage of energy intake, total kcal intake, UPF score, tertile, quintile, times per day and median of percentage energy intakes. Specific estimates of what was considered high UPF intake in primary studies were not provided in the SR.

6.23   A list of covariates adjusted for are provided for each included study. Adjustment across primary studies appears inconsistent overall. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Pagliai et al (2021)

6.24   Pagliai et al (2021) is a SR with MA of PCS (MA of PCS conducted separately to other study designs, 100% participant weighting) and cross-sectional studies which considered the relationship between UPF consumption (NOVA group 4) and various health outcomes. As data from PCS were reported independently from cross-sectional studies, for the purpose of this review only data from PCS were extracted (see Table 2, Annex 8) and included.

6.25   The review identified 6 PCS (183,491 participants, aged 18 years and over) conducted in Spain (2 studies), France (1 study), Brazil (1 study), Italy (1 study) and the USA (1 study). A MA of 5 studies (111,056 participants) found an association between the highest consumption of UPF and an increased risk of all-cause mortality (RR 1.25 [95% CI 1·14, 1·37]; $P < 0.00001$; I^2 2%; P_{het} 0.40). A MA of three studies (139,867 participants) found an association between the highest consumption of UPF and an increased risk of CVD incidence and/or mortality (RR 1.29 [95% CI 1.12, 1.48]; $P=0.0003$; I^2 7%; P_{het} 0.34). A MA of 2 studies (127,969 participants) found an association between the highest consumption of UPF and an increased risk of cerebrovascular disease incidence and/or mortality (RR 1.34 [95% CI 1.07, 1.68]; $P =0.01$; I^2 32%; P_{het} 0.22). A MA of 2 studies (41,637 participants) found an association between the highest consumption of UPF and an increased risk of depression (RR 1.20 [95% CI 1.03, 1.40]; $P=0.02$; I^2 42%; P_{het} 0.19). A MA of 2 studies (20,278 participants) found an association between the highest consumption of UPF and an increased risk of overweight or obesity (RR 1.23 [95% CI 1.11, 1.36]; $P < 0.00001$; I^2 0%; P_{het} 0.64).

6.26   UPF exposure was assessed as quartiles in all but one study, which compared tertiles. Specific values for what was considered high UPF intake in primary studies were provided, as either servings per day, times per day, grams per day or percentage of total energy intake.

6.27 SR authors provided a list of covariates adjusted for by each included study. Adjustment across primary studies appears inconsistent overall. Adjustments used in SR pooled analyses not reported. Sensitivity of SR pooled estimates to adjustments for different covariates in primary studies not reported. Values for exposure to UPF reported as percentage of energy intake for most primary studies.

6.28 SR authors note that "only a limited number of studies included total energy intake as a confounding variable in the multivariable models, thus introducing a possible limitation in the interpretation of the results. However, it should be noted that total energy intake can also be part of the causal pathway of UPF intake; therefore, this aspect is not necessarily a study limitation'. SR authors also note that 'the results of the present meta-analysis should be interpreted with caution, since not all the included studies considered unhealthy lifestyle behaviours as confounding factors in the multivariable model".

Paula et al (2022)

6.29 Paula et al (2022) is a SR with MA of PCS (MA of PCS conducted separately to other study designs, 100% participant weighting), cross-sectional studies and case-control studies. It considered the association between UPF (NOVA group 4), rich diet consumption by pregnant women, and perinatal (maternal and neonatal) outcomes. As the number of studies informing each outcome differed, for the purpose of this review outcomes informed by predominantly PCS (>70% participant weighting) were extracted (see Table 2, Annex 8).

6.30 This SR considered 'UPF-rich diet consumption' when the evaluated food, diet, or dietary pattern included at least one NOVA-defined UPF food such as 'fast' foods, 'junk' foods, processed meats, soft drinks, confectionaries, pizzas, hamburgers, candies and sweets, sweetened beverages and cookies. 'Western' and 'Prudent' diet patterns which were characterised by a higher intake of red and processed meats, beverages sweetened with sugar, sweets, desserts, industrialised 'food like' products, and refined grains with a high intake of energy-dense and processed foods, were also considered as a proxy for high UPF intake.

6.31 The review identified a total of 61 studies (698,803 participants, aged 18 years and over), conducted in Europe (23 studies), America (17 studies), Asia (16 studies), Oceania (3 studies) and Africa (2 studies). A MA of 10 PCS (including 42,477 participants) showed that higher maternal consumption of UPF increased the odds of gestational diabetes mellitus (GDM) (OR 1.48 [95% CI 1.17, 1.87]; I^2 82.70%). A MA of 4 PCS (including 112,307 participants) found that UPF-rich dietary consumption increased the odds of preeclampsia (OR 1.28 [95% CI 1.15, 1.42]; I^2 0.00%).

6.32   A MA of 5 PCS (including 4,576 participants) found no association between maternal UPF-rich diet consumption and odds of excessive gestational weight gain. Authors report that this association was also explored in 5 different PCS (including 4,384 pregnant women) where β coefficient was used as the measure of effect, but no association between UPF-rich diet consumption and gestational weight gain (GWG) was found. A MA of 3 PCS (including 58,701 participants) found no association between UPF-rich diet consumption and the odds of hypertension during pregnancy. A MA of 5 PCS studies (including 146,617 participants) found no association between maternal UPF-rich diet consumption and the odds of low birth weight. A MA of 3 PCS (including 52,468 participants) pooled in the MA found no association between maternal UPF-rich diet consumption and the odds of large for gestational age. A MA of 4 PCS (including 233,308 participants) found no association between maternal UPF-rich diet consumption and the odds of preterm birth.

6.33   Measures used to quantify exposure to UPF were not reported. Values for what was considered high UPF intake in primary studies were not provided.

6.34   Details of covariables adjusted for in each study were not provided. SR authors report that when multiple estimates were reported, the results with adjustment for the highest number of confounders were used in pooled analysis. Sensitivity of SR pooled estimates to adjustments for different covariates in primary studies not reported. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Suksatan et al (2021)

6.35   Suksatan et al (2021) is a SR with dose-response MA of PCS. It considered the relationship between UPF consumption (NOVA group 4) and mortality, including all-cause mortality, CVD-cause mortality, heart-cause mortality and cancer-cause mortality.

6.36   The review identified 7 studies (207,291 participants, aged 18 years and over), conducted in Spain (3 studies), the USA (2 studies), Italy (one study) and France (one study). A MA of 6 studies (participant numbers for individual MA not provided) reported that UPF consumption was associated with an increased risk of all-cause mortality (HR 1.21 [95% CI 1.13, 1.30]; P <0.001; I^2 0.0%). A MA of 4 studies reported that UPF consumption was associated with an increased risk of CVD-cause mortality (HR 1.50 [95% CI 1.37, 1.63]; P <0.001; I^2 0.0%). A MA of 2 studies reported that UPF consumption was associated with an increased risk of heart-cause mortality (HR 1.66 [95% CI 1.50, 1.85]; P <0.022; I^2 0.0%). A MA of 3 studies found no association between UPF consumption and risk of cancer-cause mortality (HR 1.00 [95% CI 0.81, 1.24]; P <0.976; I^2 0.0%).

6.37   Authors reported that each 10% increase in UPF consumption in daily caloric intake was associated with a 15% higher risk of all-cause mortality (HR 1.15 [95% CI 1.09, 1.21]; P <0.001; I^2 0.0%). No associations were found between each 10% increase in UPF consumption in daily caloric intake and CVDs-cause mortality (HR 1.21 [95% CI 0.90, 1.62]; P <0.001; I^2 91.4%) or heart-cause mortality (HR 1.18 [95% CI 0.95, 1.47]; P = 0.044; I^2 75.4%). The dose response analysis showed a positive linear relationship between UPF consumption and all-cause mortality ($P_{nonlinearity}$ = 0.879; $P_{dose-response}$ = P <0.001), CVDs-cause mortality ($P_{nonlinearity}$ = 0.868; $P_{dose-response}$ = P <0.001), heart-cause mortality ($P_{nonlinearity}$ = 0.774; $P_{dose-response}$ = P <0.001) and cancer-cause mortality ($P_{nonlinearity}$ = 0.340; $P_{dose-response}$ = P = 0.187).

6.38   Details of measures used to quantify exposure to UPF were not provided for each study. Quartiles, quintiles and percentage energy intake were mentioned as assessment measure in some studies. Specific values for what was considered high UPF intake in primary studies were not provided in the SR.

6.39   A list of covariates adjusted for are provided for each included study. Adjustment across primary studies appears inconsistent overall. SR authors state that covariates used for adjustments in the multivariate analyses were data extracted and that maximally adjusted hazard ratios were pooled for meta-analysis. Sensitivity of SR pooled estimates to adjustments for different covariates in primary studies not reported. SR authors did not comment on the potential impact of lack of, or inconsistency in, covariable adjustment.

Taneri et al (2022)

6.40   Taneri et al (2022) is a SR with MA of PCS. It considered the relationship between UPF consumption (NOVA group 4) and all-cause mortality as well as consumption of single UPF foods or categories. Only 5 out of the total 40 included studies analysed UPF as a category. The remaining studies evaluated single UPF foods and these have not been extracted or included.

6.41   The review identified 5 studies (110,721 participants, aged 18 years and over), conducted across a range of countries including the USA the UK, European countries, Singapore, Australia, and China. A MA of 5 studies (110,721 participants) reported that the highest consumption of UPF was associated with an increased risk of mortality (RR 1.29 [95% CI 1.17, 1.42]; I^2 0.0%) compared with lowest consumption of UPF.

6.42   Details of measures used to quantify exposure to UPF were not provided for each study. Specific values for what was considered high UPF intake in primary studies were not provided in the SR.

6.43   SR provided list of covariates adjusted for by each included primary study. SR authors reported that all but one study adjusted for age, sex (when both sexes were included in analysis) and at least one lifestyle factor but most did not adjust for socioeconomic status, overall diet quality, physical activity, income or education. SR authors reported that the most extensively adjusted RRs reported were used for analysis. Sensitivity of SR pooled estimates to adjustments for different covariates in primary studies not reported. SR authors note that "our results comparing highest vs. lowest intake could reflect a proxy for lifestyle and socioeconomic status".

Wang et al (2022)

6.44   Wang et al (2022) is a SR with MA of PCS (MA of PCS conducted separately to other study designs, 100% participant weighting) and cross-sectional studies. It considered the relationship between UPF consumption (NOVA group 4) and hypertension in adults.

6.45   The review identified 9 studies (111,594 participants, aged 18 years and over), conducted in the USA (2 studies), Canada (2 studies), Brazil (2 studies), Spain (one study), Mexico (one study) and Lebanon (one study). A pooled MA of all 9 studies (111,594 participants) reported that higher consumption of UPF was associated with increased incidence of hypertension (OR 1.23 [95% CI 1.11, 1.37]; P = 0.034; I^2 51.9%).

6.46   UPF exposure in individual studies was assessed as quintiles in all studies. Quintile comparison differed between studies, with some studies comparing Q5 with Q1, and others comparing Q3 with Q1, for example. Values for exposure to UPF were reported as percentage of energy intake for most primary studies.

6.47   SR authors stated that data on covariates used for adjustment and the most adjusted risk estimates were extracted. Authors conducted subgroup analysis on estimates adjusted for potential confounders such as body mass index, energy intake and physical activity to further investigate whether the relationship between UPFs and incidence of diabetes mellitus and hypertension was bias by some specific factors. Analyses performed based these factors were ambiguously reported by SR authors.

6.48   A list of covariates adjusted for are provided for each included study. Adjustment across primary studies appears inconsistent overall. SR authors report that when a multivariate model was reported, risk estimates with the greatest control for potential confounding effects were extracted. SR authors report that subgroup analysis was also conducted on adjustments including gender, study design, exposure assessment, outcome assessment, body mass index, energy intake, and physical activity. SR authors reported that analyses performed based these factors suggested that the results remained statistically significant.

6.49   SR authors note that "our meta-analysis was based on observational studies and thus some unmeasured confounding factors may have various degrees of influence on the results".

6.50   Table 2 below summarises the results of the 10 studies included and extracted in this scoping review. Key characteristics of the studies, as well as details of the author-reported direction of association and any adjustments made for potential confounding co-variates are provided. A number of limitations were identified in relation to assessing the evidence of processed foods and health outcomes. These are summarised in Chapter 7.

Table 2: Summary of extracted systematic reviews identified through the scoping review on associations between processed food consumption and health outcomes results

Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Mortality	Heart-cause mortality	Suksatan et al (2021) 100%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	Maximally adjusted hazard ratios pooled for meta-analysis, further detail not provided	Not reported
	Cancer-cause mortality	Suksatan et al (2021) 100%	High vs low UPF	—		See Suksatan et al (2021) above	
	All-cause mortality	Lane et al (2020) 93%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	Where multiple analyses presented in primary studies, those in abstracts were extracted as main statistical models, unless primary study authors indicated otherwise	Not reported

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[1] Participant weighting: Of the 20 SRs that met the scoping review eligibility criteria, 10 were either comprised only of PCS or included mixed observational study designs where >70% of the total participant weighting came from PCS evidence. As per the eligibility criteria (see Annex 6), these papers were fully extracted (see Tables 1 and 2, Annex 8). The remaining 10 SRs included mixed observational study designs that formed >30% of the total participant weighing and were therefore not extracted but have been listed (see Tables 3 and 4, Annex 8).

[2] Author reported.

[3] SR reporting of covariate adjustments in primary studies.

[4] Adjustments used in SR pooled analyses.

[5] Sensitivity of SR pooled estimates to adjustments for covariates in primary studies.

Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Mortality (continued)	All-cause mortality (continued)	Pagliai et al (2021) 100%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	Not reported	Not reported
		Suksatan et al (2021) 100%	High vs low UPF	↑	See Suksatan et al (2021) above		
		Taneri et al (2022) 100%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed. All but one study adjusted for age, sex and at least one lifestyle factor; most did not adjust for SE measures, diet quality or physical activity	Most extensively adjusted risk ratios reported were used for analysis	Not reported

Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Non-communicable chronic disease risk	Blood pressure or arterial hyper-tension	Barbosa et al (2022) 78%	UPF	↑	Covariates were not listed for each primary study but 8/9 adjusted for 'diverse' covariables	Pooled analysis not conducted	Pooled analysis not conducted
		Wang et al (2022) 80%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	The most adjusted risk estimates were extracted	Subgroup analysis was conducted on risk estimates adjusted for gender, study design, exposure assessment, outcome assessment, body mass index, energy intake, and physical activity but these results were ambiguously reported
	Overweight or Obesity	Jardim et al (2021) 88%	UPF	↑	Details of covariables adjusted for in each study were not provided	Risk estimates from models with the greatest control for potential confounders were extracted	Pooled analysis not conducted
		Pagliai et al (2021) 100%	High vs low UPF	↑		See Pagliai et al (2021) above	

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Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Non-communicable chronic disease risk (continued)	Type 2 diabetes	Jardim et al (2021) 88%	UPF	↑		See Jardim et al (2021) above	
	Type 2 diabetes	Delpino et al (2022) 100%	Moderate vs low UPF	—	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	Results from the full adjusted model were considered	Not reported
			High vs low UPF	↑			
	Gastrointestinal tract disease	Jardim et al (2021) 88%	UPF	↑		See Jardim et al (2021) above	
	Cardiovascular disease (including incidence and mortality)	Jardim et al (2021) 88%	UPF	↑		See Jardim et al (2021) above	
		Suksatan et al (2021) 100%	High vs low UPF	↑		See Suksatan et al (2021) above	

Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Non-communicable chronic disease risk (continued)	Cerebro-vascular diseases (including incidence and mortality)	Pagliai et al (2021) 100%	High vs low UPF	↑		See Pagliai et al (2021) above	
Mental health	Depression	Lane et al (2020) 93%	High vs low UPF	↑		See Lane et al (2020) above	
		Pagliai et al (2021) 100%	High vs low UPF	↑		See Pagliai et al (2021) above	
Maternal health	Gestational weight gain	De Oliveira et al (2022) 84%	High vs low UPF	↑	Covariates adjusted for by each primary study are listed, adjustments not consistent between studies	Pooled analysis not conducted	Pooled analysis not conducted
		Paula et al (2021) 98%	High vs low UPF	—	Details of covariables adjusted for in each study were not provided	Results adjusted for the most confounders were used in the pooled analysis	Not reported
	Gestational diabetes	Paula et al (2021) 98%	High vs low UPF	↑		See Paula et al (2021) above	

Overall health outcome	Specific health outcome	Author (date) % PCS[1]	Exposure	Direction of association[2]	SR adjustments[2] primary studies[3]	SR adjustments[2] pooled analyses[4]	SR adjustments[2] sensitivity analyses[5]
Maternal health (continued)	Hyper-tension during pregnancy	Paula et al (2021) 98%	High vs low UPF	—		See Paula et al (2021) above	
	Pre-eclampsia	Paula et al (2021) 98%	High vs low UPF	↑		See Paula et al (2021) above	
Fetal, neonatal and child health	Pre-term birth	Paula et al (2021) 98%	High vs low UPF	—		See Paula et al (2021) above	
	Low birth weight	Paula et al (2021) 98%	High vs low UPF	—		See Paula et al (2021) above	
	Large for gestational age	Paula et al (2021) 98%	High vs low UPF	—		See Paula et al (2021) above	
	Child adiposity	De Oliveira et al (2022) 84%	High vs low UPF	↑		See De Oliveira et al (2022) above	

Abbreviations: UPF, ultra processed food; PF, processed food; SR, systematic review; BMI, body mass index; MA, meta-analysis; SE, socioeconomic; ↑, author reported positive association; —, author reported no statistically significant association

Registered trials – ongoing or completed RCTs and PCS

6.51 A total of 56 ongoing or completed studies were identified from the ClinicalTrials.gov search conducted on 18 January 2023 and updated on 21 June 2023. Forty-nine studies were excluded following application of the eligibility criteria (see Annex 6): 6 studies were excluded based on the study population being out of scope of this review, 41 were excluded based on the intervention being out of scope, one study was excluded based on the outcome being out of scope and one study was excluded based on the study design being out of scope. Seven studies of potential relevance were identified, 6 RCTs and one observational study (see Annex 7).

6.52 Each study set out to evaluate 2 or more levels of food processing or high versus low consumption of UPF and associated markers of health or health outcomes. The status of 2 studies were noted as completed, one with results (Hall et al, 2019) and one without results (NCT04275843).

6.53 The only completed registered trial with results available, was published by Hall et al (2019) and is summarised below. The status of one study (NCT04280146) was noted as unknown as it had passed its recruitment completion date, but the status had not been updated on ClinicalTrials.gov. The status of the remaining 4 studies, 3 interventional (NCT04308473, NCT05290064, NCT05368194) and one observational (NCT05071170) were noted as active or recruiting.

6.54 The trial by Hall et al (2019) was a small (n=20) randomised controlled crossover trial (Hall et al, 2019) that assessed the impact of UPF (NOVA group 4) on energy intake and weight gain. Participants received either a UPF diet or an unprocessed diet for 2 weeks followed immediately by the alternate diet for 2 weeks.

6.55 Authors reported that energy intake was substantially greater during the period of the UPF diet (508±106 kcal per day; p=0.0001). Participants gained more weight (0.9±0.3 kg; p=0.009) on the UPF diet and lost more weight on the unprocessed diet (0.9±0.3 kg; p=0.007). Weight changes were highly correlated with energy intakes (r=0.8, p < 0.0001). A range of limitations were identified, which are outlined, alongside further details on the methods, findings and limitations in Annex 11.

7 Limitations

7.1 A range of limitations are noted. These are outlined below.

Limitations relating to the methods of the position statement

7.2 As this is a SACN position statement and not a full risk assessment, a full quality assessment was not completed and SACN did not undertake a formal grading of the certainty of the evidence. This is in accordance with SACN's Framework for the Evaluation of Evidence (SACN, 2023b).

7.3 A full systematic search was not undertaken to identify the available classification systems or specific aspects of their use (for example inter-assessor reliability). Known review articles were supplemented by non-systematic searches.

7.4 The inclusion cut-off date for publications considering processed foods and health was set as the date of the literature search, 12 January 2023. As this is such a rapidly evolving field there are likely to be studies published since then that would meet the inclusion criteria (see Annex 12).

7.5 It was not possible within the required time frame to carry out a systematic search of which countries make reference to food processing within their national dietary guidelines. This statement refers to the findings of a global analysis by Koios et al (2022), as well as other countries identified by SACN and the secretariat to make recommendations with respect to processing. Some countries with recommendations with respect to processing may therefore not have been identified.

7.6 The feasibility of applying the NOVA classification system to UK dietary and food composition data was restricted to National Diet and Nutrition Survey (NDNS) data and did not consider other sources of food consumption data collected in the UK.

7.7 Only one assessor considered the studies for eligibility with respect to the application of NOVA to NDNS data, introducing the potential for bias.

7.8 No detailed assessment was made of the potential for double counting of primary studies within included SRs. It was observed that a number of primary studies were included in more than one SR.

