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REVISÃO
REVIEW

Impact of the consumption of ultra-processed foods on children, adolescents and adults' health: scope review

Impacto do consumo de alimentos ultraprocessados na saúde de crianças, adolescentes e adultos: revisão de escopo

Impacto del consumo de alimentos ultraprocesados en la salud de niños, adolescentes y adultos: revisión de alcances

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Abstract

The aim of this study was to conduct a literature scope review of the association between the consumption of ultra-processed foods and health outcomes. The search was carried out in the PubMed, Web of Science and LILACS databases. Studies that assessed the association between the consumption of ultra-processed foods, identified on the NOVA classification, and health outcomes were eligible. The review process resulted in the selection of 63 studies, which were analyzed in terms of quality using a tool from the National Institutes of Health. The outcomes found included obesity, metabolic risk markers, diabetes, cardiovascular diseases, cancer, asthma, depression, frailty, gastrointestinal diseases and mortality indicators. The evidence was particularly consistent for obesity (or indicators related to it) in adults, whose association with the consumption of ultra-processed foods was demonstrated, with dose-response effect, in cross-sectional studies with representative samples from five countries, in four large cohort studies and in a randomized clinical trial. Large cohort studies have also found a significant association between the consumption of ultra-processed foods and the risk of cardiovascular diseases, diabetes and cancer – even after adjusting for obesity. Two cohort studies have shown an association of ultra-processed foods consumption with depression and four cohort studies with all-cause mortality. This review summarized the studies' results that described the association between the consumption of ultra-processed foods and various non-communicable diseases and their risk factors, which has important implications for public health.

Industrialized Foods; Food Consumption; Chronic Disease; Review

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Introduction

Ultra-processed foods, as defined by the NOVA classification, are industrial formulations of substances extracted or derived from foods, that contain little or no whole food in their composition and typically it is added flavorings, dyes, emulsifiers and other additives that modify the sensory attributes of the final product. The ingredients and procedures used in the manufacture of ultra-processed foods aim to create low-cost, hyper-palatable and convenient products, with the potential to replace fresh or minimally processed foods [1].

Food sales statistics indicate higher consumption of ultra-processed foods in high-income countries, but rapid and exponential growth in middle-income countries. Between 1998 and 2012, snacks and soft drinks sales increased by 50% in the upper-middle income countries and by more than 100% in the lower-middle income countries [2]. National surveys show that ultra-processed foods are already half or more of the total energy consumed in some high-income countries, such as the United States, Canada and the United Kingdom [34,5,6], and between one-fifth and one-third of the energy consumed in middle-income countries, such as Chile and Mexico [7,8]. In Brazil, surveys on the acquisition of foodstuffs for household consumption, carried out in the metropolitan areas between 1987-1988 and 2008-20099 and in the country as a whole between 2002-2003 and 2017-2018 [10], indicate systematic increases in the participation of ultra-processed foods and a reduction in concomitant of fresh or minimally processed foods and culinary ingredients.

Previous studies show that ultra-processed foods, together, have a higher energy density, more free sugar and unhealthy fats and less fiber, protein and micronutrients than non-ultra-processed foods, and that their acquisition or consumption is systematically associated with the deterioration of the nutritional food quality [3,4,5,6,7,8,11,12]. Experimental studies also show that when compared to non-ultra-processed foods, ultra-processed foods have a low satiety power and induce high glycemic responses [13], that are associated with a higher speed of energy intake [14] and the presence of contaminants, including toxic compounds newly formed during processing or released synthetic packaging [15,16] and create an intestinal environment that favors microbes that promote inflammatory diseases [17]. Therefore, studies with different designs have investigated the association between the consumption of ultra-processed foods and the diseases or risk factors for diseases in different populations. However, there is still no clarity about the totality of information available in this rapidly growing field of publications. Consequently, the present scope review was conducted in order to map the literature about the impact of ultra-processed foods on health.

Methods

Eligibility criteria

The question that guided the review was: "Is the consumption of ultra-processed foods (defined by the NOVA classification) associated with diseases?". To answer it, the review considered all studies that investigated the association between the consumption of ultra-processed foods (exposure) and health outcomes, including indicators related to obesity (body mass index – BMI, waist circumference and body fat), metabolic risk markers (such as blood pressure, lipid profile and blood glucose), diabetes, cardiovascular diseases, cancer, among others. The studies should have assessed the exposure (the consumption of ultra-processed foods) based on the definition by the NOVA classification [1]. Case studies, reviews, comments, editorials, conference proceedings or theses/dissertations or restricted to people with specific diseases were excluded.