7.9 No detailed assessment was made of authors' attempts to adjust for covariates and potential residual confounding. It was observed that adjustment varied between studies.

7.10 Only one trial registry (ClinicalTrials.gov) was searched for registered RCTs and PCS on the topic of processed foods and health. It was not possible, within the required timeframe to search other registries.

7.11 As the aim of this review was to assess food processing as a category, SRs focusing on the association between single food groups defined by a level of processing and health outcomes were not included. This means that, for example SRs considering the health outcomes associated with consumption of sugar sweetened beverages, infant formula, infant foods or foods for special medical purposes alone were excluded. If SACN were to undertake a full risk assessment on this topic it would be helpful to consider exposure to specific single ultra-processed food groups.

Limitations relating to classifications of processed foods

7.12 Classification systems for processed foods generally did not consider:

- the relationship between the classification system and the nutritional content of products
- known associations between specific processed foods and health (such as processed meat and cancer).

As such it remains unclear how classification systems relate to existing dietary recommendations (see paragraph 7.19)

7.13 A number of limitations regarding classification systems for processed foods have been identified:

- some systems draw on subjective concepts such as "natural"; "wholesome", "raw", "artisanal" and "mass produced". These concepts may be understood and applied differently by different users leading to potential misclassification bias
- systems inconsistently consider or provide a lack of clarity on various components. This includes, for example:
  o refined versus whole grains
  o fortified foods
  o physical and chemical changes to food resulting from processing, such as integrity of the 'food matrix' or acrylamide formation
  o additives.

7.14 Specific issues relating to the NOVA classification were identified:

- the categories are broad and capture a wide range of foods. This can lead to discordance with nutrient or other food-based classifications. For example, processed meats are classified as NOVA group 3 and not UPF NOVA group 4;

all manufactured sliced breads are classified as UPF NOVA 4 with no differentiation between white and wholemeal bread

- it is unclear how to categorise homemade dishes that contain only a proportion of UPF as part of the overall recipe

- the degree of inter-assessor reliability on application of the NOVA classification to dietary consumption data appeared to vary among the studies identified. However, a systematic search of the literature was not conducted to further assess this.

Limitations relating to applying processed food classifications to UK consumption data.

7.15   UK consumption data was only considered against one classification system, NOVA.

7.16   A number of limitations in the evidence base applying NOVA to the NDNS data were identified:

- limited assessment has been undertaken of the application of NOVA to the NDNS. One group linked to the development of the NOVA system was responsible for 9 out of 12 publications identified, with all publications citing the same methodology

- data on the application of NOVA to the UK NDNS nutrient databank (NDB) were of insufficient detail to enable comparison.

7.17   A number of practical limitations of applying the NOVA system to the NDNS data were identified, (in addition to the limitations of the NOVA system described above):

- the NDNS does not currently capture all of the detail required for classifying foods according to the NOVA system. For example, it does not include information on low or no calorie sweeteners or other additives, nor the method of food processing or packaging.

- there is a risk that researchers may under or over-estimate UPF consumption as a result of oversimplified interpretation of the NDNS food groupings.

7.18   An assessment of US National Health and Nutrition Examination Survey (NHANES) data using NOVA has reported similar limitations (Steele et al, 2023).

Limitations of the evidence on associations between processed food consumption and health outcomes

7.19 Several limitations were identified in relation to the evidence on associations between processed food consumption and health outcomes:

- the literature is dominated by NOVA. Any limitations or biases of the NOVA classification may be replicated throughout the research literature

- although a detailed assessment was not carried out for this review, authors of the extracted SRs appeared to inconsistently adjust for key confounders or covariates, which may result in residual confounding. This includes:

    o the impact of dietary or nutritional factors already known to be associated with health outcomes. Some but not all studies, report accounting for energy density, saturated fat, salt or free sugars content of foods. Many studies did not adjust for intakes of these or other dietary or nutritional components (see Table 2). Studies measured UPF intake in a variety of ways. For example, some studies reported UPF intake as a percentage of total energy intake, while others presented UPF intake in grams. These different approaches will differentially affect reported exposure to UPF

    o the impact of participant characteristics. Some but not all studies account for age, sex, ethnicity, smoking status or socioeconomic status

    o the impact of health-related covariates. Some but not all consider BMI or other anthropometric measures, medication use or presence of non-communicable diseases

- limited information is available on the impact on population subgroups and studies to date are not necessarily undertaken among socially and ethnically diverse groups. This impacts both on the potential generalisability of study findings to the UK population, and limits understanding on the potential differential effects of UPF consumption and associated adverse health outcomes

- the available evidence is almost exclusively observational and several of the SRs identified do not disaggregate prospective and cross-sectional data. In addition, much of the published research is based on a limited number of cohorts, with self-reported height and weight

- dietary data were mostly based on dietary collection methods (such as food frequency questionnaires) that were unlikely to have been designed or validated for assessing level of food processing and may provide insufficient information to robustly apply classification systems (Barbosa et al, 2022). Although many cohort studies used generic food frequency questionnaires (FFQ) not developed for the purpose of assessing food processing, some attempts have been made to verify the categorisation of items to NOVA categories (Khandpur et al, 2021)

- consumption of UPF products appears to have increased in recent years. Given that diet-related diseases may take many years to develop it is unclear how retrospective analysis of older dietary data may compare with findings from current or future prospective cohort studies

- at the time of scoping the evidence, only one small trial had been published that investigated one type of UPF diet versus one type of non UPF diet. The findings of this study cannot be generalised to all comparisons of UPF and non-UPF diets

- the evidence base is heterogeneous and the terminology used is imprecise. As a consequence, studies investigating processed food consumption and health outcomes are difficult to compare. For example:
  - primary studies may consider high UPF as quartile 4, or quartile 3 to 4 combined. Values are usually not reported to clarify intakes in specific sub-groups.

8 Summary and conclusions

Summary

8.1 In autumn 2022, the Office for Health Improvement and Disparities (OHID) asked SACN to review the evidence on processed foods and health. The terms of references for this work were to:

a) issue a position statement on processed foods and health. To include:

- evaluation of existing classifications of processed foods, including ultra-processed foods and the NOVA classification

- evaluation of the suitability and methods to apply food processing definition(s) as a dietary exposure

- consideration of the availability and quality of evidence associating different forms or levels of food processing with health outcomes

b) scope any future work on this issue.

Evaluation of existing classifications of processed foods, including ultra-processed foods and the NOVA classification

8.2 Eight classification systems were identified and considered against five initial screening criteria (as set out in paragraph 3.5). NOVA was the only system identified that met all 5 screening criteria. NOVA was found to be potentially applicable to the UK population (criterion 1) and had been used to evaluate health outcomes associated with consumption (criterion 5). It has been used in peer-reviewed publications by more than one research group (criterion 3). Assessment beyond the initial screen identified that the literature is currently dominated by NOVA (Monteiro et al, 2019; Monteiro et al, 2016) raising the risk that any limitations or biases present within the NOVA classification system may be replicated throughout the research literature. While NOVA also met the initial screening criterion 2 on a clear, usable definition and criterion 4 on the availability of data on inter-assessor reliability, assessment beyond the initial screen identified less certainty on the clarity, reliability and feasibility of the system.

8.3 Processed food classification systems identified generally did not consider the nutrient content of products nor existing dietary recommendations, or relationships with other measures of dietary patterns.

Evaluating suitability and methods to apply food processing definitions as a dietary exposure

8.4   In order to evaluate the suitability of using food processing as a dietary exposure this rapid scoping review assessed the available evidence that applied the NOVA food processing classification system to the UK National Diet and Nutrition Survey (NDNS) dataset.

8.5   A range of assumptions have to be made in order to apply NOVA to the NDNS dataset, for example the NDNS does not distinguish between manufactured and homemade for all food groups. Some key characteristics required by NOVA are not available within the NDNS, for example, whether foods are 'mass-produced' or 'artisanal' and no information is collected on low or no calorie sweeteners or other additives, packaging or preservation methods.

8.6   Twelve studies were identified which considered the application of NOVA to NDNS. Nine of the 12 studies included authors who were members of the research group that developed NOVA. All 9 studies used the same methodology for applying NOVA to NDNS data. Estimates of population UPF intake in the UK ranged from 51% to 68% of total dietary energy, varying within this range by age and socioeconomic status. The validity and reproducibility of these estimates is unclear given difficulties in disaggregating some food codes within the NDNS data.

Associations between processed food consumption and health outcomes

8.7   Twenty SRs met the inclusion criteria (Askari et al, 2020; Barbosa et al, 2022; Cascaes et al, 2022; Chen et al, 2020; De Amicis et al, 2022; de Oliveira et al, 2022; Delpino et al, 2022; Jardim et al, 2021; Lane et al, 2021; Lane et al, 2022; Mazloomi et al, 2022; Moradi et al, 2023; Moradi et al, 2021; Pagliai et al, 2021; Paula et al, 2022; Santos et al, 2020; Suksatan et al, 2021; Taneri et al, 2022; Tian et al, 2022; Wang et al, 2022). Of these, 10 were fully extracted as they contained only PCS or at least 70% of the total participant weighting from PCS (Barbosa et al, 2022; de Oliveira et al, 2022; Delpino et al, 2022; Jardim et al, 2021; Lane et al, 2021; Pagliai et al, 2021; Paula et al, 2022; Suksatan et al, 2021; Taneri et al, 2022; Wang et al, 2022).

8.8   The 10 fully extracted SRs considered associations between UPF intake and:
- overweight and obesity (2 SRs)
- chronic non-communicable diseases including type 2 diabetes, hypertension, cardiovascular disease (CVD), cerebrovascular disease and gastrointestinal tract disease (6 SRs)
- depression (2 SRs)
- mortality risk including all-cause mortality, CVD-cause mortality, heart-cause mortality and cancer-cause mortality (4 SRs)

- maternal and child health outcomes including gestational weight gain, gestational diabetes, hypertension during pregnancy, pre-eclampsia, low-birth weight, large-for-gestational age, preterm birth and child adiposity (2 SRs).

8.9 Most SRs reported that increased consumption of processed food (specifically UPF) was associated with an increased risk of the adverse health outcomes considered.

8.10 A check of a trial registry (ClinicalTrials.gov) during the drafting of this statement (carried out in January 2023 and updated in June 2023), indicated that a number of registered trials were underway on the topic of processed foods and health.

Limitations

8.11 Several limitations were noted with respect to SACN's scoping review process largely due to the limited time frame and resources available for this work.

8.12 Limitations were identified regarding processed food classification systems. Some systems draw on subjective concepts such as "natural"; "wholesome", "raw", "artisanal" and "mass produced". These concepts may be understood and applied differently between users. Systems differ in their classification of components such as refined versus wholegrains and additives.

8.13 Classification systems identified generally did not consider the nutritional content of products, or known associations between specific processed foods and health (such as processed meat and cancer).

8.14 Specific limitations of the NOVA classification system were that the categories are very broad and capture a wide range of foods. They group together foods with differing nutritional attributes. There were also different estimates of the degree of inter-assessor reliability.

8.15 A number of limitations were identified in applying NOVA to UK dietary survey data. The NDNS currently does not capture all of the detail required by NOVA. Researchers may under or over-estimate UPF consumption as a result of oversimplified interpretation of the NDNS food groupings. Data identified on the application of NOVA to the NDNS were of insufficient detail to enable comparison.

8.16 In relation to assessing the evidence on processed foods and health outcomes there are important limitations:

- the majority of included studies used the NOVA classification system for processed foods
- the available evidence is almost exclusively observational in nature

- there was inconsistent adjustment for covariables as well as inconsistency between SRs regarding which are the key covariables. Hence, although adverse health associations were consistently reported, it is unclear whether these associations are due to or independent of the 'unhealthy' nutrient contents that are typical of many UPFs (for example, high energy density, salt, saturated fat or free sugars)

- limited available information on the impact on population subgroups and the lack of studies to date undertaken among socially and ethnically diverse groups. This impacts both on the potential generalisability of study findings to the UK population, and limits our understanding on potential differential effects of UPF consumption on health

- dietary data within observational studies was mostly based on dietary collection methods unlikely to have been designed or validated for assessing level of food processing

- the method of reporting UPF intakes (for example grams UPF per day, percentage of energy from UPF per day) and the cut offs for the quantiles used varies across studies.

Conclusions

8.17 The systematic reviews identified have consistently reported that increased consumption of (ultra-) processed foods was associated with increased risks of adverse health outcomes. However, there are uncertainties around the quality of the available evidence. Studies are almost exclusively observational and confounding factors or covariates may not be adequately accounted for.

8.18 NOVA was the only processed food classification that met SACN's initial screening criteria as being potentially suitable for use in the UK. However, assessment of the NOVA approach identified some concerns around its practical application in the UK. In particular, the classification of some foods is discordant with nutritional and other food-based classifications.

8.19 Consumption of (ultra-) processed foods may be an indicator of other unhealthy dietary patterns and lifestyle behaviours. Diets high in (ultra-) processed foods are often energy dense; high in saturated fat, salt or free sugars; high in processed meat; and/or low in fruit and vegetables and fibre.

8.20 It is unclear to what extent observed associations between (ultra-) processed foods and adverse health outcomes are explained by established relationships between nutritional factors and health outcomes on which SACN has undertaken robust risk assessments (SACN, 2003; SACN, 2010; SACN, 2011; SACN, 2015; SACN, 2019).

8.21 The observed associations between higher consumption of (ultra-) processed foods and adverse health outcomes are concerning, however, the limitations in the NOVA classification system, the potential for confounding, and the possibility that the observed adverse associations with (ultra-) processed foods are covered by existing UK dietary recommendations, mean that the evidence to date needs to be treated with caution.

Scoping future SACN work

8.22 There is currently insufficient evidence for SACN to carry out a full risk assessment on the topic of processed foods and health. However, given SACN's concern on this issue, the committee will formally add this topic to its watching brief and re-consider at the next scheduled horizon scan (June 2024).

8.23 SACN are aware that there are a number of on-going registered trials on this topic; further observational data and systematic reviews are also likely to be published. These studies may address some of the limitations identified in this position statement and enable a full risk assessment.

8.24 Any future risk assessment by SACN would require detailed consideration of UK population exposure to processed foods, via the NDNS or other UK dietary datasets. In order to undertake further assessment of (ultra-) processed food intakes using the NDNS, consideration would need to be given to:

- the impact of assumptions about coding (ultra-) processed food categories on error, bias and interpretation of findings if no adjustments to NDNS methodology were made
- the potential for adjustments to NDNS methodology to better capture population exposure to (ultra-) processed foods and the potential impact of these on resource needs, participant burden and response rates.

8.25 Any future risk assessment would need to consider the full range of potential benefits and risks of food processing on health to the UK population. This may include, for example, the benefits of food fortification or reformulation versus the contribution of processed products to energy and nutrients intakes among different population groups in the UK.

9 Research recommendations

9.1 A number of limitations in the available evidence on processed foods and health were identified. Further research is required in particular in the following areas:

- further assessment and development of a (ultra-) processed foods classification system that can reliably be applied to estimate consumption of processed foods in the UK

- further evidence exploring relationships between (ultra-) processed foods and health outcomes, based on a classification system that can reliably be applied in the UK (see above). This includes:

  o good quality randomised controlled trials (RCTs) that may help to identify potential mechanisms and establish whether they are independent of energy density or other dietary factors which have been considered in previous SACN risk assessments

  o good quality prospective cohort studies that can address concerns relating to confounding and reverse causality for observed associations between (ultra-) processed foods and health outcomes

  o good quality studies that consider the benefits of consuming products with minimal processing in comparison with existing UK dietary recommendations and/or other dietary patterns for which there is evidence of beneficial health outcomes

  o assessing any role of food additives or other processing methods in observed associations between (ultra-) processed foods and health

- further assessment and refinement of NDNS methodology to better estimate and monitor processed food consumption, while minimising impact on participant burden.

Abbreviations

Abbreviation	Definition
ACNFP	Advisory Committee on Novel Foods and Processes
ADHD	Attention deficit hyperactivity disorder
AH	Arterial hypertension
ANSES	The French Agency for Food, Environmental and Occupational Health and Safety
ASB	Artificially sweetened beverages
BP	Blood pressure
BMI	Body mass index
CI	Confidence intervals
COMA	Committee on Medical Aspects of Food and Nutrition Policy
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DHSC	Department of Health and Social Care
DLW	Doubly labelled water
EFSA	European Food Safety Authority
FCS	Food classification system
FFQ	Food frequency questionnaire
FOPL	Front of pack labelling
FSA	Food Standards Agency
GDM	Gestational diabetes mellitus
GWG	Gestational weight gain
HDL-C	High density lipoprotein cholesterol
HFSS	High in saturated fat, salt or free sugars
HR	Hazard ratio
HDP	Hypertensive disorders of pregnancy
IARC	International Agency for Research on Cancer
IFIC	International Food Information Council
IFPRI	International Food Policy Research Institute in Guatemala
LBW	Low birth weight

Abbreviation	Definition
LGA	Large for gestational age
LSMS	Living Standard Measurement Survey
MA	Meta-analysis
MNIPH	Mexican National Institute of Public Health
MPF	Minimally processed food
NCD	Non-communicable disease
NDB	Nutrient Databank
NDNS	UK National Diet and Nutrition Survey
NOS	Newcastle-Ottawa scale
NHANES	National Health and Nutrition Examination Survey
NOVA	Classification system for processed foods
NR	Not reported
OHID	Office for Health Improvement and Disparities
OR	Odds ratio
PCS	Prospective cohort study
PF	Processed food
PI	Processed ingredient
RCT	Randomised controlled trial
RR	Relative risk
RTB	Ready-to-bake
RTE	Ready-to-eat
RTH	Ready-to-heat
SACN	Scientific Advisory Committee on Nutrition
SBP	Systolic blood pressure
SDIL	Soft drinks industry levy
SR	Systematic review
SSB	Sugar sweetened beverages
UKHSA	UK Health Security Agency
UPF	Ultra-processed foods
UPFD	Ultra-processed foods and drinks
WHO	World Health Organization
WWEIA	What We Eat in America

Annex 1: Identified classification systems and definitions of food processing

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
NOVA (Monteiro et al, 2019; Monteiro et al, 2016)	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Considered Place of change (eg at home or in a factory) Considered Purpose of change (eg essential, cosmetic, palatability) Considered	1). Unprocessed or minimally processed foods Unprocessed/natural foods: edible parts of plants (seeds, fruits, leaves, stems, roots) or of animals (muscle, offal, eggs, milk), and also fungi, algae and water, after separation from nature Minimally processed foods: natural foods altered by processes such as removal of inedible or unwanted parts, drying, crushing, grinding, fractioning, filtering, roasting, boiling, pasteurisation, refrigeration, freezing, placing in containers, vacuum packaging, or non-alcoholic fermentation. None of these processes adds substances such as FSS to the original food. The main purpose of the processes used in the production of group 1 foods is to extend the life of unprocessed foods, allowing their storage for longer use, such as chilling, freezing, drying, and pasteurising. Other purposes include facilitating or diversifying food preparation, such as in the removal of	Fresh, squeezed, chilled, frozen, or dried fruits and leafy and root vegetables; grains such as brown, parboiled or white rice, corn cob or kernel, wheat berry or grain; legumes such as beans of all types, lentils, chickpeas; starchy roots and tubers such as potatoes and cassava, in bulk or packaged; fungi such as fresh or dried mushrooms; meat, poultry, fish and seafood, whole or in the form of steaks, fillets and other cuts, or chilled or frozen; eggs; milk, pasteurised or powdered; fresh or pasteurised fruit or vegetable juices without added sugar, sweeteners or flavours; grits, flakes or flour made from corn, wheat, oats, or cassava; pasta, couscous and polenta made with flours, flakes or grits and water; tree and ground nuts and other oil seeds without added salt or sugar; spices such as pepper, cloves and cinnamon; and herbs such as thyme and mint, fresh or dried; plain yoghurt with no added sugar or artificial sweeteners added; tea, coffee, drinking water. Also includes foods made up from two or more items in group 1, such as dried mixed fruits, granola made from cereals, nuts and dried fruits with no added sugar, honey or oil; and foods with vitamins and minerals added generally to replace nutrients lost during processing, such as wheat or corn flour fortified with iron or folic acid

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		inedible parts and fractioning of vegetables, the crushing or grinding of seeds, the roasting of coffee beans or tea leaves, and the fermentation of milk to make yoghurt	
		2). Processed culinary ingredients – Includes substances obtained directly from group 1 foods or from nature by processes such as pressing, refining, grinding, milling, and spray drying. The purpose of processing is to make products used in home and restaurant kitchens to prepare, season and cook group 1 foods.	Vegetable oils crushed from seeds, nuts or fruit (notably olives); butter and lard obtained from milk and pork; sugar and molasses obtained from cane or beet; honey extracted from combs and syrup from maple trees; starches extracted from corn and other plants; vegetable oils with added antioxidants; salt mined or from seawater, and table salt with added drying agents. Also includes products consisting of group 2 items, such as salted butter, and group 2 items with added vitamins or minerals, such as iodised salt.
		3). Processed foods Relatively simple products made by adding FSS or other group 2 substances to group 1 foods. Most processed foods have two or three ingredients. Processes include various preservation or cooking methods, and, in the case of breads and cheese, non-alcoholic fermentation. The main purpose of the manufacture of processed foods is to increase the durability of group 1 foods, or to modify or enhance their sensory qualities	Canned or bottled vegetables or legumes (pulses) preserved in brine; whole fruit preserved in syrup; tinned fish preserved in oil; some types of processed animal foods such as ham, bacon, pastrami, and smoked fish; most freshly baked breads; and simple cheeses to which salt is added; alcoholic drinks such as beer, cider and wine.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		4). Ultra-processed foods The main purpose of industrial ultra-processing is to create products that are ready to eat, to drink or to heat, liable to replace both unprocessed or minimally processed foods that are naturally ready to consume, such as fruits and nuts, milk and water, and freshly prepared drinks, dishes, deserts, and meals. Common attributes of UPF are hyper-palatability, sophisticated and attractive packaging, multi-media and other aggressive marketing to children and adolescents, health claims, high profitability, and branding and ownership by transnational corporations Several industrial processes with no domestic equivalents are used in the manufacture of UPFs, such as extrusion and moulding, and pre-processing for frying	carbonated drinks; sweet or savoury packaged snacks; ice-cream, chocolate, candies (confectionery); mass-produced packaged breads and buns; margarines and spreads; cookies (biscuits), pastries, cakes, and cake mixes; breakfast 'cereals', 'cereal' and 'energy' bars; 'energy' drinks; milk drinks, 'fruit' yoghurts and 'fruit' drinks; cocoa drinks; meat and chicken extracts and 'instant' sauces; infant formulas, follow-on milks, other baby products; 'health' and 'slimming' products such as powdered or 'fortified' meal and dish substitutes; and many ready to heat products including pre-prepared pies and pasta and pizza dishes; poultry and fish 'nuggets' and 'sticks', sausages, burgers, hot dogs, and other reconstituted meat products, and powdered and packaged 'instant' soups, noodles and desserts; alcohol, such as whisky, gin, rum and vodka

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
International Agency for Research on Cancer (IARC) (Chajès et al, 2011; Slimani et al, 2009)	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Not considered Place of change (eg at home or in a factory) Considered Purpose of change (eg essential, cosmetic, palatability) Not considered	1). Non-processed Foods consumed raw without any further processing/preparation, except washing, cutting, peeling, squeezing.	Raw fruits, non-processed nuts, fresh raw vegetables, fresh raw grated vegetable, raw egg white, raw meat, crustaceans, molluscs, honey, fresh Farmer's milk (not enriched), whole fresh cream, fresh fruit juices, tap water, ice cubes.
		2). Moderately processed 2.1). Modest processing and consumed with no further cooking	2.1). Dried fruits, raw vacuum-packed or under controlled atmosphere foods (such as salads and potatoes), frozen basic foods, extra virgin olive oil, vegetables canned in own juice or in water/brine, legumes canned in own juice or in water/brine, dried or semi-dried fruits, nuts and seeds, frozen or vacuum-packed raw meat, virgin olive oil; fat from cooked fish/meat, dripping, green tea, camomile tea, dried herbs.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		2.2). Foods processed at home and prepared/cooked from raw or moderately processed foods.	2.2). Fresh vacuum-packed or frozen cooked potato (including homemade French fries), fresh or frozen cooked vegetables, dried boiled legumes, fresh fruit, compote, boiled; cooked fruit, boiled grain, wholemeal boiled rice, fresh or vacuum-packed cooked meat, fresh or frozen cooked offal, fresh or frozen cooked fish, whole cooked egg, fresh cooked frogs' legs.
		3). Highly processed Foods that have been industrially prepared and involving a high degree of processing such as drying, flaking, hydrogenation, heat treatment, use of industrial ingredients and industrial deep frying, including those from bakeries and catering outlets, and which require no or minimal domestic preparation apart from heating and cooking.	UHT-treated or pasteurized, enriched, condensed milk, milk beverages reconstituted from powder; buttermilk beverages; kefir; non homemade yogurt in general, cheese in general, commercial cream dessert, UHT-treated or pasteurized or reconstituted from powder dairy cream, coffee creamer, thickened milk for coffee; starch, flakes, flour, wheat germ, wheat bran, ravioli canned in tomato sauce, fresh or dried boiled pasta, cooked couscous, white boiled rice, bread, bread crumbs, cream crackers, crispbread, rusks, breakfast cereals, salty biscuits, plain popcorn, commercial baked dough; meat canned in gravy; ham, sausages, bacon, pâte; gizzard confit, battered and fried pigs' or sheep's trotters; fish canned in oil, tomato sauce, vinegar or pickled, marinated salmon, salted anchovy; cod roe, crabsticks, fish pâte; egg powder; oils, butter, margarine, deep frying fat, cooking fat; sugar, candied fruit/peel, jam, marmalade, chocolate products, confectionery, ice cream, sorbet, syrup; commercial cakes; alcohol-free beer, commercial juice, commercial juice reconstituted from condensed fruits, soft drinks with artificial sugar

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
			(light) or sweetened, diluted syrup, instant and brewed coffee, flavoured tea, ready-to-drink iced tea, powdered tea, black tea, powdered sweetened fruit tea, chicory, mineral water, sparkling water; wine, beer, cider, spirits, brandy, aniseed drinks (Pastis), liquors; sauce reconstituted from powder or commercial; bouillon cube/powder, salt, yeast, vinegar, spices; commercial soup, soup reconstituted from condensed tomatoes, soup reconstituted from powder; broth from a cube; commercial vegetarian food, aspartame, saccharine, meal replacements, muesli bars, protein powder; commercial snacks; marinated frogs' legs.
		Highly processed foods are further split into those considered: 3.1). Staple/basic foods And 3.2). Highly processed foods	3.1). Bread, pasta, rice, milk, butter, vegetable oils 3.2). Cakes, biscuits, breakfast cereals, crisp bread, confectionary, processed meat and fish, yogurt, cheese, cream. Bread, pasta, breakfast cereals, cheese, commercial sauces, canned foods including jams, commercial cakes, biscuits and sauces.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
Siga (Fardet, 2018) (Siga, 2019)	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Considered Place of change (eg at home or in a factory) Not considered Purpose of change (eg essential, cosmetic, palatability) Not considered	Eight technological groups: A). Un/minimally processed A0). Un-/minimally processed A1). Un-/minimally processed foods with degraded raw matrix A2). Culinary ingredients used at home	A0). - Raw foods: cut, peeled... (undegraded matrix) A1). - Raw foods: cooked, filtrated, ground, powdered, juices... (degraded matrix) Limited used of additives without risk A2). - Culinary ingredients: distinction of fat and sugar types
		B). Processed B1). Processed foods with added salt, sugars, and fat in proportions in agreement with official recommendations B2). Processed foods with added salt, sugars, and fat in proportions above official recommendations	B1 and B2 Products made from A0 and/or A1 foods with A2 ingredients: Limited use of additive without risk – Filter on quantities of added salt, fat, and sugars

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		C). Ultra-processed C1). Ultra-processed foods with loose of matrix effect and/or with added unprocessed industrial ingredients and/or limited number of additives C2). Ultra-processed foods with loose of matrix effect and/or with added processed industrial ingredients and/or a high number of additives C3). Ultra-processed foods with loose of matrix effect and with added ultra-processed industrial ingredients and/or a very high number of additives. In C group the quantity, number and function of ingredients and/or additives is also taken into consideration for dispatching foods within C1, C2, or C3. Additional groups in Sadler et al (2021). • C01. Balanced nutritional profile & one industrial ingredient/ additive (acceptable) • C02. High added fat/sugar/salt	C1 to C3 Evaluation of processing (C1–C3) as a function of: Food matrix un-structuration– Use of esthetic additives, aromas, and processed ingredients (sequestrant, taste enhancer, colouring, texture agents...)– Types and quantities of salt, sugar, and fat – At risk ingredients and/or additives

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
International Food Information Council (IFIC) (Eicher-Miller et al, 2012; Eicher-Miller et al, 2015)	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Considered Place of change (eg at home or in a factory) Not considered Purpose of change (eg essential, cosmetic, palatability) Considered	1). Minimally processed Foods that require little processing or production and retain most of their inherent properties.	Washed and packaged fruits and vegetables; bagged salads; roasted and ground nuts; coffee beans; and homemade soups
		2). Foods processed for preservation Foods processed to help preserve and enhance nutrients and freshness of foods at their peak.	Canned tuna, beans and tomatoes; frozen fruits and vegetables; pureed and jarred baby foods; soups from canned vegetables or broth.
		3). Mixtures of combined ingredients Foods that combine ingredients such as sweeteners, spices, oils, flavours, colours, and preservatives to improve safety and taste and/or add visual appeal. (Does not include "ready-to-eat" foods listed below).	Some packaged foods, such as instant potato mix, rice, cake mix, jarred tomato sauce, spice mixes, dressings and sauces, gelatine and ready-to-serve, canned and condensed soups.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		4). Ready-to-eat processed foods "Ready-to-eat" foods needing minimal or no preparation.	Breakfast cereal, flavoured oatmeal, crackers, jams and jellies, nut butters, ice cream, yogurt, garlic bread, granola bars, cookies, fruit chews, rotisserie chicken, luncheon meats, honey-baked ham, cheese spreads, fruit drinks and carbonated beverages.
		5). Prepared foods/meals Foods packaged to stay fresh and save time.	Prepared deli foods and frozen meals, entrées, pot pies and pizzas

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
Variation of NOVA; NUPENS/USP (Louzada et al, 2015; Sadler et al, 2021)	Extent of change (from the natural state) Not considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Considered Place of change (eg at home or in a factory) Considered Purpose of change (eg essential, cosmetic, palatability) Not considered	1). Unprocessed, minimally, or moderately processed foods 1.1). Unprocessed foods were defined as having not undergone any kind of industrial processing. 1.2). Minimally processed foods were defined as processed in ways that did not add substances or subtract edible parts. 1.3). Moderately processed foods were defined as those that had an edible part subtracted, but no substance added. This category also included handmade dishes made from these foods and culinary ingredients such as oils, salt, and sugar.	Rice, reans, red meat, fruits and 100% fruit juices, corn, oatmeal, wheat (including pasta), milk, poultry, roots and tubers, coffee and tea, fish, vegetables, eggs, other foods (nuts and seed, lentil, peas and soy, plain yogurt, shellfish and other mixed dishes)
		2). Processed foods Processed foods were defined as products made by the food industry with at least two ingredients and characterised as foods as those manufactured by adding salt, sugar, or oil to unprocessed, minimally processed or moderately processed foods.	Salted meat and fish, cheese, vegetables in brine or oil and fruits in syrup

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		3). Ultra-processed foods Ultra-processed foods were defined as products made by the food industry with at least two ingredients characterised as food formulations mostly made from substances extracted from foods or obtained with the further processing of constituents of foods or through chemical synthesis, such as oils, hydrogenated fats, starches, sugars, protein isolates, amino acids, and additives like flavours and colours.	Industrialised bread, pizzas, hamburgers, sandwiches, cakes, pies and cookies, sugar-sweetened beverages, candies, chocolates, gelatine, flan and ice cream, crackers and chips, reconstituted meat products, flavoured or sweetened yogurts or milk beverages, alcoholic beverages, other products (margarine, RTE sauces and breakfast cereals)

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
International Food Policy Research Institute in Guatemala (IFPRI) (Asfaw, 2011; Moubarac et al, 2014)	Extent of change (from the natural state) Not considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Not considered Place of change (eg at home or in a factory) Not considered Purpose of change (eg essential, cosmetic, palatability) Not considered	1). Unprocessed - No definition given	Staple foods such as corn and other grains, fruits, vegetables, roots and tubers, beans, meat, fish, eggs and dairy (fresh or dried milk and cream).
		2). Primary or partially processed - No definition given	Corn products (including tortillas), vegetable oils, other flours and processed grains, sugars and sweeteners, dairy products (such as evaporated milk, cheese and yogurt), bread, animal fats (such as lard and butter).
		3). Highly processed - Food items that have undergone secondary processing into a readily edible form, likely to contain high levels of added sugars, fats or salt.	Pastries, cookies and crackers, sausage and prepared meats, ice cream and frozen desserts (eg granizados), breakfast cereals, confectionary (such as sweets and chocolate), fat spreads and shortening, pasta products, soft drinks (eg packaged juices), prepared meals (such as dried soup), formula and complementary foods.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
Poti et al (Poti et al, 2015)[1]	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Considered Place of change (eg at home or in a factory) Not considered Purpose of change (eg essential, cosmetic, palatability) Considered	1). Less processed 1.1). Unprocessed/minimally processed 1.1.1). Unprocessed/minimally processed - single-ingredient foods with no or very slight modifications that do not change inherent properties of the food as found in its natural form 1.2). Basic processed 1.2.1). Processed basic ingredients - single isolated food components obtained by extraction or purification using physical or chemical processes that change inherent properties of the food 1.2.2). Processed for basic preservation or precooking - single minimally processed foods modified by physical or chemical processes for the purpose of preservation or precooking but remaining as single foods	1.1.1). Fresh plain milk, coffee (whole or ground beans), bottled plain water, tea leaves or bags; fresh, frozen, or dried plain fruit, vegetables, or legumes plain nuts; eggs, unseasoned meat (refrigerated or frozen); whole-grain plain hot cereal, brown rice, popcorn kernels; cream; honey, herbs, spices, pepper 1.2.1). Unsweetened fruit juice not from concentrate; egg whites; wholegrain flour, wholegrain pasta; oil, unsalted butter, sugar, pure maple syrup, salt 1.2.2). Unsweetened fruit juice from concentrate or frozen concentrate, dry milk, instant coffee; unsweetened/ unflavoured canned fruit, vegetables, or legumes; unsweetened/unsalted peanut butter; unseasoned canned meat; refined-grain pasta, refined-grain flour, white rice, instant rice, plain refined-grain hot cereal; sour cream, plain yogurt, evaporated milk

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		2). Moderately processed 2.1). Moderately processed for flavour - single minimally or moderately processed foods with addition of flavour additives for the purpose of enhancing flavour; directly recognizable as original plant/ animal source	2.1). Sweetened/flavoured fruit or vegetable juice, tea, soy milk, chocolate milk, cocoa mix; sweetened/flavoured canned, dried, refrigerated, or frozen fruit, vegetables or legumes, jam, potato chips, frozen French fries, salted peanut butter, nuts with salt or oil; seasoned refrigerated, frozen, or canned meat, smoked or cured bacon, ham, or seafood; sweetened/flavoured hot cereal, flavoured pasta, flavoured popcorn (microwaveable or pre-popped); cheese, sweetened/flavoured yogurt, sweetened condensed milk, whipped cream; salted butter, flavoured oil, seasoning salts
		2.2). Moderately processed grain products - grain products made from whole-grain flour with water, salt, and/or yeast	2.2). Wholegrain breads, tortillas, crackers, or RTE cereals with no added sugar or fat
		3). Highly processed 3.1). Highly processed ingredients - multi-ingredient industrially formulated mixtures processed to the extent that they are no longer recognizable as their original plant/animal source and consumed as additions (condiments, dips, sauces, toppings, or ingredients in mixed dishes)	3.1). Tomato sauce, salsa, hummus, jelly; breadcrumbs/breading with refined grains or added sugar/fat; creamer, whipped topping, dairy-based chip/veggie dip, cheese dip/queso, Alfredo sauce; margarine, mayonnaise, salad dressing, shortening, pancake syrup, artificial sweetener, baking chocolate, icing, ketchup, barbecue sauce, marinades, and other condiments, sauce/seasoning mixes

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		3.2). Highly processed stand-alone - multi-ingredient industrially formulated mixtures processed to the extent that they are no longer recognizable as their original plant/animal source and not typically consumed as additions	3.2). Soda, alcohol, fruit drinks, sports drinks, energy drinks, flavoured waters, coffee beverages; fruit snacks, gelatine fruit salads, chocolate or yogurt covered dried fruit or nuts, vegetable-based soups, frozen vegetables in sauce, onion rings, entrée garden salads, restructured potato chips, tater tots, hash brown patties, reformed French fries, RTH or instant potato dishes (mashed potatoes, stuffed baked potatoes), RTE potato salad, canned baked beans or beans with pork; sausage, hot dogs, pressed/formed lunchmeats (bologna, salami) or ham, Spam, RTH meat dishes (meatloaf, crab cakes, buffalo wings, pot roast, barbecue), meat-based frozen meals (Salisbury steak), breaded meat (chicken nuggets, fish sticks), meat-based soups; bread, tortillas, rolls, bagels, or RTE breakfast cereals with refined grains or added sugar/fat, pancakes, waffles, or biscuits (RTH, RTB, mixes), grain-based desserts (cookies, cake, pie, pastries, RTE/RTB, mixes), processed salty snacks (crackers, pretzels, tortilla chips, cheese puffs), frozen pizza, RTH or RTE grain-based dishes (burritos, sandwiches, pot pies), frozen or canned pasta dishes (lasagne, ravioli, spaghetti and meatballs), pasta or rice-based frozen meals, boxed macaroni and cheese, instant rice/pasta dish mixes, noodle or rice-based soups, stuffing mix; ice cream, frozen yogurt, pudding (RTE and mixes), processed cheese, cheesecake; candy, chocolate, popsicles, sorbet, gelatine (RTE and mixes), broth, bouillon

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
Mexican National Institute of Public Health (MNIPH) - devised in 2007 (Moubarac et al, 2014)	Extent of change (from the natural state) Considered Nature of change (eg change to food's natural properties, addition of ingredients, or food additives) Not considered Place of change (eg at home or in a factory) Considered Purpose of change (eg essential, cosmetic, palatability) Not considered	1). Non-industrialised (split into 4 subcategories) - 1.1). Non processed foods: Raw foods not processed except by collection, selection, cleaning. 1.2). Locally made traditional foods: Typical Mexican cuisine. Home-made or artisanal on a small and very small scale. 1.3). Traditional preparations outside the home: Preparations with ingredients often impossible to separate. Prepared locally or at home, and that have been part of the traditional food culture of Mexico. 1.4). Modern preparations outside the home: Preparations, ingredients not typical of Mexican food.	1.1). Fruits, vegetables, legumes, cereals, tubers, red and white meats, fish, eggs. 1.2). Corn tortillas, salty and sweet bread (*bolillo*), animal fats such as pig skin or lard, home-made sugar and drinks 1.3). Beans or stews with beans, *tacos, atoles, tamales*, fresh water, artisanal sweetened drinks, *gordassolas o rellenas*, broths, salsas, fish, meat stews, fried fish; vegetable or legume pies, *pozole, chilaquiles*, soups, salads, *carnitas*. 1.4). Burgers, sandwiches, pizza, milkshakes.
		2). Industrialised traditional - Foods that have been part of the traditional Mexican food culture according to customs and traditions since before the 20th century and that nowadays are being produced at a large scale in an industrial way.	Corn flour for tortillas or *atoles*, whole cow milk.

Food classification system (FCS)	4 core themes (as noted by Sadler et al, 2021) 'considered' or 'not considered' in the development of classification system	Definition of each level of processing	Foods included in each level of processing
		3). Industrialised modern - Foods that have been incorporated into the Mexican diet. They can be found as a single product or mixed with other ingredients, impossible to separate.	Powdered milk, non-fat milk, 1% milk, breakfast cereals, whole wheat bread, salty wheat bread, sausages, packaged sweet breads, oil and modified oils, granulated and liquid sugar, sweetened drinks, instant coffee, baby formulas, compotes, supplements.

Annex 2: Processed food classification system assessment

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
NOVA (Monteiro et al, 2019; Monteiro et al, 2016)	Yes Although developed in Brazil, items included at each level of food processing are recognisable within the UK diet.	Yes 4 distinct groups defining each level of food processing and extensive list of foods that fall within each group.	Yes Systematic review evidence identified in this scoping review of available evidence on associations between processed food consumption and health outcomes was published by more than one research group (Askari et al, 2020; Barbosa et al, 2022; Cascaes et al, 2022; Chen et al, 2020; De Amicis et al, 2022; de Oliveira et al, 2022; Delpino et al, 2022; Jardim et al, 2021; Lane et al, 2021; Lane et al, 2022; Mazloomi et al, 2022;	Yes Braesco et al (2022) evaluated whether the NOVA classification system leads to consistent food assignments by users. Authors concluded that "overall consistency among evaluators was low, even when ingredient information was available. These results suggest current NOVA criteria do not allow for robust and functional food assignments". Mean Fleiss' κ (inter-assessor value) was	Yes Systematic review evidence identified in the scoping review of available evidence on health outcomes identified X studies (Askari et al, 2020; Barbosa et al, 2022; Cascaes et al, 2022; Chen et al, 2020; De Amicis et al, 2022; de Oliveira et al, 2022; Delpino et al, 2022; Jardim et al, 2021; Lane et al, 2021; Lane et al, 2022; Mazloomi et al, 2022; Moradi et al, 2023; Moradi et al, 2021; Pagliai et al, 2021; Paula et al, 2022; Santos et al,

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
			Moradi et al, 2023; Moradi et al, 2021; Pagliai et al, 2021; Paula et al, 2022; Santos et al, 2020; Suksatan et al, 2021; Taneri et al, 2022; Tian et al, 2023; Wang et al, 2022). It is likely that significantly more primary and secondary research has been published by further research groups.	0.32 and 0.34 for marketed foods and generic foods respectively, ie agreement between assessor was about one third.	2020; Suksatan et al, 2021; Taneri et al, 2022; Tian et al, 2023; Wang et al, 2022).
International Agency for Research on Cancer (IARC) (Chajès et al, 2011; Slimani et al, 2009)	Yes IARC was developed using data from 10 countries participating in the European Prospective Investigation into Cancer and Nutrition	Yes 3 main groups defining each level of food processing (or which 2 groups are further split into 2 subgroups. An extensive list of foods that fall within each group is reported.	No No articles identified reporting the used of IARC by more than one research group.	No No data identified.	No No data identified. IARC has been used to estimate nutrient intake which could be a marker for health outcomes.