Search strategy

The search for indexed articles was carried out in three databases: PubMed and Web of Science, of international scope, and LILACS, covering Latin America and the Caribbean. The keywords used for the exhibition of interest were "ultra-processed" combined with "food OR product" for international databases, and "ultraprocessado OR ultraprocesado OR ultra-processed" combined with

"alimento OR produto OR food OR product" for the Lilacs database. No topic, language or publication date limits were used. The search included records published as of August 18th, 2020. Additionally, records identified through other sources, such as articles in press/published after the search were incorporated.

Studies selection

All titles and abstracts found in the electronic search were imported for assessment using EndNote version X9 (http://www.endnote.com/) software, with duplicate studies removed from the list. The titles and abstracts of the remaining articles were analyzed by two independent reviewers, considering the inclusion criteria mentioned above. Articles with insufficient information in the abstract were not discarded. After the selection by titles and abstracts, the same reviewers independently read the full texts to select the studies to be included. In the case of discordant selection, the studies were evaluated by a third reviewer.

Data-mapping process

Relevant data were extracted from each selected article, with the aid of a standardized spreadsheet, including the author and year of publication, study design, participants, operational definition of exposure and outcome, control variables and results. The studies were organized into three large groups according to the outcomes found and presented, within each outcome group, for adults, pregnant women, children/adolescents (in that order) and, within each population subgroup, by type of study design – randomized clinical trial, cohort, case-control, cross-sectional with national representativeness and local cross-sectional (in that order).

Methodological quality assessment

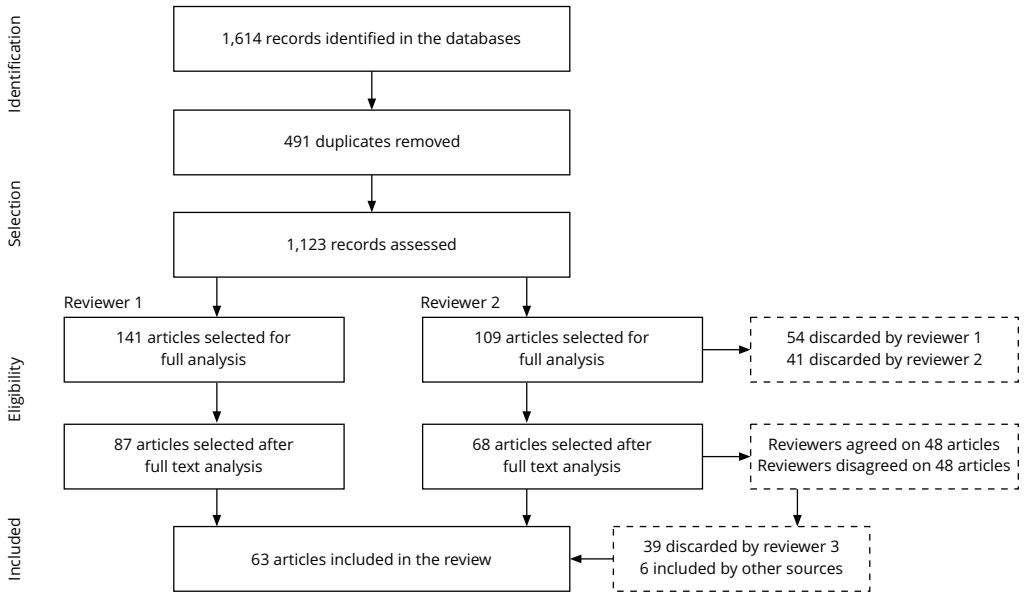
The selected articles were analyzed by the same reviewers, independently, in terms of methodological quality using the tool from the National Institutes of Health (NIH) [18]. This tool provides 14 questions (specific to each study design) to be answered by the reviewers in order to assist in the internal validity assessment (or risk of bias) of each study (Supplementary Material: http://cadernos.ensp.fiocruz.br/static//arquivo/suppl-e00323020-ingles_2541.pdf). The questions are focused on key concepts related to the study design, the research question, eligibility, sample selection and recruitment, the validity of the exposure and outcome measures, losses to follow-up and statistical analysis. Reviewers can select "yes", "no" or "cannot be determined/not reported/not applicable" in response to each question. The instrument does not provide an objective rating scale, but, for each item in which "no" was selected, reviewers are instructed to consider the risk of bias that could be introduced by this failure. For each question, there is a detailed instruction for its assessment, which has also been developed by the NIH. It was considered important for the methodological study quality, for example, the purpose clarity, the definition and appropriate description of the exposure and the outcomes, the loss of follow-up below 20% (in the case of the cohort studies) and the statistical control for at least age, sex and socioeconomic characteristics. From the questions, the reviewers attributed to each article a high, mean or low assessment of its methodological quality. Disagreements were resolved by consensus or by the third reviewer.