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
	(EPIC) study, including the UK.				
The Siga Index (Fardet, 2018) (Siga, 2017)	Yes The Siga Index claims to be based on European regulatory guidelines, follows advice from WHO, EFSA and ANSES on risk assessment of ingredients and additives, and follows 'nutritional thresholds' set by the FSA UK.	No 3 main groups split into 8 subgroups. Limited information is available defining each level of food processing. Images of foods that fall into each level of food processing are provided but not a definitive list.	No No articles identified.	No No data identified.	No No data identified.
International Food Information Council (IFIC) (Eicher-Miller et al, 2012; Eicher-Miller et al, 2015)	Yes IFIC was developed using US data from NHANES.	Yes 5 distinct groups. Limited information is available defining each level of food processing. Some levels of food processing include more definitive lists of	No No articles identified.	No No data identified.	No No data identified.

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
		foods that fall within each group.			
(Louzada et al, 2015; Sadler et al, 2021)	Yes Based on the NOVA system which incorporates items included that are recognisable within the UK diet.	No 3 main groups defining each level of food processing (based upon an earlier iteration of NOVA) with the first group further split into 3 subgroups (unprocessed, minimally processed and moderately processed). Foods in group 1 sub-groups are not defined by subgroup and limited information is provided on group 2 foods.	No No articles identified based on this variation of NOVA.	No No data identified based on this variation of NOVA.	No No data identified based on this variation of NOVA.
International Food Policy Research Institute in	No Based on data collected for the 2000 Living Standard	No 3 different levels of food processing. No definition is provided	No No articles identified.	No No articles identified.	No No articles identified.

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
Guatemala (IFPRI) (Asfaw, 2011; Moubarac et al, 2014)	Measurement Survey (LSMS) of Guatemala which includes staples of the traditional Guatemalan diet.	for groups 1 (unprocessed) and 2 (primary or partially processed). Foods that fall within each level of food processing are provided.			
Poti et al (Poti et al, 2015)	Yes Based on nationally representative sample data collected from the 2000–2012 Nielsen Homescan Panel, a longitudinal study of food and beverage consumer packaged goods purchased by US households.	Yes 3 main groups defining each level of food processing, each with subgroups with detailed definitions. An extensive list of foods that fall within each group is also provided.	No No articles identified.	No No data identified.	No No data identified.
Mexican National Institute of Public Health (MNIPH) -	No Based on data collected in 1 to 4 year olds from the 1999 Mexican National	No	No No articles identified.	No No data identified.	No No data identified.

Food classification system (Author, year)	Can the classification system be applied to a UK population?	Is there a clear 'useable definition' of the classification system (as provided in studies)?	Has the classification system been published as used by more than one research group?	Is data available on inter-assessor reliability when applying the classification system?	Has the classification system been used to evaluate health outcomes?
devised in 2007 (Moubarac et al, 2014)	Nutrition Survey which includes staples of the traditional Mexican diet.				

Annex 3: Search strategies - to identify studies applying the NOVA classification system to NDNS data

Database: Ovid MEDLINE(R) ALL 1946 to January 11, 2023

Line	Search term	Results
1	"national diet and nutrition survey".tw,kw.	327
2	NDNS.tw,kw.	142
3	exp Nutrition Surveys/ and exp United Kingdom/	925
4	or/1-3	1106
5	NOVA.tw,kw.	6937
6	((ultra-process* or ultraprocess*) adj3 food*).tw,kw.	1159
7	(processed adj3 food*).tw,kw.	6030
8	((overprocess* or Over-process*) adj3 food*).tw,kw.	4
9	*Fast Foods/	1725
10	or/5-9	13969
11	4 and 10	31

Database: Embase 1974 to 2023 January 11

Line	Search term	Results
1	"national diet and nutrition survey".tw,kw.	510
2	NDNS.tw,kw.	265
3	exp *health survey/ and exp *diet/ and exp United Kingdom/	6
4	or/1-3	595
5	NOVA.tw,kw.	9474
6	((ultra-process* or ultraprocess*) adj3 food*).tw,kw.	1353
7	(processed adj3 food*).tw,kw.	7238
8	((overprocess* or Over-process*) adj3 food*).tw,kw.	5
9	*fast food/	2257
10	or/5-9	18489
11	4 and 10	35

Scopus

TITLE-ABS-KEY ((ndns OR "national diet and nutrition survey") AND (((ultra-process* OR ultraprocess*) W/2 food*) OR (processed W/2 food*) OR ((ov erprocess* OR over-process*) W/2 food*) OR nova)) - 20 results

PubMed

 (((("processed food"[Title/Abstract:~3]) OR ("ultraprocessed food"[Title/Abstract:~3])) OR ("ultra-processed food"[Title/Abstract:~3])) OR ("overprocessed food"[Title/Abstract:~3])) OR ("over-processed food"[Title/Abstract:~3]) OR NOVA[Title/Abstract]

AND

("national diet and nutrition survey"[Title/Abstract] OR NDNS[Title/Abstract] OR united kingdom AND nutrition survey) – 30 results

BioaRxiv and MedRxiv

"national diet and nutrition survey" – phrase search in title and abstract – 1 result (not downloaded as did not contain mention of NOVA in title or abstract).

Annex 4: Studies identified applying the NOVA classification system to National Diet and Nutrition Survey (NDNS) data

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Characterisation of UK diets according to degree of food processing and associations with socio-demographics and obesity: cross-sectional analysis of UK National Diet and Nutrition Survey (2008–12) (Adams and White, 2015)	NOVA, 2010 (Monteiro et al, 2010) NOVA groups 1 to 3: • MPF • PI • UPF	Describe: • the nutritional content of UK foods classified according to degree of processing • the nutritional content of UK diets with different relative intakes of processed foods • the socio-demographic characteristics of UK individuals with different relative intakes of processed foods • the association between intake of processed foods and overweight and obesity in the UK	Adult only (n=2,174) Results: Percentage of total energy intake from NOVA groups, mean: • MPF - 28% • PI - 13% • UPF - 53%	NDNS rolling programme years 1 to 4 (2008 to 2012) • Applies NOVA classification to NDB codes based on retail and homemade subgroups – where retail codes are typically UPF: • For homemade dishes or in cases of uncertainty, codes were classified individually "As far as possible, subsidiary groups were coded in their entirety according to degree of processing [see Adams and White, 2015]. In cases of uncertainty (n=15), all foods within a subsidiary food group were individually coded. An example of where this occurred was the subsidiary food group 'yoghurt'. As this group contains both unsweetened yoghurt (defined as MPF, [see Adams and White, 2015]) and sweetened yoghurt (defined as UPF as it involves the additional of a PI (sugar) to a MPF (unsweetened yoghurt), [see Adams and White, 2015], all foods within the group were individually coded."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
				"Foods in NDNS are not always disaggregated into constituent ingredients. For example, 'macaroni and cheese' may be listed, rather than 'pasta', 'cheese', 'milk', and 'flour'. However, such dishes are identified as homemade or manufactured. As previously, homemade dishes were categorised according to the main constituent ingredient brought into the home, as identified in NDNS. Thus 'macaroni and cheese, homemade' is listed as a 'pasta dish' and so was coded as pasta, and hence a PI. 'Macaroni and cheese, manufactured' was coded as UPF." "We found applying the coding harder than anticipated. More explicit information on the definitions of each group or standard coding frameworks may be useful."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Association between home food preparation skills and behaviour, and consumption of ultra-processed foods: Cross-sectional analysis of the UK National Diet and nutrition survey (2008–2009) (Lam and Adams, 2017)	NOVA, 2010 (Monteiro et al, 2010) NOVA groups 1 to 3: • MPF • PI • UPF	Examine the relationship between home food preparation skills and behaviour and consumption of UPF	Adults aged 19 years and over (n=509), who completed three or four days of the food diary, and did not report any health problems limiting or preventing them from cooking. Results: Percentage of total dietary energy intake from UPF, mean - 51.3%	NDNS rolling programme years 1 and 2 (2008 to 2009) Analysis used previous coding from Adams and White (2015) to calculate energy intake from UPF foods. Same methodology and issues noted.

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Ultra-Processed Food Consumption and Chronic Non-Communicable Diseases-Related Dietary Nutrient Profile in the UK (2008–2014) (Rauber et al, 2018)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4: • MPF • PI • PF • UPF	Describe the contribution of ultra-processed foods in the UK diet and its association with the overall dietary content of nutrients known to affect the risk of chronic non-communicable diseases (NCDs).	Adults (n=4,738) and children (n=4,636), total (n=9,374) Results: Percentage of total dietary energy intake from NOVA groups, mean: • MPF - 30.1% • PI - 4.2% • PF - 8.8% • UPF - 56.8%	NDNS rolling programme years 1 to 6 (2008 to 2014) • Applies NOVA classification to NDB codes based on retail and homemade subgroups – where retail codes are typically UPF • For homemade dishes or in cases of uncertainty, codes were classified individually "All foods in NDNS are coded and grouped into subsidiary food groups (n=155). When possible, subsidiary food groups were directly classified according to NOVA [see Rauber et al, 2018]. When foods within a subsidiary food group belonged to different NOVA groups (n=52), the food codes were individually classified. Thus, we were able to classify each underlying ingredient of homemade dishes in the corresponding NOVA group". "Most food items in the NDNS were systematically disaggregated into their individual components, but about 4% of composite food codes were still mixed dishes compiled from two or more single-ingredient food codes [see Rauber et al, 2018]. Using the core sample of years 1 to 4 (n=4,125), we estimated that these represented only 3% of total dietary energy. In these cases, dishes were

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
				categorised according to the main constituent ingredient. Dishes in which a main constituent ingredient was not clearly identified (for example, chicken and vegetable soup) were classified as a specific subgroup of freshly prepared dishes based on one or more unprocessed or minimally processed food (group 1). Non-caloric supplements were not included in the analyses".

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Ultra-processed foods and excessive free sugar intake in the UK: a nationally representative cross-sectional study (Rauber et al, 2019)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4. 3 groups included overall due to groups 1 and 2 being combined as "foods belonging to these two groups are usually mixed together in culinary preparations and, therefore, consumed together." • MPF and PI • PF • UPF	Describe the dietary sources of free sugars in different age groups of the UK population considering food groups classified according to the NOVA system and estimate the proportion of excessive free sugars that could potentially be avoided by reducing consumption of their main sources.	Adults (4,729) and children (n=4,635), total (n=9,364) Results: Percentage of total dietary energy intake from NOVA groups, mean: • MPF and PI - 34.3% • PF - 8.8% • UPF - 56.8% • UPF (in children) - 63.5% • UPF (in adolescents) - 68% Percentage of total dietary energy intake from free sugars by NOVA group: • MPF and PI - 23.8% • PF - 11.5% • UPF - 64.8% The average UK daily intake of free sugars was 12.4% (SE 0.1) of total energy intake and 61.3% of British exceeded the recommended limit of 10% energy from free sugars. This proportion was even higher among children	NDNS rolling programme years 1 to 6 (2008 to 2014) • Same methodology as Rauber et al, 2018 "All foods in NDNS are coded as food number and grouped into subsidiary food groups (n=155). When possible, subsidiary food groups were directly classified according to NOVA [see Rauber et al, 2019]. When foods within a subsidiary food group pertained to different NOVA groups (n=52), it was the food codes instead of the group, which were individually classified. By doing so, we were able to classify each underlying ingredient of homemade dishes in its corresponding NOVA group. Subsidiary food groups as classified by NOVA are described." [see Rauber et al, 2019] "Although the NDNS database was provided with most food items systematically disaggregated into their individual components, about 4% of composite food codes were still mixed dishes compiled from two or more single-ingredient food code. The method we adopted to disaggregate food codes has been described previously [see Rauber et al, 2019]. Using the core sample of years 1 to 4 (2008/2009 to 2011/2012)

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
			(74.9%) and adolescents (82.9%)	(n=4,125), we estimated that composite food codes represented only 3% of total calories. In this case, dishes were categorised according to the main constituent ingredient. Dishes in which a main constituent ingredient was not clearly identified (eg, chicken and vegetable soup) were classified as a specific subgroup of freshly prepared dishes based on one or more unprocessed or minimally processed food (group 1). Non-caloric supplements were not included in the analyses."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Ultra-processed food consumption and indicators of obesity in the United Kingdom population (2008-2016) (Rauber et al, 2020)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4: • MPF • PI • PF • UPF	Examine the association between the consumption of ultra-processed foods and adiposity in a nationally representative sample of the UK adult population.	All adults aged 19 years and over (n=6,143) Results: Percentage of total dietary energy intake from NOVA groups, mean: • MPF - 30.7% • PI - 4.9% • PF - 10.1% • UPF - 54.3%	NDNS rolling programme years 1 to 8 (2008 to 2016) • Same methodology as Rauber et al, 2018 "We classified foods by considering the NDNS variables 'Food Number' and 'Subsidiary food groups'. When foods were judged to be homemade dishes, we applied the classification to the underlying ingredients in order to ensure more accurate classification. The NDNS database was provided with most food items systematically disaggregated into their individual components and the method adopted to disaggregate the food codes has been described in a previous paper [see Rauber et al, 2020]. Despite this, a few composite dishes were not disaggregated into constituent ingredients (less than 4%). In these cases, homemade dishes were categorised according to the main constituent ingredient. Details of how food item classification was undertaken are further explained in previously published papers [see Rauber et al, 2020]. We used the mean of all available days of food diary for each person to estimate the dietary contribution of ultra-processed foods (as a percentage of total energy intake)."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Association between watching TV whilst eating and children's consumption of ultraprocessed foods in United Kingdom (Martines et al, 2019)	NOVA, 2016 (Monteiro et al, 2016) NOVA group 4 - UPF only "This study specifically assessed consumption of ultraprocessed foods and its subcategories: ultraprocessed breads, packaged ready meals, breakfast cereals, confectionary, sausages and other reconstituted meat products, biscuits, pastries, buns and cakes, industrial French fries, soft drinks and sweetened fruit drinks, milk-based beverages, packaged salty snacks, industrial pizza, margarine and other spreads, sauces, dressing and gravies, industrial desserts, and other ultraprocessed foods (baked beans, meat alternatives, and soy and other beverages as milk substitutes)."	Assess the association between watching TV whilst eating and consumption of ultraprocessed foods amongst children aged 4 to 10 years old in the United Kingdom.	Children aged 4 to 10 years (n=1,277) Results: • Mean total dietary energy intake from UPF was 65.84% • Ultraprocessed breads were the greatest contributor (11.06%)	NDNS rolling programme, years 1 to 4 (2008 to 2012) • Same methodology as Rauber et al, 2018 "All foods in NDNS are coded as food number and grouped into subsidiary food groups (n=155). When possible, subsidiary food groups were directly classified according to NOVA [see Martines et al, 2019]. When foods within a subsidiary food group pertained to different NOVA groups (n=52), food codes were used instead of the group, and they were individually classified."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Consumption of ultra-processed foods and the eating location: can they be associated? (Souza et al, 2022)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4: • MPF • PI • PF • UPF	Analyse the association between different places of consumption and the intake of ultra-processed foods in the UK in 2014 to 2016.	Adults (n=1,401) and children (n=1,048), total (n=2,449) Results: Percentage contribution of UPFs to the total dietary energy intake consumed at each location: • fast-food restaurants - 88.6% • on the go - 72.2% • leisure and sports places - 71.8% • institutional places 61.1% • other places - 57.7% • home - 55.0% • friends and relatives' houses - 50.0% • sit-down restaurants - 44.9%	NDNS rolling programme years 7 and 8 (2014 to 2016) • Same methodology as Rauber et al, 2018 "Foods were classified according to key variables of the NDNS, the "Food Number" and "Subsidiary food groups". For the classification of dishes, their respective food items were disaggregated in order to ensure a more accurate classification, then each single ingredient of the dish was classified according to the NOVA system".

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Eating context and ultraprocessed food consumption among UK adolescents (Rauber et al, 2022)	NOVA, 2016 (Monteiro et al, 2016) NOVA group 4 - UPF only "This study specifically assessed the consumption of ultraprocessed foods"	Evaluate the association between eating context patterns and ultraprocessed food consumption at two main meal occasions in a representative sample of UK adolescents.	Children aged 11 to 18 years (n=542) Results: Mean total dietary energy intake from UPF was 67.8%. Food groups contributing to total dietary energy intake from UPF were: • packaged pre-prepared meals - 13.4% • packaged breads - 11.6% • sweets - 9.7% • industrial French fries and pizza - 8.6% • biscuits and snacks - 7.6% • beverages - 6.1% • breakfast cereals - 4.5% • spreads, sauces and others - 6.1%	NDNS rolling programme years 7 and 8 (2014 to 2016) • Same methodology as Rauber et al, 2018 "All foods included in food diaries were classified into one of the four NOVA food groups". "Details on how food item classification was accomplished are explained in previously published papers." [see Rauber et al, 2022]

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Eating context and its association with ultra-processed food consumption by British children (Onita et al, 2021)	NOVA, 2016 (Monteiro et al, 2016) NOVA group 4 - UPF only	Investigate the patterns of eating context and its association with ultra-processed food consumption by British children.	Children aged 4 to 10 years (n=1,772) Results: • Mean total dietary energy intake from UPF was 65.4% • Ultra-processed bread was the main contributor to total dietary energy intake at lunch and dinner in all eating contexts Eating contexts evaluated at lunch were eating with family watching TV, eating at school with friends and eating away from home Eating contexts evaluated at dinner were Eating with family watching TV and eating alone in the bedroom	NDNS rolling programme years 1 to 6 (2008 to 2014) • Same methodology as Rauber et al, 2018 "All foods presented in the NDNS database are coded as a food number and grouped into subsidiary food groups (n=155). When possible, subsidiary food groups were classified directly according to NOVA. For the subsidiary food groups, including food items belonging to different NOVA groups (n=52), the food codes were individually classified instead of categorizing the entire group. Thus, a classification of each underlying ingredient of homemade preparations was feasible within its corresponding NOVA group. The NDNS database presented most food items systematically broken down into their individual components [see Onita et al, 2021]. Notwithstanding, certain preparations have not been broken down into constituent ingredients (less than 4%). In this case, homemade preparations were categorized according to the main constituent ingredient. It is noteworthy that details on food items classification are well documented in previously published articles (Rauber et al, 2018)."

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Trends in food consumption according to the degree of food processing among the UK population over 11 years (Madruga et al, 2022)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4: • MPF • PI • PF • UPF	Evaluate the trends of the dietary share of foods categorised according to the NOVA classification in a historical series (2018 to 2019) among the UK population	Adults and children (n=15,643) Results: Changes in percentage of total dietary energy intake over 11 years by NOVA group, mean: • MPF - remained similar from 2008 to 2019 ($\cong$30%, P for linear trend = 0.505) • PI - increased from 3.7% in 2008 to 4.9% in 2019 (P for linear trend <0.001) • PF - decreased from 9.6% in 2008 to 8.6% in 2019 (P for linear trend = 0.002) • No changes were observed in the proportion of UPF, which accounted for more than half of total energy consumed throughout the period ($\cong$56%, P for linear trend = 0.580)	NDNS rolling programme years 1 to 11 (2008 to 2019) • Same methodology as Rauber et al, 2018 "All food items were classified according to NOVA". "All foods presented in the NDNS database are coded as food number and grouped into subsidiary food groups (n=155). When possible, the subsidiary food groups were classified directly according to NOVA. When foods within a subsidiary food group belonged to different NOVA groups (n=52), it was the food codes instead of the group, which were classified individually. Hence, it was possible to allocate each underlying ingredient of homemade dishes into the appropriate NOVA group. Food classification details can be found in a previously published article." [see Madruga et al, 2022]

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
The Ultra-Processed Food Content of School Meals and Packed Lunches in the United Kingdom (Parnham et al, 2022)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1 to 4: • MPF • PI • PF • UPF	• Describe the UPF content of school food in the UK among primary and secondary school children between 2008 and 2017. • Explore differences between school meals and packed lunches. • Compare the UPF content of school food consumed by children with different household incomes.	Children aged 4 to 18 years (n=3,303) Results: Percentage of total energy intake from UPF at lunch, median: • primary school children - 72.6% • secondary school children 77.8% Percentage of total energy intake of UPF from school meals, median: • primary school children - 61.0% • secondary school children - 70.1% Percentage of total energy intake of UPF from packed lunches, median: • primary school children - 81.2% • secondary school children - 83.5%	NDNS rolling programme years 1 to 9 (2008 to 2017) "The dietary diaries recorded the meal type for each food item; that is, whether it was consumed as part of a school meal or packed lunch. If the item was described as 'food from home' it was categorised as a 'packed lunch' and if it was described as 'bought at the canteen' in the dataset it was categorised as a 'school meal'." No further description of how NOVA was applied to these datasets (although Rauber is co-author)

Title (Author, year)	Classification system	Author stated objective(s)	Participants included in analyses and key metrics	National Diet and Nutrition Survey rolling program (NDNS) dataset and method
Nutritional Quality, Environmental Impact and Cost of Ultra-Processed Foods: A UK Food-Based Analysis (Aceves-Martins et al, 2022)	NOVA, 2016 (Monteiro et al, 2016) NOVA groups 1, 3 and 4: • MPF • PF • UPF NOVA group 2 (PI) was excluded from the analysis	Determine how ultra-processed and processed foods compare to fresh and minimally processed foods in relation to nutritional quality, greenhouse gas emissions and cost on the food and food group level.	Out of 5,927 items included in the NDB (year 11), 1,015 items were excluded from the analysis. NOVA classification was applied to the remaining 4,912 items in the NDB. Proportion of items in the NDB attributed to NOVA groups: • MPF - 20% • PF - 32% • UPF - 48%	NDNS rolling programme year 11 (2018 to 2019) "The characteristics of each product contained in the nutrient bank database were considered while using the NOVA classification. Because of the lack of information on the recipes of certain items and the debate surrounding the classification of homemade dishes versus industrially prepared ready meals [see Aceves-Martins et al, 2022], homemade products were classified as NOVA 3 foods, while ready meals were classified as NOVA 4 foods."

Abbreviations: MPF, unprocessed or minimally processed food; NDB, nutrient database; NDNS, National Diet and Nutrition Survey; PF, processed food; PI, processed culinary ingredients; UPF, ultra-processed food

Annex 5: Search strategies to identify systematic reviews and meta-analyses examining the relationship between two or more levels of food processing and health outcomes

Database: Ovid MEDLINE(R) ALL 1946 to January 12, 2023

Line	Search term	Results
1	((ultra-process* or ultraprocess*) adj3 food*).tw,kw.	1,163
2	(processed adj3 food*).tw,kw.	6,038
3	((overprocess* or Over-process*) adj3 food*).tw,kw.	4
4	*Fast Foods/	1,725
5	or/1-4	7,426
6	exp *Diet/	150,266
7	Intake*.tw,kw.	321,710
8	Consumption.tw,kw.	354,055
9	(Diet* adj3 (habit* or pattern* or practice* or poor or unhealthy or behavio?r*)).tw,kw.	47,282
10	or/6-9	728,088
11	5 and 10	3,850
12	limit 11 to (english language and yr="2015 -Current" and "reviews (maximizes specificity)")	95

Database: Embase 1974 to 2023 January 12

Line	Search term	Results
1	((ultra-process* or ultraprocess*) adj3 food*).tw,kw.	1,354
2	(processed adj3 food*).tw,kw.	7,241
3	((overprocess* or Over-process*) adj3 food*).tw,kw.	5
4	*fast food/	2,257
5	or/1-4	9,453
6	exp *diet/	119,944
7	Intake*.tw,kw.	421,502
8	Consumption.tw,kw.	445,889
9	(Diet* adj3 (habit* or pattern* or practice* or poor or unhealthy or behavio?r*)).tw,kw.	61,314
10	or/6-9	898,018
11	5 and 10	5,139
12	limit 11 to (english language and "reviews (maximizes specificity)" and yr="2015 -Current")	113

PubMed top-up

Line	Search term	Filters	Results
1	(((("processed food"[Title/Abstract:~3]) OR ("ultraprocessed food"[Title/Abstract:~3])) OR ("ultra-processed food"[Title/Abstract:~3])) OR ("overprocessed food"[Title/Abstract:~3])) OR ("over-processed food"[Title/Abstract:~3]) OR NOVA[Title/Abstract]		9,213
2	(intake*[Title/Abstract] OR consumption[Title/Abstract]) OR ("diet"[MeSH Terms]) OR (Dietary habit or dietary pattern or dietary practice or poor diet or unhealthy diet or dietary behavio?r)		1,011,937
3	#1 AND #2		2,009
4	(pubstatusaheadofprint OR publisher[sb] OR pubmednotmedline[sb])		5,033,928
5	#3 AND #4		284
6	#3 AND #4	from 2015 - 2023	255
7	#3 AND #4	Meta-Analysis, Review, Systematic Review, English, from 2015 - 2023	46

BioRxiv and MedRxiv

"processed food" OR "ultraprocessed food" phrase searched in title and abstract, date limited to 1/1/2015 (date of search 12 January 2023) – 15 results downloaded to EndNote.

Prospero

"processed food" OR "ultraprocessed food" – limited to search terms in title field only, no date limit applied – 38 results downloaded to EndNote.

Annex 6: Review of available evidence on food processing and health outcomes - eligibility criteria

Category	Include	Exclude

Population	• Studies including healthy adult and/or child populations
	• Studies including otherwise healthy overweight/ obese participants
		• Studies including non-healthy populations (participants with specified medical conditions) eg:
		  o type 2 diabetes
		  o hypertension
		  o cardiovascular disease

Intervention / Exposure	• Consumption of at least 2 different levels of processed foods, for example:
	  o unprocessed
	  o minimally processed
	  o processed
	  o ultra-processed
	or a combination of the above
	• Comparison of intakes (ie high vs low) for one level of food processing
	Classification system has been clearly defined by authors
		• Systematic reviews (SRs) not evaluating the consumption of processed foods
		• SRs evaluating single food groups (for example sugar sweetened beverages and processed meats)
		
		Studies that do not clearly report a specific classification system

Outcomes	• Any health outcome	• None

Study type and design	• SRs and/or meta-analyses (MA) of:
	  o randomised controlled trials (RCTs)
	  o prospective cohort studies (PCSs)
	
	• SRs that include RCTs, PCSs and other observational study designs (non-randomised clinical studies, retrospective studies, cross-sectional studies, case-series, case-control, case-report)[6]
		• Non-randomised clinical studies
		• Retrospective studies
		• Cross-sectional studies
		• Case-series, case-control, case-report
		• Narrative reviews
		• Animal studies
		• *In vitro* studies
		• Studies on cells

Literature type	• Peer-reviewed papers published in scientific or medical journals	• Protocols • Commentaries • Editorials • Letters to the editor • Grey literature (including PhD theses, extended abstracts, conference proceedings), or other publications not peer-reviewed
Date	• 2015 to present	• Published 2014 or earlier
Language	• English	• Languages other than English

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[6] Only extract data from SRs that include mixed observational study designs providing PCS or RCT evidence form ≥70% of the total participant weighting. SRs including mixed observational study designs that form >30% of the total weighing would be included but not data extracted.

Annex 7: Registered trial search strategy

Clinicaltrials.gov – searched 18 January 2023 and updated on 21 June 2023

56 studies identified for: (ultra processed food OR UPF)

Search term or synonym	Search results
ultra processed food	42 studies
processed food	44 studies
convenience food	No studies found
fast food	No studies found
food	49 studies
processed	50 studies
process	11 studies
ultra	49 studies
UPF	18 studies

Annex 8: Data extraction

Table 1 Evidence on the relationship between two different levels of food processing and health outcomes from predominantly PCS

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
A Systematic Review on Processed/Ultra-Processed Foods and Arterial Hypertension in Adults and Older People **Barbosa et al (2022)**	• **Research question:** Is there an association between consumption of processed/ultra-processed foods and arterial hypertension in adults and older people? • **Eligibility criteria:** - Population - adults (20 to 59 years of age) and/or older people (60 years of age or older) - Intervention/Exposure - high consumption of processed and ultra-processed foods based on the NOVA classification - Comparison - low consumption of processed and ultra-processed foods based on the NOVA classification - Outcome - arterial hypertension defined based on any diagnostic criteria - Type of Study - observational (cohort, case-	• **Countries covered:** Countries of the Americas (n=7) Europe (n=2) Brazil (n=3) USA (n=2) Canada (n=1) Mexico (n=1) Spain (n=2) • **Participant numbers:** A total of 114,849 individuals participated in the nine studies. Of those, 89,116 were participants of cohort studies. • **Association:** Nearly all studies (n=7) found a positive association between the consumption of UPFs and AH/BP. Only two cross-sectional studies found no statistically significant difference in the average systolic blood pressure (SBP) and diastolic blood pressure (DBP) based on the consumption of these foods.	The results reveal the high consumption of ultra-processed foods in developed and middle-income countries, warning of the health risks of such foods, which have a high energy density and are rich in salt, sugar and fat. The findings underscore the urgent need for the adoption of measures that exert a positive impact on the quality of life of populations, especially those at greater risk, such as adults and older people	Studies with different methodological designs (cross-sectional and cohort) were included. This decision was made due to the scarcity of studies investigating the association between PFs/UPFs and BP/AH in adults and older people. Some of the studies used a food frequency questionnaire not specifically validated for the collection of data on food intake according to the NOVA classification, which may have resulted in the underestimation or over estimation of the consumption of PFs/UPFs. Third, few studies were found that evaluated the consumption of PFs and involved the older	In this review, authors were very clear with regards to studies needing to adhere to the NOVA classification system explicitly in order to be included, whereas other reviews identified in this scoping review, studies which included single UPFs were included, rather than needing to adhere to a whole level of processing according to NOVA. Details of measures used to quantify UPF intakes were not provided for each study, but terciles and quintiles were measured as assessment measure in some studies.

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	control and cross-sectional) and intervention studies • **Study populations:** Adults (20 to 59 years of age) and/or older people (60 years of age or older). Studies with pregnant women, children and adolescents and those that addressed a disease other than AH were excluded • **Classification system as defined by authors:** Studies that used the terms "processed" or "ultra-processed" but did not follow the requirements of the NOVA classification proposed by Monteiro et al. (2010) were not included.			population, possibly due to the fact that PFs are not considered to be as harmful as UPFs and that more discerning methodological criteria are needed for the assessment of older people." **Funding/declarations of interest:** This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal deNível Superior—Brasil (CAPES)—Finance Code 001. The authors declare that there are no conflicts of interest.	

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Ultra-processed foods increase noncommunicable chronic disease risk **Jardim et al (2021)**	• **Research question:** the association between the intake of NOVA food groups and NCDs. • **Eligibility criteria:** **Inclusion:** - Observational studies in which the NOVA food classification was used to evaluated food intake in adults and its association with the development or presence of NCDs. **Exclusion:** - A priori, randomized controlled trials, ecological studies, commentaries, general reviews, case reports, animal studies, and studies with non–adult subjects. • **Study populations:** No restrictions were reported on age or health of the populations. • **Classification system as defined by authors:** NOVA	• **Countries covered:** Brazil (n=8) France (n=7) Canada (n=5) Spain (n=4) United Kingdom (n=4) United States (n=3) Japan (n=2) Lebanon (n=1) Israel (n=1) Australia (n=1) Mexico (n=1) Latin America (Chile, Colombia, Costa Rica and Mexico) (n=1) • **Participant numbers:** PCS (16 studies, 762,947 participants), CS (19 studies, 95,160 participants) and CCS (3 studies, 2,968 participants) • **Association:** **Obesity (5 studies)** - All 5 PCS found that participants with higher Ultra-processed foods and drinks (UPFD) consumption had obesity more often than those with lower consumption **Hypertension (7 studies)** - All 7 PCS studies demonstrated that greater UPFD consumption increased the chances of having	In conclusion, UPFD may increase the risk of NCDs, and natural foods and MPF may possibly reduce it. Up until now, NOVA food classification is less known than other food classifications. Our results reinforce the need for more research to determine the link of UPFD consumption to the risk of disease.	Most of the studies were developed in Brazil, there are few studies from other countries. Also noteworthy is the presence of Brazilian researchers involved in the team that prepared most of the work carried out in other countries. There was also a lack of comparability with the findings of studies carried out outside Brazil. NOVA classifications have some limitations, and it is not the only way to categorize food to stablish guidelines recommendations. Studies may be using other dietary pattern classification, diet quality index, or even isolated nutrients as factors associated with the occurrence of NCDs, which would also explain the failure to adopt this food classification.	Results are not reported for each study, and it appears just a select few results are provided in the narrative for each outcome. Results reported for UPFD and some results for other NOVA groups but from the study characteristics table it appears that all NOVA groups were reported for most studies and it is unclear if the results for UPFD is in comparison to all other groups. Studies reported consumption of UPF in a variety of ways, including: ○ % of energy ○ Quartiles (in weight and g/day) ○ Quintiles (servings/day) ○ Tertiles (% of total daily energy intake) ○ Total daily % kcal ○ Proportion of each NOVA category (continuous data)

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
		systemic arterial hypertension. **Diabetes (3 studies)** - All 3 PCS found that UPFD energy contribution was positively associated with diabetes mellitus **Cardiovascular disease (2 studies)** - In 1 study, a 10% increase in UPFD intake was associated with an increase in cardiovascular, coronary and cerebrovascular disease rates by 12% (P = .001), 13% (P = .02), and 11% (P = .02), respectively. - 1 study demonstrated that greater UPFD intake quartile was associated with inadequate cardiovascular health, assessed through several variables, including diabetes diagnosis. **Gastrointestinal tract disease (2 studies)** - 1 study found that patients with higher UPFD intake were more susceptible to developing irritable bowel syndrome and functional dyspepsia - 1 study found that UPFD intake was associated with incident inflammatory bowel diseases		Other terms that could be indirectly related to UPFD, such as unhealthy diet or processed foods, were not considered in the present review, as the researchers used the term 'ultra-processed'. Some outcomes were self-reported, like high blood pressure and diabetes, and it may introduce bias to the results and some of them takes time to develop, like cancer and others are difficult to perform the diagnosis, like depression. Other limitations include the nature of the study itself. Several associations were observed in cross-sectional studies and, therefore, it could not be used to infer causality because temporality is not known. Although a wide search was performed, with no language- or time-related limits, a small number of articles were found for each NCD.	

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
				Funding/declarations of interest: This research did not receive any funding support from public, commercial, or not-for-profit agencies.	

Table 2 Evidence on the association between high vs low consumption of UPF and health outcomes from predominantly PCS

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Ultra-processed food and risk of type 2 diabetes: a systematic review and meta-analysis of longitudinal studies **Delpino et al (2022)**	• **Research question:** the association between consumption of ultra-processed food and the risk of type 2 diabetes • **Eligibility criteria:** **Inclusion:** - observational study with longitudinal design - ultra-processed food as the main exposure (according to the NOVA food classification system or that did not use the NOVA food classification system but evaluated foods according to the classification) - assessed the association with type 2 diabetes - results reported as odds ratios, relative risks or hazard ratios, with 95% confidence intervals. - No restrictions on years or language of publication **Exclusion:** - Animal or in vitro - Review articles	• **Countries covered:** the 3 studies of interest were in the UK, France and Spain. • **Participant numbers:** 1.1 million individuals (full review) and 146, 497 in the 3 studies which specifically used NOVA. • **Association** (meta-analysis using random-effects model): - To note, only studies that classified foods according to a defined classification system (NOVA in this case) were included here - The association between ultra-processed food consumption and risk of diabetes using meta-analysis (random-effects model): - **Moderate intake (3 studies, 146,497 participants):** RR 1.10 (95% CI 0.99 to 1.23) - **High intakes (2 studies, 41, 790 participants):** RR 1.48 (95% CI 1.48 to 1.89)	In conclusion, our results showed that the consumption of ultra-processed foods substantially increased the risk for type 2 diabetes, with a dose-response effect and moderate to high credibility of evidence	There were significant variations in the measures to assess food consumption, the number of subjects included in each cohort and the follow-up duration. Also, many studies evaluated only processed meats (which are in the ultra-processed category), and only three studies categorized their foods according to the NOVA food system classification **Funding/declarations of interest:** F.M.D. received a doctoral fellowship from the National Council for Scientific and Technological Development (CNPq) during the writing of the manuscript.	Studies that assessed only one specific food or including only beverages were excluded Authors stated that they included studies which defined ultra-processed food according to the NOVA food classification system or that did not use the NOVA food classification system but evaluated foods according to the classification. Studies reported consumption of UPF in a variety of ways, including: o Times per week o Times per month o Grams per day o Grams per week o Quartile o Quintile o Tertile o Increments of 10%

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	- Studies assessing gestational diabetes. • **Study populations:** no age restrictions were applied, but included studies were of individuals aged 18 years or older. The 3 studies of interest (which specifically used the NOVA classification system) were in participants ages 18 to 90 years. • **Classification system as defined by authors:** Studies were included that classified foods according to the NOVA food classification system or that did not use the NOVA food classification system but evaluated foods according to the classification				

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Ultra processed food and chronic noncommunicable diseases: A systematic review and meta-analysis of 43 observational studies **Lane et al (2021)**	• **Research question:** the association between consumption of ultra-processed food and noncommunicable disease risk, morbidity and mortality. • **Eligibility criteria:** **Inclusion:** - written in English - conducted in humans of any age - used an observational study design (for example, cross-sectional - prospective, case-control and retrospective designs) - investigated the relationship between consumption of ultra processed food and noncommunicable diseases, associated risk factors and all-cause mortality - compared either different levels of ultra processed food consumption (e.g., lower versus higher) or ultra processed food versus unprocessed or minimally processed food. **Exclusion:**	• **Countries covered:** Brazil (n=17) France (n=8) Spain (n=7) Canada (n=3) USA (n=3) United Kingdom (n=2) Norway (n=1) Lebanon (n=1) Malaysia (n=1) • **Participant numbers:** A total of 891,723 participants were included. For prospective outcomes of interest: depression: N=41,637) and all-cause mortality (n=88,247). • **Association:** **All-cause mortality (4 studies, 88,247 participants)** - Higher consumption of ultra processed food (ranging from >35.7% to >36.0% of calories or from 5.2 to <29.8 times per day) significantly increased risk of all-cause mortality compared with lower consumption in adults (ranging from 14.1% to <21.6% of calories or <2.6 times per day) (hazard ratio: 1.28; 95% CI, 1.11-1.48; P = 0.001; I^2 = 45%) **Depression (2 studies, 41,637 participants)**	The present review and meta-analysis provides evidence associating higher consumption of ultra processed food with a 20% to 81% increased risk of various noncommunicable diseases when assessed cross-sectionally and a 22% to 28% increased risk of depression and mortality when examined prospectively in adults. However, evidence for an association between ultra processed food consumption and adverse health outcomes in children and adolescents was limited. Further rigorously executed studies that address the noted limitations and between-study disparities are required to investigate and more clearly define associations between ultra processed consumption and intermediate risk factors. Nevertheless, the weight of evidence is sufficient, especially given the precautionary	First, approximately half of the included studies were cross-sectional by design and the reported dietary intake at the time of measurement may not be representative of habitual dietary intake (for example, a possible discrepancy exists between individuals with excess weight undertaking a healthier or weight-loss diet at the time of measurement versus the diet that led to their current weight status). Second, the observational nature of the studies eligible for inclusion in our review demonstrates associations rather than causation. Observational studies run the risk of residual confounding by many factors, such as socioeconomic status. While the majority of studies in the present review adjusted for potential covariates, residual confounding remains possible Lastly, it has been argued that the widespread success and adoption of the NOVA food classification system depends on sensitivity to factors impacting consumer choices,	Studies reported consumption of UPF in a variety of ways, including: o average intake of ultra processed food expressed as a percentage of total caloric intake. o weight (absolute or Percentage g per day) o absolute caloric intake per day o servings or times per day o ultra processed food consumption scores o ultra processed items consumed per day o quartiles o quintiles o sex-specific cut-off ranges

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Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	- they did not use the NOVA food classification system - did not assess the direct consumption of ultra processed food (e.g., household availability, access to, price of and purchase of ultra processed food). • **Study populations:** no age or health criteria was applied to the search. • **Classification system as defined by authors:** NOVA	- Higher consumption of ultra processed food (ranging from between 19.0% and 76.0% to >33.0% of calories) significantly increased the risk of depression compared to lower consumption in adults (ranging from ≤10.0% to <15.0% of calories) (hazard ratio: 1.22; 95% CI, 1.16-1.28; $P < 0.001$; $I^2 = 0\%$).	principle, to address consumption of ultra processed food in diverse preventive and treatment efforts'.	including the time, effort and expense required to prepare non ultra processed food. It was beyond the scope of our review to investigate such factors. However, it is important to reemphasize that the NOVA system is endorsed by United Nations and World Health Organization. Compared with traditional approaches that have typically focused on isolated nutrients, the NOVA system provides a novel area of research into the possible effects of the nature, extent and reasons for food processing, including the food matrix and artificial food additives. **Funding/declarations of interest:** Long list of affiliations, declarations and grants awarded to each author listed in review (see review for extensive details).	