Results

The selection process was described in Figure 1. The search originated 1,614 articles. After removing duplicates and sorting by title and abstract, 141 articles were selected for review of the full text by reviewer 1 and 109 by reviewer 2. With the complete reading, 48 articles were selected by both reviewers and 48 conflicting articles were evaluated by the third reviewer, including 9 more articles. It was added 6 articles in press/published after the search, totaling 63 articles included and evaluated qualitatively.

Figure 1

Flowchart of study selection.



The studies evaluated the association between the consumption of ultra-processed foods and weight gain (n = 3), BMI (n = 17), overweight/obesity (n = 25), waist circumference (n = 9), body fat (n = 4), hypertension/blood pressure levels (n = 4), serum lipid levels (n = 4), blood glucose (n = 1), serum levels of C-reactive protein (n = 1), subclinical atherosclerosis (n = 1), short telomeres (n = 1), urinary levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) (n = 1), metabolic syndrome (n = 4), gestational diabetes (n = 1), cardiovascular disease (n = 1), type 2 diabetes (n = 2), breast cancer (n = 2), prostate cancer (n = 2), colorectal cancer (n = 1), wheezing/asthma (n = 3), mortality from cardiovascular diseases (n = 2), all-cause mortality (n = 4), depression (n = 3), frailty syndrome (n = 1) and gastrointestinal diseases (n = 2). The studies were carried out in Brazil (n = 24), France (n = 9), Spain (n = 9), United States (n = 6), United Kingdom (n = 4), Canada (n = 4), Australia (n = 1), Norway (n = 1), Lebanon (n = 1) and Iran (n = 1). Three ecological studies evaluated data from 19 European countries, 13 Latin American countries and 80 countries from different regions, respectively. Author and year of publication, design, participants (covering sample size), operational definition of exposure and outcome, control variables and main results of these studies are described in separate tables according to the type of health outcome.

Obesity and obesity-related indicators and metabolic risk markers

- **Adults**

Box 1 describes the studies' main characteristics that assessed the association of the consumption of ultra-processed foods with the indicators related to obesity and metabolic risk markers in adults.

Box 1

Characteristics of studies that assessed the association between the consumption of ultra-processed foods and obesity and obesity-related indicators and metabolic risk markers (hypertension, serum C-reactive protein and metabolic syndrome) in adults.

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Hall et al. [19] (2019)	Randomized clinical trial	Adults from the United States aged between 18 to 50 years old in 2018 (n = 20) (NIH Study).	*Ad libitum* offer for two weeks of diets made with, on average, 83% of calories from ultra-processed foods or diets without ultra-processed foods.	Daily energy intake and change in weight and body fat in two weeks.	The ultra-processed and non-ultra-processed diets were paired for calories, energy density, macronutrients, sugar, sodium and fiber.	When exposed to an ultra-processed diet, participants consumed, on average, 508 ± 106Kcal more per day than when exposed to diets without ultra-processed foods. At the end of two weeks, the participants increased 0.9kg ± 0.3kg in weight and 0.4kg ± 0.1kg in body fat consuming the ultra-processed diet and decreased 0.9kg ± 0.3kg in weight and 0.3kg ± 0.1kg of body fat consuming the non-ultra-processed diet (p-value < 0.001).	High