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Impacts of Consumption of Ultra-Processed Foods on the Maternal-Child Health: A Systematic Review **de Oliveira et al (2022)**	• **Research question:** identify the presence of health outcomes associated with UPF consumption by pregnant women, lactating women, newborns and infants • **Eligibility criteria:** **Inclusion** - Pregnant, lactating/ breastfeeding, children (neonates, infants, and children under 10 years old). - Percentage of total energy consumed from UPF as defined by NOVA classification - Original research studies which reported health outcomes associated with UPF consumption in the population described - Diseases (morbidities, clinical complications), nutrition (anthropometric nutritional status, eating practices, and diet quality) and toxicity as the primary health outcomes. We applied no language limitations to the records searched **Exclusion:**	Note: Data on associations between exposure and outcome are extracted from cohort studies only as data are reported by individual study • **Countries covered:** Brazil (53.3%; n=8) European countries (n=4 [Norway, England, UK, Spain]) USA (n=2) Chile (n=1) • **Participant numbers:** **Pregnant women:** 4 cohorts including 78,114 participants; 1 cross sectional study including 784 participants **Children:** 4 cohorts including 11,808 participants; 5 cross sectional studies including 15,833 participants • **Association:** **Gestational weight gain in pregnant women (3 studies)**	Despite little evidence in the phase of lactation and pregnancy, the selected studies showed a negative impact on health associated with the high UPF consumption in the three cycles of life, which reflected in different aspects. The repercussions are seen in several spheres, more importantly on nutritional indicators (overweight, adiposity measures, low levels of serum alpha-tocopherol and in breast milk, inadequate dietary practices, lower nutritional quality of the diet), but also on metabolic alterations (high glycemic levels and lipid profile), presence of diseases (depression, attention deficit hyperactivity disorder (ADHD), caries, and respiratory diseases), and toxicity (high levels of toxic compounds from plastics in the urine).	This study has some limitations. The current analysis is limited to the data currently available. The limited number of studies with infants, wide variation between existing instruments to assess UPF intake – often quite limited in scope and assessing only one aspect (such as, cumulative UPF consumption). Finally, we suggest that the weaknesses observed in the studies included in this systematic review are addressed in future studies evaluating UPF consumption and its impacts on maternal-child health. **Funding/declarations of interest:** This study was financed in part by the CAPES Foundation (Coordination for the Improvement of Higher Education Personnel in Brazil), under the finance code 001, and by the CAPES Foundation and CNPQ (The Brazilian National Council for Scientific and Technological	High and low consumption level was not explicitly reported by review authors. UPF exposure in individual studies was reported in a variety of ways (Table 2): ○ % of total energy intake ○ total (kcal) ○ UPF score ○ tertiles of % energy intake ○ quintiles of % energy intake ○ consumption ≥ 4 times per day ○ median of % energy intake (2 groups: high and low) In several instances, foods were classified differently across surveys due to different contexts. For example, some FFQs had few or did not specify food items and were not developed for UPF analysis. Additional complexities included application to food databases with a lack of information on the differentiation of canned food into processed food

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	- reviews, conference abstract, opinions, experimental studies, research protocols, clinical trials, case reports, comments, letters to editors - studies that did not assess dietary patterns using the NOVA classification - studies that did not include the separate analysis of the population of interest (pregnant women, lactating women, infants, or children), studies that did not present health outcomes that would allow us to observe the association with UPF consumption • **Study populations**: Pregnant, lactating/ breastfeeding, children (neonates, infants, and children under 10 years old). • **Classification system as defined by authors:** NOVA classification	- cohort studies found a positive association between UPF consumption and gestational weight gain (GWG) in the third gestational trimester, indicating that the 1% or Kcal point increased in the calorie intake from UPF increased total (Kg) or weekly (g) gestational weight gain **Adiposity measures in children (2 studies)** • cohort studies found a positive association between adiposity measurements (body mass index-BMI, weight, fat mass index, waist circumference) and high UPF consumption: ○ 1 study found every adiposity indicator increased per year of follow up [10 years], showing a greater and faster progression of these in the group of individuals in the highest UPF consumption quintile when compared to the group in the 1st quintile		Development) – Finance code 421916/2018-4. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.	(PF) or UPF, databases disaggregating foods to nutrient content rather than processing type (for example, cake disaggregated to component ingredients could inadvertently be classed as PF, and not correctly as UPF if it were ultra-processed), and disaggregating handmade dishes (for example, pizza) into major food-items in the recipe (for example, group 1) rather than underlying ingredients (flour, cheese, meat, sauce, salt, and oil), which is the recommended approach

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Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
		○ 1 study reported UPF consumption at age 4 years was a predictor of an increase in delta waist circumference from age 4 to 8 (β = 0.07; 95%CI 0.01–0.14). No significant associations were observed for BMI and glucose metabolism			
Consumption of ultra-processed foods and health status: a systematic review and meta-analysis **Pagliai et al (2021)**	• **Research question:** Our study aimed to assess the relationship between UPF consumption as defined by NOVA and health status by conducting a comprehensive systematic review with meta-analysis of all the cross-sectional and cohort studies published so far. • **Eligibility criteria:** **Inclusion:** - Clinically healthy subjects aged ≥18 years, all ethnicities - Exposure to high consumption of ultra-processed foods as defined by the NOVA Food Classification System compared with low consumption of ultra-processed foods as defined	Note: Data extracted from prospective cohort studies only as data are reported separately to cross-sectional • **Countries covered:** Cohorts: Spain (n=2; 6 articles) France (n=1; 4 articles) Brazil (n=1; 1 article) Italy (n=1; 1 article) USA (n=1; 1 article) • **Participant numbers:** Overall analysis included 183,491 participants from 13 articles reporting on 6 cohorts • **Association** **All-cause mortality (5 studies, 111,056 participants)** - The highest consumption of UPF was found to be associated with an increased risk of all-cause mortality	In conclusion, we reported for the first time in a systematic review with meta-analysis the possible association between high UPF consumption, worse cardiometabolic risk profile (reported mainly by an increased risk of overweight/obesity, elevated waist circumference, reduced HDL-cholesterol levels and increased risk of the metabolic syndrome), and greater risk of all-cause mortality, CVD, cerebrovascular disease and depression. The available literature still has several limitations and the methods used	The present study has several limitations that should be addressed. First, the included studies evaluated UPF consumption through self-reported tools (FFQ, food records and 24-h recalls), which are generally accepted, but which are susceptible to recall bias, and which are not specifically designed to collect UPF data as described by the NOVA classification. This may result in an over or underestimation of the UPF intake level. Indeed, the application of the National Institutes of Health study quality assessment tool suggested that the methodological quality of all the cross-sectional studies	Authors report "comparing the highest v. the lowest UPF consumption" rather than defining 'high' and 'low' levels of UPF consumption "All but one of the included cohort studies had good methodological quality, with an adequate follow-up, and high participation rates" "A leave-one-out sensitivity analysis was performed by iteratively removing one study at a time to confirm that results were not determined by a single study. There were few

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Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	by the NOVA Food Classification System - Any health [outcome] indicator - Cross-sectional studies, prospective cohort studies - No language limitations were applied **Exclusion:** - Subjects aged <18 years, pregnant women - Review articles, letters to the editor, comments, case reports, case-control studies, randomized controlled trials • **Study populations:** Clinically healthy subjects aged ≥18 years, all ethnicities • **Classification system as defined by authors:** NOVA Food Classification System	RR 1.25 (95% CI 1.14, 1.37) P <0.00001, I^2 2%, P_{het} 0.40 **CVD incidence/mortality (3 studies; 139,867 participants)** - The highest consumption of UPF showed a significant association with increased risk of CVD incidence and/or mortality RR 1.29 (95% CI 1.12, 1.48) P 0.0003, I^2 7%, P_{het} 0.34 **CV incidence/mortality (2 studies; 127,969 participants)** - The highest consumption of UPF showed a significant association with increased risk of cerebrovascular disease incidence and/or mortality RR 1.34 (95% CI 1.07, 1.68) P 0.01, I^2 32%, P_{het} 0.22 **Depression (2 studies; 41,637 participants)** - The highest consumption of UPF showed a significant association with increased risk of depression RR 1.20 (95% CI 1.03, 1140) P 0.02, I^2 42%, P_{het} 0.19 **Overweight/obesity (2 studies; 20,278 participants)**	to classify these foods need careful review, so reducing the applicability and transferability of these results to the general population. However, these findings have important public health implications, especially for food policymakers who should discourage the consumption of UPF and promote fresh and minimally processed foods to improve health status.	included was fair or poor, mainly due to the lack of details on the validity and reliability of the questionnaires used to assess UPF consumption. Secondly, the overall analyses for each different outcome were carried out in a limited number of studies, thus reducing the statistical power of the analysis. Third, only a limited number of studies included total energy intake as a confounding variable in the multivariable models, thus introducing a possible limitation in the interpretation of the results. However, it should be noted that total energy intake can also be part of the causal pathway of UPF intake; therefore, this aspect is not necessarily a study limitation. In addition, it is well known that unhealthy eating habits (such as high consumption of UPF) are commonly associated with other unhealthy lifestyle behaviours, such as sedentary habits, which in turn are associated	changes in the quantitative measurements of OR, RR and the 95 % CI, without any study affecting the results for almost all of the outcomes investigated. The only exceptions were found in cross-sectional study analyses" "The publication bias was evaluated for all-cause mortality. The shape of the funnel plot did not show any evident asymmetry, suggesting the absence of possible publication biases."

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
		- The highest consumption of UPF showed a significant association with increased risk of overweight/obesity RR 1.23 (95% CI 1.11, 1.36), P <0.00001, I^2 0%, P_{het} 0.64 P value is for Z test of no overall association between exposure and outcome I^2 estimates from heterogeneity rather than sampling error P_{het} is for test of no differences in association measure among studies		with adverse health outcomes. Thus, the results of the present meta-analysis should be interpreted with caution, since not all the included studies considered unhealthy lifestyle behaviours as confounding factors in the multivariable models. **Funding/declarations of interest:** "This research received no specific grant from any funding agency, commercial or not-for-profit sectors." "The authors declare that there are no conflicts of interest."	

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Maternal Consumption of Ultra-Processed Foods-Rich Diet and Perinatal Outcomes: A Systematic Review and Meta-Analysis **Paula et al (2022)**	• **Research question:** this study aimed to determine the association between UPF-rich diet consumption by pregnant women and perinatal (maternal and neonatal) outcomes through a comprehensive systematic review with meta-analysis. The hypothesis was that a higher intake of UPF-rich diet during pregnancy is associated with adverse perinatal outcomes • **Eligibility criteria:** **Inclusion:** - observational studies (cross-sectional, longitudinal, case-control) - reported a measure of association (relative risk, odds ratio, or β-coefficients with confidence interval) between UPF-rich diet consumption and perinatal outcomes. - For this review, we considered it UPF-rich diet consumption when the evaluated food, diet, or dietary pattern included at least one food from the UPF	• **Countries covered:** Continents included: Africa (n=2) Asia (n=16) America (n=17) Europe (n=23) Oceania (n=3) • **Participant numbers:** Total – 698,803 participants 47 cohorts included 684,010 participants; 9 cross-sectional studies included 10,170 participants; 5 case-control studies included 4,274 participants • **Association:** **Gestational weight gain (5 studies, 4,567 participants):** - No association observed - This association was also explored using β coefficient in five articles reporting prospective cohorts, including 4,384 pregnant women, but no significant association between UPF-rich diet consumption and GWG was found. **Gestational Diabetes Mellitus (10 studies, 42,477 participants):**	This study indicates a positive association between maternal UPF-rich diet consumption during pregnancy and increased risk of developing gestational diabetes mellitus and preeclampsia. These findings corroborate the adverse effects of consumption of diets rich in UPF during pregnancy and highlight the need to monitor and reduce UPF-rich diet consumption specifically during the gestational period, as a strategy to prevent adverse perinatal outcomes.	Some limitations are also noteworthy. First, the study did not exclusively evaluate UPF consumption, but we speculate that unhealthy and Western dietary patterns may be considered as a proxy for UPF intake. Second, applied dietary assessments of the included studies were not specifically designed for the NOVA classification system. Third, high heterogeneity between studies was observed in many analyses considering the nature of the observational nutritional studies. This is expected because of the diverse characteristics of subjects, the different dietary approaches, and the variance between outcome assessment methods. Fourth, the lack of significant results in perinatal outcomes may be due to the small number of included articles for each outcome, thus it was not possible to perform subgroups	Publication bias analysis for UPF consumption and GDM risk by funnel plot inspection showed asymmetry among the studies, which was confirmed by Egger test (p = 0.001). Certainty of Evidence - The GRADE assessment was moderate for maternal UPF-rich diet consumption and preeclampsia and very low for GWG, GDM, LBW, LGA, and preterm birth Of 47 cohort studies, 24 (51%) were considered at low risk of bias. Two indicators were accomplished in all studies: "confounding factors identified" and "strategies to deal with confounding factors stated". Most studies were at high risk of bias due to not presenting the strategies to address incomplete follow-up, which is considered a potential source of bias.

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	group defined by the NOVA Food Classification System, such as fast foods, junk foods, processed meats, soft drinks, confectionaries, pizzas, hamburgers, candies and sweets, sweetened beverages and cookies. Diet patterns described as unhealthy dietary patterns compared to healthy patterns, and Western and Prudent diet patterns which are characterized by a higher intake of red and processed meats, beverages sweetened with sugar, sweets, desserts, industrialized food-like products, and refined grains with a high intake of energy-dense and processed foods, were also considered as a proxy for high UPF intake. No date of publication or language restriction was applied. **Exclusion:** - studies including pregnant women with pre-existing diseases, - animal studies, letters to editors, reviews, personal opinions, reviews, book	- Higher consumption of diets rich in UPF significantly increased odds of GDM by 48% [(OR: 1.48; 95% CI: 1.17, 1.87) I^2 = 82.70%]. **Hypertensive Disorders of Pregnancy (3 studies, 58,701 participants):** - No association observed **Preeclampsia (4 studies, 112,307 participants):** - Consumption of UPF-rich diets was found to be associated with 28% higher odds of preeclampsia [(OR: 1.28; 95% CI: 1.15, 1.42) I^2 = 0.00%] **Low Birth Weight (5 studies, 146,617 participants):** - No association observed **Large for Gestational Age (3 studies, 52,468 participants):** - No association observed **Preterm Birth (4 studies, 233,308 participants)** - No association observed		analysis to seek the source of heterogeneity. Lastly, publication bias was observed, so, studies that had negative results might not have been submitted for publication and were not included. **Funding/declarations of interest:** DPG/DPI/University of Brasilia and PPGNH/UnB The authors declare no conflict of interest	As reported in inclusion criteria diets were considered 'UPF-rich' when the evaluated food, diet, or dietary pattern included at least one food from the UPF group defined by the NOVA Food Classification System, such as fast foods, junk foods, processed meats, soft drinks, confectionaries, pizzas, hamburgers, candies and sweets, sweetened beverages and cookies. Diet patterns described as unhealthy dietary patterns compared to healthy patterns, and Western and Prudent diet patterns which are characterized by a higher intake of red and processed meats, beverages sweetened with sugar, sweets, desserts, industrialized food-like products, and refined grains with a high intake of energy-dense and processed foods, were also considered as a proxy for high UPF intake.

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	chapters, editorials, congress abstracts, or any publication without primary data were excluded - studies that evaluated individual nutrient or diet scores and studies without the required data being available even after at least two attempts to contact the authors by e-mail were also excluded. • **Study populations:** Pregnant women • **Classification system as defined by authors:** NOVA Food Classification System				

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose–Response Meta-Analysis of 207,291 Participants **Suksatan et al (2021)**	• **Research question:** Perform a systematic review and dose–response meta-analysis to determine if UPF intake is associated with mortality risk. • **Eligibility criteria:** **Inclusion:** - Observational studies (cohort, case-control, or cross-sectional studies) - undertaken in adults (≥18 years) - reported on the association between UPF consumption and the risk of mortality - provided effect estimates in the form of hazard ratio (HR), relative risk (RR), or odds ratios (OR) with 95% confidence interval (95% CI). No language or date limitations were applied **Exclusion:** - Studies performed in children and adolescents (<18 years) - reviews, conference letters, notes, reports, short surveys, and case reports • **Study populations:** Adults (≥18 years)	Note: participant numbers not provided • **Countries covered:** Spain (n=3) USA (n=2) Italy (n=1) France (n=1) • **Participant numbers:** The study-specific, maximally adjusted HR was reported for 207,291 participants • **Association:** **All-cause mortality risk (4 studies):** - UPF consumption was associated with an enhanced risk of all-cause mortality HR 1.21 (95% CI 1.13, 1.30) P <0.001, I^2 0.0% **CVDs-cause mortality risk (4 studies):** - UPF consumption was associated with an enhanced risk of CVD-cause mortality HR 1.50 (95% CI 1.37, 1.63) P <0.001, I^2 0.0% **Heart-cause mortality risk (2 studies):** - UPF consumption was associated with an enhanced risk of heart-cause mortality	Note: authors do not explicitly state conclusions. The excerpt below is the final paragraph from the discussion. The present dose–response meta-analysis showed that each 10% increase in UPF as a proportion of daily caloric intake was associated with a 15% higher risk of all-cause mortality. Although there was no association between UPF consumption and cancer-related mortality, a significant positive association was found between UPF consumption and cardiovascular disease-related mortality. Future longitudinal studies with sufficient control for confounding factors should focus on developing high-quality studies in diverse human populations to translate	Despite several crucial strengths of the current quantitative review, including cohort design of all included studies, evaluating the association between UPFs consumption and risk of mortality for the first time, adjustment of findings for numerous probable confounders in the included studies, no evidence of publication bias, and performing a dose–response analysis, some potential limitations should be considered for interpreting our conclusions. Firstly, this investigation based on observational studies could not firm causation nor avoid the possibility of residual confounding for the proposed associations. Secondly, recall bias and misclassification of participants in terms of UPFs consumption were also possible. Thirdly, the component of UPFs varied across studies	The classification system was not reported by study authors, however, the NOVA classification system was used by all studies included in this systematic review and meta-analysis. "NOVA" and related variations were also included in the search terms for each database searched. High and low consumption level was not explicitly reported by review authors UPF intake in individual studies was reported in a variety of ways (Table 1): ○ frequency of ultra-processed food intake ○ proportion of UPF in the total weight of food and beverages consumed (g/day) ○ proportion of total energy The included articles' quality evaluation was completed applying the Newcastle–Ottawa scale, which indicated that all

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	• **Classification system as defined by authors:** Not reported	HR 1.66 (95% CI 1.50, 1.85) P <0.022, I^2 0.0% **Cancer-cause mortality (2 studies):** - No association was observed **Each 10% increase in UFP consumption in daily calorie intake was associated with a 15% increased risk of all-cause mortality** HR 1.15 (95% CI 1.09, 1.21) P < 0.001, I^2 0.0% **Each 10% increase in UFP consumption in daily calorie intake and risk of CVDs-cause mortality** HR 1.21 (95% CI 0.90, 1.62) P < 0.001, I^2 91.4% **Each 10% increase in UFP consumption in daily calorie intake and risk of heart-cause mortality** HR 1.18 (95% CI 0.95, 1.47) P = 0.044, I^2 75.4% **The dose response analysis revealed a positive linear relationship between UPF consumption and:** **All-cause mortality**	recommendations into practice. Several issues require further investigation in future studies. Existing instruments for assessing UPF intake are subjective and rather limited in scope, with most assessing only one aspect (such as, cumulative UPF consumption). To more accurately assess the actual burden of UPF consumption, a specific food intake frequency questionnaire or dietary recording tool should be adapted or further developed to assess all aspects of UPF consumption, for example, food class, specific components of UPF foods, their health effects, and specific procedures or additives. In addition, it is necessary to determine whether such associations are due to ultra-processing itself or to the nutritional or non-	and could be dependent on the type of processing that food products have undergone. Lastly, dietary intake was assessed by 24 h dietary recall instead of food frequency questionnaire (FFQ) in two included studies. **Funding/declarations of interest:** "Funding: This research received no external funding." "Conflicts of Interest: The authors declare no conflict of interest."	studies had high quality. Moreover, our outcomes showed that the level of agreement between reviewers for data collection and quality evaluation was suitable (Kappa = 0.813). Sensitivity analysis was carried out by removing each study and recalculating the pooled effect estimates (as in, one study removed analysis). The study results were not affected by any study. The outcome of publication bias among studies did not show publication bias according to Egger's regression asymmetry (p = 0.168) or Begg's rank correlation tests (p = 0.217). This result was confirmed by a symmetric funnel plot.

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		$P_{nonlinearity} = 0.879$ $P_{dose-response} = P < 0.001$ **CVDs-cause mortality** $P_{nonlinearity} = 0.868$ $P_{dose-response} = P < 0.001$ **Heart-cause mortality** $P_{nonlinearity} = 0.774$ $P_{dose-response} = P < 0.001$ **Cancer-cause mortality** $P_{nonlinearity} = 0.340$ $P_{dose-response} = P = 0.187$	nutritional properties of UPF. Future studies should also investigate whether ultra-processing indices can demonstrate an association between diet and mortality compared with other nutritional quality scores/indices. Ultimately, assessment of associated variables such as genetic variants, lifestyle characteristics, demographic and socioeconomic status, and psychological disorders, as well as differences in therapy, may accelerate the discovery of potential mechanisms of UPFs in relation to mortality.		

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Association Between Ultra-Processed Food Intake and All-Cause Mortality: A Systematic Review and Meta-Analysis **Taneri et al (2022)**	**Research question:** investigate the prospective association between all-cause mortality and not only UPF consumption overall but also consumption of different UPF categories **Eligibility criteria:** **Inclusion:** - prospective design (nested case-control studies, case-cohort studies, prospective cohort studies) - adult populations (≥18 years old) - evaluated consumption of UPF (every food item in NOVA classification were taken into consideration) - evaluated the risk of all-cause mortality - No limitations on publication date or language were applied **Exclusion:** - abstracts, cost effectiveness studies, randomized and nonrandomized clinical trials intervention studies, cross-sectional studies, case-control studies, letters to the	**Countries covered:** USA (n=18) Sweden (n=4) Spain (n=3) Denmark (n=3) UK (n=2) Europe (cohort studies that included participants from multiple European countries) (n=2) Netherlands (n=2) Italy (n=2) Singapore (n=1) Australia (n=1) China (n=1) France (n=1) **Participant numbers:** 40 unique prospective cohort studies across 47 articles, comprising 5,750,133 individuals **Association:** **All-cause mortality (5 studies; 110,721 participants):** - Compared with lowest consumption, highest consumption of UPF was significantly associated with increased risk of mortality RR 1.29 (95% CI 1.17, 1.42) P = 0.519, I^2 0.0%	We found that consumption of UPF, SSB, ASB, processed meat, and processed red meat is associated with an increased risk of all-cause mortality. On the other hand, breakfast cereals/ready-to-eat cereals have an inverse relationship with mortality. We conclude that the health consequences of UPF must be carefully assessed, given that this broad term includes various food components that can cause different health outcomes. Further comprehensive prospective studies with standardized reporting are necessary.	We would like to note that there are just a few observational studies in the literature about UPF and their relationship with overall mortality; for this reason, some of our analyses have a small number of studies. Current literature provides prospective studies that report the health outcomes of processed meats, which involve both processed and ultra-processed meats as defined by NOVA. For this reason, we could not make this distinction in the analysis of processed meat and mortality, so the results on processed meat should be interpreted with caution. Due to limited studies and different categories with different levels of consumption provided by the included studies, we were not able to perform meta-analysis for some of our exposures comparing consumers with non-consumers. The majority of studies in our meta-analyses adjusted for a	Authors report comparing the highest v. the lowest consumption of UPF rather than defining 'high' and 'low' levels of UPF consumption. Individual studies included in the UPF consumption and risk of all-cause mortality meta-analysis report highest vs. lowest intake as: o highest: fourth quartile; lowest: first quartile o highest: fourth quarter; lowest: first quarter o highest: fourth quarter (>4 servings/day); lowest: first quarter (<2 servings/day) o 18.5 vs. 4.8 weight ratio in % Funnel plotting and Egger's test were used to assess publication bias in meta-analyses that included 5 or more studies, however, results were not reported for UPF

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	editor, conference proceedings, systematic reviews, or meta-analyses. • **Study populations:** Adult population, aged ≥18 years • **Classification system as defined by authors:** NOVA classification			range of relevant confounders, although 1 study was entirely unadjusted. Also, most of the studies did not adjust for lifestyle factors and socioeconomic status, such as overall quality of diet, physical activity, income, and education. Therefore, our results comparing highest vs. lowest intake could reflect a proxy for lifestyle and socioeconomic status. Nevertheless, restriction of some of our analysis to studies that considered all these factors did not materially change the results. In addition, the level of consumption across different populations we studied could be different, and thus comparing lowest vs. highest intake could result in biased estimates. However, the results comparing consumers with non-consumers were generally in line with the findings comparing highest vs. lowest intake. Similarly, stratifying by location did not change the	consumption and risk of all-cause mortality All studies included in this review were of fair (14.9%) to good quality (85.1%), except 1 study, classified as poor quality. The 5 studies included in the meta-analysis of UPF consumption and all-cause mortality were all classified as good quality. Results are also reported (not extracted) for associations between: o sugar sweetened beverages (SSB) consumption and risk of all-cause mortality o artificially sweetened beverages (ASB) consumption and risk of all-cause mortality o processed meat/processed red meat consumption and all-cause mortality o breakfast/ready-to-eat cereal consumption and all-cause mortality

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
				main results; it is noteworthy that this comparison was between the United States and European countries, including mainly countries of high and upper-middle income, hence the generalizability of the findings is limited. Also worth mentioning, we could not address the association between all kinds of cereals and all-cause mortality, since the initial search term included only "ready to eat cereal," excluding specific publications regarding wholegrain, oat cereals, which points in a direction for the future research. Last, we would like to point out that, depending on how it has been cooked, a food item can be classified as UPF or processed food. With that in mind, we have to consider that food frequency questionnaires might not be able to make this distinction, and thus in these studies, the UPF items may be under-reported or over-reported. We acknowledge	o other UPF components and risk of all-cause mortality

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
				that different dietary assessment methods may cause potential misclassification in identifying UPF; however, we were not able to stratify by the dietary assessment method since only one of the total UPF studies was using 24-hour recall to assess the consumption. **Funding/declarations of interest:** Funding: not reported "Conflict of interest: none declared."	

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
Ultra-Processed Foods Consumption Increases the Risk of Hypertension in Adults: A Systematic Review and Meta-Analysis **Wang et al (2022)**	• **Research question:** conduct a comprehensive meta-analysis and systematic review of observational studies to assess the relationship between UPFs consumption and hypertension in adults • **Eligibility criteria:** **Inclusion:** - observational studies (such as cohort, cross-sectional, and case–control studies) - population-based studies - participants were ≥18 years old at baseline - the exposure interested was UPFs (as defined by the NOVA classification system) - the primary outcome of interest was hypertension - data provided as risk ratio, hazard ratio, or odds ratio (OR) and corresponding 95% confidence intervals (CIs) for the risk of hypertension - No restriction on language was applied **Exclusion:** - duplicate reports - not population-based studies	• **Countries covered:** USA (n=2) Canada (n=2) Brazil (n=2) Spain (n=1) Mexico, (n=1) Lebanon (n=1) • **Participant numbers:** 4 cohort studies (89,699 participants) and 5 cross-sectional studies (21,895 participants) • **Association:** - Higher consumption of UPFs was significantly associated with incidence of hypertension OR: 1.23 (95% CI 1.11, 1.37) P = 0.034), I^2 51.9%	Based on our findings, consumption of UPFs is significantly associated with an increased risk of hypertension in adults. As the current evidence is limited, more longitudinal studies and intervention studies are needed in the future to further explore the potential association between UPFs consumption and hypertension.	Nevertheless, there are also several limitations to be acknowledged. Firstly, our meta-analysis was based on observational studies and thus some unmeasured confounding factors may have various degrees of influence on the results. Secondly, the studies included in this meta-analysis were used to assess UPFs consumption through food-frequency questionnaire, food recording, and 24-hour recall, which are likely to recall bias. Thirdly, the definition of UPFs consumption was not exactly the same in the included studies of this meta-analysis, which made these comparisons less straightforward; thus, we could only obtain a quantitative rate of the association between the UPFs consumption and hypertension but not a specific range. Finally, subgroup meta-analyses by common study characteristic do not	The Begg's rank correlation test and the Egger's regression test confirmed that there was no publication bias for hypertension (P = 0.348 and P = 0.247, respectively). The funnel plots were symmetrical, which revealed no clear publication bias The Newcastle-Ottawa scale (NOS) which was adapted for cross-sectional and cohort studies was used to assess study quality. All studies included in the meta-analysis were classified as high quality. Sensitivity analysis indicated that none of the included studies had significant impact on the results of the meta-analysis

Reference (Title, author, year)	Methods	Results	Author-stated conclusions	Author-stated limitations	Reviewer comments/notes
	- case reports, comments, reviews, and conference summary - non-observational design - not examined the association between UPFs and the risk of hypertension - not provided the relevant effect sizes and corresponding 95% confidence - unavailable full text or incomplete data • **Study populations:** participants were ≥18 years old at baseline • **Classification system as defined by authors:** NOVA classification system			completely eliminate substantial heterogeneity across studies. Improved analyses should be carried out as more information becomes available in the future. **Funding/declarations of interest:** Funding: "This study was supported by the Sichuan Science and Technology Program, Sichuan, China (grant numbers: 2020YFS0456 and 2019YFS0537) and the Luzhou-Southwest Medical University cooperation project, Luzhou, Sichuan, China (grant number: 2018LZXNYD—PT01). Disclosure: "The authors declared no conflict of interest."	

Abbreviations: AH, arterial hypertension; ASB, artificially sweetened beverage; BP, blood pressure; CCS, case control study; CI, confidence interval; CS, cross sectional study; CVD, cardiovascular disease; DBP, diastolic blood pressure; FFQ, food frequency questionnaire; GDM, gestational diabetes mellitus; GWG, gestational weight gain; HDL, high density lipoprotein; HDP, hypertensive disorders of pregnancy; HR, hazard ratio; LBW, low birth weight; MPF, minimally processed food; NCD, non-communicable disease; OR, odds ratio; PCS, prospective cohort study; PF, processed food; RR, risk ratio; SBP, systolic blood pressure; SSB, sugar sweetened beverage; UPF, ultra processed food; UPFD, ultra processed food and drink; USA, United States of America

Table 3 Evidence on the relationship between two different levels of food processing and health outcomes from SRs with >30% cross-sectional studies

Reference (Title, author, year)	Health outcomes	Participant weighting (% cross-section)
Food processing and cardiometabolic risk factors: a systematic review (Santos et al, 2020)	Cardiometabolic risk factors	86.3

Table 4 Evidence on the association between high vs low consumption of UPF and health outcome from SRs with >30% cross-sectional studies

Reference (Title, author, year)	Health outcomes	Participant weighting (% cross-sectional)
The association of ultra-processed food consumption with adult mental health disorders: a systematic review and dose-response meta-analysis of 260,385 participants (Mazloomi et al, 2022)	Adult mental health	46.2
Ultra-processed food consumption and adult obesity risk: a systematic review and dose-response meta-analysis (Moradi et al, 2023)	Adult obesity risk	32.6
Ultra-processed food intake and risk of depression: a systematic review (Tian et al, 2023)	Risk of depression	49.9
Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies (Askari et al, 2020)	Risk of overweight and obesity	96.0
Ultra-processed foods consumption and dental caries in children and adolescents: A systematic review and meta-Analysis (Cascaes et al, 2022)	Dental caries in children and adolescents	89.8
Ultra-Processed Food Consumption and Mental Health: A Systematic Review and Meta-Analysis of Observational Studies (Lane et al, 2022)	Mental Health	87.9
Ultra-Processed Food Consumption and Adult Diabetes Risk: A Systematic Review and Dose-Response Meta-Analysis (Moradi et al, 2021)	Adult Diabetes Risk	67.4
Consumption of ultra-processed foods and health outcomes: a systematic review of epidemiological studies (Chen et al, 2020)	Multiple health outcomes (including all cause mortality, cardiocerebrovascular diseases, mental health diseases, metabolic syndrome, overweight and obesity)	67.5
Ultra-processed foods and obesity and adiposity parameters among children and adolescents: a systematic review (De Amicis et al, 2022)	Obesity and adiposity parameters	60.5

Annex 9: Reference approach to guide the NOVA classification of food items in What We Eat in America (WWEIA), National Health and Nutrition Examination Survey (NHANES)

1. Steele et al (2023) describe the "reference approach" of classifying WWEIA, NHANES data according to the NOVA classification system. Steele et al considered this the reference approach because it was developed by the creators of the NOVA classification system and has been used in most previous studies (Baraldi et al, 2021; Juul et al, 2018; Juul et al, 2022; Liu et al, 2022; Livingston et al, 2021; Martínez Steele et al, 2016; Martínez Steele et al, 2019; Martínez Steele et al, 2020; Martínez Steele and Monteiro, 2017; Martínez Steele et al, 2017; Neri et al, 2022; Wang et al, 2021; Yang et al, 2020; Zhang et al, 2021; Zhang et al, 2022).

2. The decisions made to classify WWEIA, NHANES, according to the NOVA classification system in the reference approach (including examples) are displayed in Annex 9a Appendix.

3. The NOVA classification was determined by taking into account the following 3 variables from the NHANES recall databases:

   - "main food description"

   - "additional food description" which qualitatively describes food codes

   - "standard reference code description," which qualitatively describes each of the underlying standard reference codes

4. Standard reference codes (or ingredient codes) were taken from the USDA National Nutrient Database for Standard Reference.

5. For each food code, a decision was made on whether food codes or underlying standard reference codes would be used to estimate NOVA group energy contributions. The decision to use a standard reference code rather than a food code depended on whether there was any indication that the food code could have been homemade.

6. Food codes that were likely to be homemade or artisanal and linked to a list of scratch ingredient standard reference codes, such as "Beef stroganoff" and "Cookie, chocolate chip, made from home recipe or purchased at a bakery," were classified at the standard reference code level (referred to as "disaggregated food codes" or "disaggregated mixed dishes"), decision A (see Annex 9a Appendix).

7. Conversely, foods likely purchased as ready-to-eat/heat/drink items, such as "Milk, fat-free (skim)," "Cereal (Kellogg's Apple Jacks)" or "Lasagna with meat, canned" were classified at the food code level (referred to as "non-disaggregated food code"

or "non-disaggregated mixed dishes"). Mixed dishes were assumed to be homemade unless the food item description or standard reference codes clearly suggested that it was ready-to-eat.

8. When necessary, the list of ingredients of branded food products, obtained through supermarket, Amazon, and Fooducate websites and from the USDA Branded Food Products Database (available from 2019 onward and relevant to the 2017–2018 WWEIA, NHANES cycles only) (Kretser et al, 2017; Pehrsson et al, 2018) were used to decide upon the most appropriate NOVA group and subgroup. The USDA Branded Food Products Database is the result of a public–private partnership, furnishing private label data of branded foods provided by the food industry (Fukagawa et al, 2022; Kretser et al, 2017)

9. For example, food code "Salsa, red, cooked, not homemade" linked with standard reference code "Sauce, ready-to-serve, salsa" was classified as ultra-processed (rather than processed) based on the list of ingredients of branded products such as Lizano Salsa [water, sugar, iodized salt, vegetables, chili, pepper, molasses, spices (mustard, celery), modified corn starch, acetic acid, hydrolysed corn protein, and sodium benzoate (used to protect quality); treated with ionizing energy and contains traces of soy and milk].

10. In contrast, food code "Salsa, red, cooked, homemade," which is linked to a list of scratch ingredient standard reference codes ["Peppers, hot chili, sun-dried" (unprocessed/minimally processed), "Tomatoes, red, ripe, canned, packed in tomato juice" (processed), "Onions, raw" (unprocessed/minimally processed), "Garlic, raw" (unprocessed/minimally processed), "Vegetable oil, not further specified" (processed culinary ingredient), "Salt, table" (processed culinary ingredient), and "Water, tap, drinking" (unprocessed/minimally processed)] was classified at the standard reference code level.

11. This reference approach of NOVA application to NHANES generally used a conservative approach, with some exceptions such as ready-to-eat cereal, salty snacks, and bread. This meant that ambiguous food items, where a brand name or further details would have been needed to assign a NOVA group with certainty, were classified into a lower degree of processing (conservative criteria) (such as cured meats, jellies, jams, apple sauce, cottage and cream cheese, creams, and evaporated milks), decision B (see Annex 9a Appendix).

12. Ready-to-eat breakfast cereals, salty snacks, and industrial bread were classified as ultra-processed (although some specific brands could have been processed or minimally processed) because most foods that fall into these categories met the NOVA criteria for ultra-processed, and these foods are not commonly homemade in the United States, decisions C and D (see Annex 9a Appendix).

13. Potential homemade recipes with unlisted constituent ingredients (standard reference codes) were classified into 1 of the 4 NOVA groups based on the expected principal ingredients (for example, food code "Sesame chicken" linked to standard

reference code "Restaurant, Chinese, sesame chicken" was classified as "unprocessed/minimally processed meat"), decision E (see Annex 9a Appendix).

14. Finally, the participant-specific variables of "combination food type" and "source of food" from the dietary recall were used to check the appropriateness of the NOVA group. Some items were reclassified based on the information provided by these variables, decision F (see Annex 9a Appendix). For instance, some food codes (mainly mixed dishes, including sauces and cakes, cookies, and pies) initially classified at the standard reference code level were reclassified as ultra-processed foods at the food code level in participants who consumed the food code as "Frozen meals" or "Lunchables" (combination food types) or from "Restaurant fast food/pizza" or "Vending machine" (food source).

15. The classification of most food items, however, did not change (for example, raw apple from a fast food place or vending machine remained classified as an unprocessed/minimally processed food).

Annex 9a: Appendix

Decisions made to classify What We Eat in America, NHANES, according to the NOVA classification system in the reference approach

Decision	Description	Examples
Decision A: Likely homemade dishes classified at the standard reference code level	Food codes that were likely to be homemade or artisanal and linked to a list of scratch ingredient standard reference codes were classified at the standard reference code level (referred to as "disaggregated mixed dishes"). Mixed dishes were assumed to be homemade unless the food item description or standard reference codes clearly suggested that it was ready-to-eat.	• "Beef stroganoff" and "Cookie, chocolate chip, made from home recipe or purchased at a bakery" were classified at the standard reference code level • Foods likely purchased as ready-to-eat/heat/drink items, such as "Milk, fat-free (skim)," "Cereal (Kellogg's Apple Jacks)" or "Lasagna with meat, canned," were classified at the food code level
Decision B: More conservative classification	Absence of needed descriptive data for food codes or discrepancies between coders regarding the degree of processing were generally solved by opting for the lesser degree of processing (conservative criterion), with some exceptions including bread, ready-to-eat cereal, and salty snacks.	• Cured meats were classified as processed (group 3), as guided by the NOVA classification system, although some would be considered ultra-processed. Food code "Pork bacon, not specified as to fresh, smoked or cured, cooked" was classified as processed, although some brands such as "Sliced bacon, hickory smoked" should be considered ultra-processed because of sodium nitrite and flavourings in the following ingredient list: pork cured with water, salt, cane, and brown sugar, sodium phosphate, sodium erythorbate, sodium nitrite, flavourings (Kretser et al, 2017) • Jellies, jams, and applesauce were classified as processed foods (although some brands could be ultra-processed) • Animal fats such as creams and evaporated milks were classified as processed culinary ingredients (although some brands could be ultra-processed) • Cottage and cream cheese were classified as processed cheese (although some brands could be ultra-processed)

Decision	Description	Examples
Decision C: Classifying breakfast cereals and salty snacks as ultra-processed	Ready-to-eat breakfast cereals and salty snacks were generally classified as ultra-processed, as guided by the NOVA classification system, although some specific brands may be processed.	● For example, food code "Cereal, Corn Flakes" was classified as ultra-processed consistent with the ingredient list of Kellogg's Corn Flakes containing malt flavour (milled corn, sugar, contains ≤2% of malt flavour, salt, BHT for freshness, vitamins, and minerals) or Springfield Cereal, Corn Flakes containing high fructose corn syrup (milled corn, sugar, salt, malt syrup, high fructose corn syrup, vitamins and minerals), although some brands might be processed, such as Barbara's Cereal, Corn Flakes (organic corn, organic fruit juice concentrate (pear or apple), sea salt) ● Regarding salty snacks, although Corn Nuts Crunchy Corn Kernels are ultra-processed because of monosodium glutamate and natural flavour in their ingredient list (corn, salt, corn oil, contains <2% of maltodextrin, spice, onion powder, garlic powder, tomato powder, monosodium glutamate, citric acid, paprika extract (for colour), natural flavour), Corn Nuts Original Crunchy Corn Kernels (corn, corn oil, salt) would be processed
Decision D: Classifying industrial bread as ultra-processed	Regarding bread, the NOVA classification distinguishes between handmade bread (either homemade or made in restaurants or artisanal bakeries) and industrial bread (made in industrial bakeries or factories), either processed (when manufactured with ingredients used in culinary preparations) or ultra-processed (when manufactured with food substances not used in culinary preparations). Because of the large amount of industrial breads with unknown ingredients in the NHANES dietary data (~3.7% of all	No information provided

Decision	Description	Examples
	industrial bread had fully known ingredients in cycle 2009–2010) and the very low consumption of processed breads when ingredients were reported (~2.3% of industrial breads were processed in cycle 2009–2010), all industrial bread were classified as ultra-processed foods (Martínez Steele et al, 2016).	
Decision E: Classifying non-disaggregated mixed dishes based on principal ingredient	Potential homemade mixed dishes with unlisted scratch ingredients (because Food Code was linked to recipe/mixed dish and not to a list of scratch ingredient standard reference codes) were classified based on expected principal ingredients.	● For example, a standard reference code "Restaurant, Chinese, sesame chicken" (36633) used to code the "Sesame chicken" (food code 27146360), was classified as "meat" within unprocessed/minimally processed foods
Decision F: Using "combination food type" and "source of food" to review NOVA classification	Participant-specific "Combination Food Type" and "Source of food" variables from the dietary recall were used to check the appropriateness of NOVA classification. Some items were reclassified based on the information provided by these variables, if needed. Some food codes (mainly mixed dishes, including sauces and cakes, cookies, and pies) initially classified at the standard reference code level were reclassified as ultra-processed foods at the food code level if consumed as "frozen meals" or "lunchables" (combination food types) or from "restaurant fast food/pizza" or "vending machine" (food source). The classification of most food items, however, did not change (for example, a raw apple from a fast-food place or vending machine remained classified as an unprocessed/minimally processed food).	● For example, "Rice with vegetables (including carrots, broccoli, and/or dark-green leafy), no sauce, not specified as to fat added in cooking" was initially classified at the standard reference code level under the assumption that it was a homemade recipe. This was reclassified at the food code level as an ultra-processed ready-to-eat meal when reported as a "frozen meal" ● "Coffee cake, yeast type, made from home recipe or purchased at a bakery" coded according to standard reference codes was reclassified as ultra-processed "cake" when consumed at a "restaurant fast food/pizza"

Annex 9b: Sensitivity analyses (1 to 4) conducted comparing potential alternative approaches

- Sensitivity analysis 1: items were coded with uncertain classification using the lowest potential processing level (most conservative).