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Canhada et al. [20] (2019)	Cohort	Brazilian adults aged 35 years old or older with a mean follow-up of 3.8 years between 2008/2010-2012/2014 (n = 11,827) (ELSA-Brasil).	Participation of ultra-processed foods in the food's total energy.	Incidence of overweight and obesity and weight gain and waist circumference.	Age, sex, race/color, family income, education, physical activity and smoking status.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of weight gain (adjusted RR = 1.27; 95%CI: 1.07; 1.50) and waist circumference (adjusted RR = 1.33; 95%CI: 1.12; 1.58), excessive and higher incidence of overweight and obesity (adjusted RR = 1.20; 95%CI 1.03; 1.40) when compared to those in the lowest quartile.	High
Mendonça et al. [21] (2016)	Cohort	Spanish middle-aged adults with a mean follow-up of 8.9 years between 1999-2012 (n = 8,541) (The Sun).	Consumption of ultra-processed foods servings/day.	Incidence of overweight and obesity.	Age, sex, education, marital status, physical activity, smoking status, hours watching television, nap times, BMI at baseline, following a special diet at baseline, snacking between meals and consumption of fruits and vegetables.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of overweight/obesity (adjusted HR = 1.26; 95%CI: 1.10; 1.45) when compared to those in the lowest quartile.	High

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Rauber et al. [22] (2020)	Cohort	British adults aged between 40 to 69 years old with a mean follow-up of 5 years between 2006-2019 (n = 22,659) (UK Biobank).	Participation of ultra-processed foods in the food's total energy.	Incidence of obesity and abdominal obesity and gain of BMI, waist circumference and body fat.	Sex, socioeconomic deprivation index, physical activity, smoking status and hours of sleep.	Participants in the highest quartile of consumption of ultra-processed foods had a higher risk of obesity (adjusted HR = 1.58; 95%CI: 1.32; 1.90) and high waist circumference (adjusted HR = 1.38; 95%CI: 1.21; 1.57) and to experience an increase of ≥ 5% in BMI (adjusted HR = 1.30; 95%CI: 1.19; 1.42), in waist circumference (adjusted HR = 1.30; 95%CI: 1.21; 1.40) and in the percentage of body fat (adjusted HR = 1.14; 95%CI: 1.04; 1.26) when compared to those with the lowest consumption quartile.	High

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Beslay et al. [23] (2020)	Cohort	French adults aged 18 years old or over and a mean follow-up of 4.1 years (n = 110,260)	Participation of ultra-processed foods in the total of food grams.	Incidence of overweight and obesity and BMI gain.	Sex, age, marital status, education, physical activity, smoking status, number of dietary records, alcohol intake, energy intake.	The consumption of ultra-processed foods was positively associated with a higher risk of overweight (adjusted HR associated with a 10% increase in the consumption of ultra-processed foods = 1.11; 95%CI: 1.08; 1.14), obesity (adjusted HR associated with a 10% increase in the consumption of ultra-processed foods = 1.09; 95%CI: 1.05; 1.13) and BMI gain (adjusted B associated with a 10% increase in the consumption of ultra-processed foods: 0.02; 95%CI: 0.01; 0.02)	High
Adams & White [24] (2015)	Cross-sectional	British adults aged 18 years old or older in 2008-2012 (n = 2,174).	Participation of ultra-processed foods in the food's total energy.	BMI, overweight and obesity.	Age, sex, social class and alcohol consumption.	The consumption of ultra-processed foods was not significantly associated with the outcomes.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Louzada et al. [25] (2015)	Cross-sectional	Brazilians aged 10 years old or older in 2008/2009 (n = 32,898).	Participation of ultra-processed foods in the food's total energy.	BMI, overweight and obesity.	Age, sex, race/color, income, education, region, urbanity, physical activity, smoking status, intake of fruits, vegetables and beans.	Participants in the largest quintile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 0.94; 95%CI: 0.42; 1.42) and a greater chance of being overweight (adjusted OR = 1.26; 95%CI: 0.95; 1.69) and obesity (adjusted OR = 1.98; 95%CI: 1.26; 3.12) when compared to those in the lowest quintile.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Juul et al. [26] (2018)	Cross-sectional	Adults from the United States aged between 20 to 64 years old in 2005-2014 (n = 15,977).	Participation of ultra-processed foods in the food's total energy.	BMI, waist circumference, overweight and obesity.	Age, sex, ethnicity, socioeconomic status, education, marital status, physical activity and smoking status.	Participants in the largest quintile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 1.61; 95%CI: 1.11; 2.10) and waist circumference (adjusted coefficient: 4.07; 95%CI: 2.94; 5.19), greater chance of having obesity (adjusted OR = 1.53; 95%CI 1.29; 1.81), overweight (adjusted OR = 1.48; 95%CI: 1.25; 1.76) and abdominal obesity (adjusted OR = 1.62; 95%CI: 1.39; 1.89) when compared to those in the lowest quintile.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Machado et al. [27] (2020)	Cross-sectional	Australian adults aged 20 years old or older between 2011-2012 (n = 7,411).	Participation of ultra-processed foods in the food's total energy.	BMI, waist circumference, obesity and abdominal obesity.	Age, sex, income, education, area of residence, country of birth, physical activity and smoking status.	Participants in the largest quintile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 0.97; 95%CI: 0.42; 1.51), and waist circumference (adjusted coefficient: 1.92cm; 95%CI: 0.57; 3.27) and greater chance of having obesity (adjusted OR = 1.61; 95%CI: 1.27; 2.04) and abdominal obesity (adjusted OR = 1.38; 95%CI: 1.10; 1.72) when compared to those in the lowest quintile.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Rauber et al. [28] (2020)	Cross-sectional	British adults aged 19 years old or older in 2008-2016 (n = 6,143).	Participation of ultra-processed foods in the food's total energy.	BMI, waist circumference, obesity and abdominal obesity.	Age, sex, ethnicity, region, occupation, physical activity, smoking status, hours of sleep, year of research and whether they were on a diet for weight loss.	Participants in the largest quartile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 1.66; 95%CI: 0.96; 2.36) and waist circumference (adjusted coefficient: 3.56; 95%CI: 1.79; 5.33), and a greater chance of having obesity (adjusted O =: 1.90; 95%CI: 1.39; 2.61) when compared to those in the lowest quartile.	Mean
Nardocci et al. [29] (2018)	Cross-sectional	Canadian adults aged 18 years old or older in 2004 (n = 19,363).	Participation of ultra-processed foods in the food's total energy.	Overweight and obesity.	Age, sex, income, education, immigration, area of residence, physical activity, smoking status, group's total energy intake and type of weight and height measurement (self-reported or directly measured).	Participants in the largest quintile of consumption of ultra-processed foods were more likely to have obesity (adjusted OR = 1.32; 95%CI: 1.05; 1.57) when compared to those in the lowest quintile.	Low
Seale et al. [30] (2020)	Cross-sectional	Canadian adults aged 18 years old or older in 2014/2015 (n = 10,942).	Number of different types of ultra-processed foods consumed in the previous seven days.	BMI.	Age, sex, income and region.	The consumption of ultra-processed foods was positively associated with BMI (adjusted coefficient: 0.04; 95%CI: 0.02; 0.07).	Low