- Sensitivity analysis 2: items were coded with uncertain classification using the highest potential processing level and coded non-disaggregated mixed dishes as a separate group without a NOVA assignation ("non-disaggregated mixed dishes").

- Sensitivity analysis 3: items were coded making the same decisions as in the reference approach, except without taking into consideration participant-specific variables of "combination food type" and "source of food" from the dietary recall.

- Sensitivity analysis 4: items were coded making the same decisions as in the reference approach (including taking into consideration participant-specific variables of "combination food type" and "source of food" from the dietary recall) but used Standard Reference codes for all food items.

Annex 9c: Methods and assumptions for assigning food codes

- The methods by which foods were categorised, the 'reference approach', were based on a number of assumptions

- For each food code, a decision was made on whether food codes or underlying standard reference codes would be used to estimate NOVA group energy contributions. The decision to use a standard reference code rather than a food code depended on whether there was any indication that the food code could have been homemade

- Food codes that were likely to be homemade or artisanal and linked to a list of scratch ingredient standard reference codes, such as "Beef stroganoff" and "Cookie, chocolate chip, made from home recipe or purchased at a bakery," were classified at the standard reference code level (referred to as "disaggregated food codes" or "disaggregated mixed dishes")

- Foods likely purchased as ready-to-eat/heat/drink items, such as "Milk, fat-free (skim)," "Cereal (Kellogg's Apple Jacks)" or "Lasagna with meat, canned" were classified at the food code level (referred to as "non-disaggregated food code" or "non-disaggregated mixed dishes")

- Mixed dishes were assumed to be homemade unless the food item description or standard reference codes clearly suggested that it was ready-to-eat

Annex 10: Registered clinical trials identified

NCT Number	Study design	Title	Status	Study results	Primary completion date; completion date
NCT04308473	Interventional	Analysis of MicroBial Metabolites After Eating Refined Food	Recruiting	No results available	June 2023; as above
NCT05290064	Interventional	Effect of Ultra-processed Versus Unprocessed Diets on Energy Metabolism	Recruiting	No results available	24 January 2024; 29 February 2024
NCT04280146	Interventional	Speed Limits: Food Intake and Eating Behaviour of Ultra-processed and Unprocessed Foods	Unknown	No results available	30 April 2020; 31 July 2020
NCT04275843	Interventional	The Effects of Western Diet Patterns on Plasma Inflammatory and Cardio Metabolic Health Signatures in Middle-aged Adults	Completed	No results available	21 December 2021; as above
NCT05368194	Interventional	Food Intake and Epigenetic Alteration in the Spermatozoa of Singletons and Twins	Active, not recruiting	No results available	1 July 2022; 31 December 2026
NCT03407053	Interventional	Effect of Ultra Processed Versus Unprocessed Diets on Energy Intake	Completed	Has results	26 February 2020; as above
NCT05071170	Observational	Satiety Responses and Oral Processing Characteristics of Commonly Consumed Meals	Recruiting	No results available	4 May 2022; as above

Annex 11: Hall et al (2019). Ultra-processed diets cause excess calorie intake and weight gain: An inpatient randomized controlled trial of ad libitum food intake

Introduction

1. Hall et al (2019) examined the effects of ultra-processed versus unprocessed diets on energy intake and body weight.

2. The authors reported that findings from their study suggest eliminating ultra-processed foods from the diet decreases energy intake and results in weight loss whereas a diet with a large proportion of ultra-processed food increases energy intake and leads to weight gain.

Methods

3. The study by Hall et al (2019) was a randomised controlled crossover trial of 4 weeks duration. Participants resided in a metabolic unit of the study centre for the duration of the study and all meals were provided.

4. The study was powered to detect a difference in mean ad libitum energy intake (the primary endpoint) over each 14-day test diet period of 125–150 kcal/d in 20 subjects with 80% power) with a type I error probability of 0.05.

5. Ultra-processed and unprocessed foods were categorised according to the NOVA classification (Monteiro et al, 2018).

6. Participants (n=20, 10 female/10 male; age, 31.2±1.6 y; BMI=27±1.5 kg/m^2) were randomly assigned to receive either an ultra-processed or an unprocessed diet for 2 weeks followed immediately by the alternate diet for 2 weeks. During each diet phase, participants were provided with 3 meals per day and instructed to consume as much or little as they liked. They were allotted up to 60 minutes to consume each meal. Menus rotated on a 7-day schedule (see Annex 11 Appendix). Snacks appropriate to the prevailing diet were also provided ad libitum throughout the day.

7. Meals were matched across diets for total calories, energy density, macronutrients, fibre, sugars, and sodium but differed widely in the percentage of calories derived from ultra-processed versus unprocessed foods. They also differed substantially in the proportion of added to total sugar (about 54% versus 1%, respectively), insoluble

to total fibre (about 16% versus 77%, respectively) and saturated to total fat (about 34% versus 19% respectively).

8. Daily body weight was measured at 06.00 am each morning after the first void. Body composition measurements were performed at baseline and weekly using dual-energy X-ray absorptiometry. Changes in body energy stores were calculated using the measured changes in body fat and fat-free mass along with the corresponding energy densities of 9300 kcal/kg and 1100 kcal/kg, respectively.

9. Energy intake was calculated from the measured foods and beverages consumed using their estimated nutrient composition and metabolisable energy densities.

10. Overall physical activity was quantified by calculating average daily metabolic equivalents (MET) from small accelerometers worn on the hip.

11. Energy expenditure over 24 hours was measured via respiratory chamber (where participants stayed 1 day each week) and by the doubly labelled water (DLW) method.

Results

Energy and food intake

12. Energy intake was 508±106 kcal/d greater during the ultra-processed diet ($p=0.0001$).

13. Neither order of diet assignment ($p=0.64$) nor sex ($p=0.28$) had significant effects on the energy intake differences between the diets. Baseline BMI was not correlated with the energy intake differences between the diets ($r=0.11$; $p=0.66$).

14. During the unprocessed diet, energy intake did not significantly change over the two week period ($-7.7±6.4$ kcal/d; $p=0.23$); during the ultra-processed diet there was a significant linear decrease in energy intake over the two weeks ($-25.5±6.4$ kcal/d; $p<0.0001$).

15. The increased energy intake during the ultra-processed diet resulted from consuming greater quantities of carbohydrate (280±54 kcal/d; $p<0.0001$) and fat (230±53 kcal/d; $p=0.0004$) but not protein ($-2±12$ kcal/d; $p=0.85$).

16. Sodium intake was significantly increased during the ultra-processed versus the unprocessed diet (5.8±0.2 g/d vs. 4.6±0.2 g/d; $p<0.0001$) but there were no significant differences in consumption of total fibre (48.5±2.3 g/d vs. 45.8±2.3 g/d; $p=0.41$) or total sugars (93.3±4.0 g/d vs. 96.6±4.0 g/d; $p=0.57$).

17. Foods and beverages consumed during the ultra-processed diet had greater energy density than the unprocessed diet (1.36±0.02 kcal/g vs 1.09±0.02 kcal/g; $p<0.0001$).

Although energy densities of the meals in both diets were similar, this was due to inclusion of beverages as vehicles for the dissolved fibre supplements in the ultra-processed meals (that were otherwise low in fibre). The energy density of the non-beverage foods in the ultra-processed diets was about 85% higher than the unprocessed diets (1.96 kcal/g vs 1.06 kcal/g) and the authors suggested that this most likely contributed to the observed excess energy intake.

18. Meal eating rate was significantly greater during the ultra-processed diet whether expressed as kcal/min (17±1 kcal/min; $p < 0.0001$) or g/min (7.4±0.9 g/min; $p < 0.0001$).

19. Participants did not report significant differences in the pleasantness (4.8±3.1; $p = 0.13$) or familiarity (2.7±4.6; $p = 0.57$) of the meals between the ultra-processed and unprocessed diets.

Body weight and composition

20. Body weight increased (0.9±0.3 kg; $p = 0.009$) during the ultra-processed diet and decreased (0.9±0.3 kg; $p = 0.007$) during the unprocessed diet. The individual differences in weight change between the diets were highly correlated with energy intake differences between the diets ($r = 0.8$, $p < 0.0001$).

21. Body fat mass increased by 0.4±0.1 kg ($p = 0.0015$) during the ultra-processed diet and decreased by 0.3±0.1 kg during the unprocessed diet ($p = 0.05$).

Energy expenditure, physical activity and energy balance

22. The 24-hour energy expenditure was greater during the ultra-processed diet (51±27 kcal/d; $p = 0.06$) but there were no differences in sleeping energy expenditure, sedentary energy expenditure, or physical activity.

23. The ultra-processed diet led to slightly higher energy expenditure by DLW compared to the unprocessed diet (171±56 kcal/d; $p = 0.006$). The authors suggested that, since overall physical activity did not differ between the diet periods, the DLW energy expenditure differences were probably due to differing states of energy balance between the diets.

24. Energy intake was more (417±121 kcal/d; $p = 0.003$) than energy expenditure by DLW during the ultra-processed diet in accordance with the observed gain in body weight and fat. However, despite significant body weight and fat loss during the unprocessed diet, energy intake was slightly higher than energy expenditure by DLW (by 116±111 kcal/d; $p = 0.31$).

Limitations

25. These results should be treated with caution due to:

- the small sample size and short duration of the test diets. Energy intake on the UPF diet decreased over time suggesting the observed effects may be transient.

- the RCT had a crossover design but there was no washout period between the ultra-processed and unprocessed diets so there may have been carryover effects from the previous diet.

- this was a carefully controlled feeding study where all meals were provided and participants consumed only ultra-processed or unprocessed meals for the study period. Findings may not be applicable to free-living conditions where dietary patterns may be more varied.

- the energy density of non-beverage foods and snacks in the UPF diet was greater which may have contributed towards the higher energy intakes and weight gain. The meal eating rate was faster on the UPF diets which may also have contributed to the higher energy intakes. The ultra-processed meals provided in this study generally comprised foods that were softer and easier to chew while the unprocessed meals included a greater number of foods overall and more raw foods (for example, salad ingredients, vegetables and fruits) which would have taken more time to consume.

Annex 11: Appendix

Seven-day menus for ultra-processed and unprocessed diets

Day	Ultra-processed diet	Unprocessed diet
1	BREAKFAST Honey Nut Cheerios Whole milk with NutriSource fiber Blueberry muffin, margarine	BREAKFAST Greek yogurt parfait with strawberries, bananas, walnuts, salt and olive oil Apple Slices with fresh squeezed lemon
	LUNCH Beef ravioli, parmesan cheese White bread, margarine Diet lemonade with NutriSource fiber Oatmeal raisin cookies	LUNCH Spinach salad with chicken breast, apple slices, Bulgur, sunflower seeds and grapes Vinaigrette (olive oil, fresh squeezed lemon juice, apple cider vinegar, ground mustard seed, black pepper, salt)
	DINNER Steak, gravy, mashed potatoes, margarine, corn (canned) Diet lemonade with NutriSource fiber Low fat chocolate milk with NutriSource fiber	DINNER Beef tender roast, rice pilaf (basmati rice with garlic, onions, peppers, olive oil), steamed broccoli Side salad (Green leaf lettuce, tomatoes, cucumbers) with balsamic vinaigrette (balsamic vinegar) Orange slices, pecans, salt, pepper

Day	Ultra-processed diet	Unprocessed diet
2	BREAKFAST Croissant Margarine Turkey sausage Blueberry yogurt with NutriSource fiber	BREAKFAST Scrambled egg (made from fresh eggs) Hash brown potatoes (potato, garlic, paprika, ground turmeric, cream and onions) Salt and Pepper
	LUNCH Deli turkey and cheddar and Monterey Jack cheese quesadilla, refried beans, sour cream Salsa Diet lemonade with NutriSource fiber	LUNCH Salad with grilled chicken breast, baked sweet potato, corn (from frozen), avocado, onions, tomatoes, carrots on green leaf lettuce, vinaigrette (red wine vinegar, olive oil) Skim milk Apple slices with fresh squeezed lemon juice
	DINNER Chicken salad (canned chicken, Heinz pickle relish, Hellmann's mayonnaise) sandwich on white bread Peaches canned in heavy syrup Shortbread cookies Fig Newtons (Nabisco) Diet lemonade with NutriSource fiber	DINNER Stir fried beef tender roast with broccoli, onions, sweet peppers, ginger, garlic and olive oil Basmati rice Orange slices Pecan halves Salt and pepper

Day	Ultra-processed diet	Unprocessed diet
3	**BREAKFAST** Egg, turkey bacon and American cheese on an English muffin Tater tots with ketchup Orange juice with NutriSource Fiber	**BREAKFAST** Oatmeal (Quaker) with blueberries and raw almonds, salt, 2% milk
	LUNCH Tempura fried chicken nuggets with ketchup Baked potato chips Diet lemonade with NutriSource fibre	**LUNCH** Entrée salad with grilled chicken breast, farro, apples, grapes, vinaigrette (fresh squeezed lemon juice, apple cider vinegar, olive oil) salt and pepper
	DINNER Turkey meatballs with marinara sauce on a hoagie roll with provolone cheese Diet lemonade with NutriSource fibre Cheese and peanut butter sandwich crackers	**DINNER** Beef tender roast, couscous with fresh squeezed lemon juice, garlic, olive oil; green beans, from frozen; side salad with green leaf lettuce, cucumber and tomatoes. Vinaigrette (red wine vinegar, honey, olive oil, salt, pepper) Black bean hummus (black beans cooked from dried, garlic, sweet pepper, olive oil, fresh squeezed lemon juice, ground cumin, chili powder and baby carrot

Day	Ultra-processed diet	Unprocessed diet
4	BREAKFAST Scrambled egg, prepared from liquid, pork sausage Honey bun Orange juice with NutriSource fibre	BREAKFAST Spinach, onion and tomato omelette (fresh eggs) cooked in olive oil Sweet potato hash (sweet potato, olive oil and cinnamon), salt and pepper Skim milk
	LUNCH Hot dog on bun with ketchup and yellow mustard Baked potato chips Cranberry juice with NutriSource fibre Blueberry yogurt with NutriSource fibre	LUNCH Baked cod fillet with fresh squeezed lemon juice Baked russet potato with olive oil, steamed broccoli with olive oil and garlic; side salad (green leaf lettuce, tomatoes, cucumber and carrots), vinaigrette (balsamic vinegar, olive oil), salt, pepper
	DINNER Steak and Cheddar and Monterey JackcCheese burrito with canned black beans, sour cream, salsa Tortilla chips Diet Lemonade with NutriSource fibre	DINNER Salad with green leaf lettuce, tomatoes, cucumbers, carrots, black beans (cooked from dried), corn (cooked from frozen), and avocado; vinaigrette (red wine vinegar, fresh squeezed lemon juice, flaxseed oil, salt and pepper) Raw almonds, grapes

Day	Ultra-processed diet	Unprocessed diet
5	BREAKFAST Plain bagel and cream cheese with NutriSource fibre Turkey bacon	BREAKFAST Oatmeal with skim milk, cinnamon, salt, walnuts, bananas, coconut and fresh squeezed lemon juice
	LUNCH Spam sandwich with American cheese on white bread Potato chips Diet lemonade with NutriSource fibre	LUNCH Grilled beef tender roast, barley with olive oil and garlic, steamed broccoli, side salad (green leaf lettuce, tomatoes, cucumber and baby carrots), vinaigrette (apple cider vinegar and olive oil) salt and pepper Apple slices with fresh squeezed lemon juice
	DINNER Beef and bean chili, shredded cheddar and Monterey Jack cheese, sSour cream, tortilla chips, salsa Diet Ginger Ale Peaches, canned in heavy syrup	DINNER Shrimp, scampi with spaghetti, olive oil, garlic, cream, tomatoes, parsley, basil and fresh squeezed lemon juice, side salad (green leaf lettuce, tomatoes, cucumber), vinaigrette (balsamic vinegar, olive oil), salt and pepper Plain Greek yogurt with blueberries (no sugar added)

Day	Ultra-processed diet	Unprocessed diet
6	BREAKFAST Pancakes, margarine, syrup Turkey sausage, Tater tots Apple juice with NutriSource fibre	BREAKFAST Berry and walnut quinoa breakfast cereal, skim milk, ground cinnamon, salt, frozen strawberries and blueberries (no sugar added, and chopped walnuts
	LUNCH Cheeseburger with American cheese on a Kaiser roll French fries, ketchup Diet lemonade with NutriSource fibre	LUNCH Salmon with garlic and fresh squeezed lemon juice, baked sweet potato with olive oil, ground cumin and chili powder, green beans (from frozen) with olive oil' garlic Plain Greek yogurt with strawberries (from frozen, no sugar added) salt and pepper
	DINNER Deli turkey with American cheese and mayonnaise on white bread, baked potato chips Peaches canned in heavy syrup Vanilla non-fat Greek yogurt with NutriSource fibre Diet lemonade with NutriSource fibre	DINNER Entrée salad with beef tender roast, barley, spinach, cucumber and tomatoes Vinaigrette (balsamic vinegar, garlic, olive oil, basil, parsley, rosemary), salt and pepper Orange slices

Day	Ultra-processed diet	Unprocessed diet
7	BREAKFAST Cinnamon french toast sticks, butter, pancake syrup Turkey sausage Diet lemonade with NutriSource fibre	BREAKFAST Spinach, onion and tomato omelette (fresh eggs) cooked with olive oil and salt, hash browned potatoes (russet potatoes with garlic, olive oil, rosemary, salt, skim milk
	LUNCH Macaroni and cheese Chicken tenders Canned green beans Diet lemonade with NutriSource fibre	LUNCH Grilled chicken breast quinoa salad with raisins, onions, chopped walnuts, parsley, fresh lemon juice and olive oil Side salad (spinach, tomato and cucumber) with vinaigrette (balsamic vinegar and olive oil), salt, pepper
	DINNER Peanut butter and jelly sandwich on white bread 2% milk with NutriSource fibre, baked Cheetos, crackers Chocolate pudding with NutriSource fibre	DINNER Penne pasta primavera (olive oil, garlic, pinto beans (cooked from dried), spinach, basil, tomatoes); side salad (lettuce, baby carrots, broccoli), vinaigrette (red wine vinegar and olive oil), salt and pepper Grapes

Daily snacks

Ultra-processed daily snacks	Unprocessed
Baked Potato Chips, Dry Roasted Peanuts, Cheese & Peanut Butter Sandwich Crackers, Goldfish Crackers, Applesauce	Fresh oranges and apples, raisins, raw almonds, chopped walnuts

Annex 12: Evidence published after scoping search date (12 January 2023)

Reference (Title, author, year)	Study design	Date published
Food Processing and Risk of Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis (Narula et al, 2023)	Systematic review and meta-analysis	29 January 2023
Dose–response meta-analysis of ultra-processed food with risk of cardiovascular events and all-cause mortality: evidence from prospective cohort studies (Yuan et al, 2023)	Systematic review and meta-analysis	6 February 2023

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