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Julia et al. [31] (2018)	Cross-sectional	French adults aged 18 years old or older between 2009-2014 (n = 74,470).	Participation of ultra-processed foods in the total of food grams.	Overweight and obesity.	Age, sex, income, education, marital status, smoking status, BMI and energy intake.	Higher consumption of ultra-processed foods was significantly associated with overweight and obesity (p-value < 0.0001).	Mean
Silva et al. [32] (2018)	Cross-sectional	Brazilian adults aged between 35 and 74 years in 2008-2010 (n = 8,977).	Participation of ultra-processed foods in the food's total energy.	BMI, waist circumference, overweight, obesity, high waist circumference and significantly high waist circumference.	Age, sex, race/ color, family income per capita, physical activity, smoking status, hypertension, diabetes, consumption of fresh and minimally processed foods added to culinary ingredients and energy intake.	Participants in the largest quartile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 0.64; 95%CI: 0.33; 0.95) and waist circumference (adjusted coefficient: 0.95; 95%CI: 0.17; 1.74) and greater chance of overweight (adjusted OR = 1.32; 95%CI: 1.15; 1.53), obesity (adjusted OR: 1.43, 95%CI: 1.20; 1.72) and high waist circumference (OR = 1.21; 95%CI: 1.01; 1.46) when compared to those in the lowest quartile.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Djupegot et al. [33] (2017)	Cross-sectional	Norwegian parents of 2-year-old children in 2014/2015 (n = 497).	Frequency score of the consumption of ultra-processed foods.	Overweight and obesity.	Age, sex, education, shortage of time and number of children in the household.	Overweight/ obese people were more likely to have a high consumption of ultra-processed foods at dinner (adjusted OR = 1.54; 95%CI: 1.04; 2.30) when compared to those with normal weight.	Low
Pan-American Health Organization [34] (2015)	Ecological	Latin American countries between 2000-2013 (n = 13).	Total volume, in kg/per capita, of sales of ultra-processed foods.	BMI trajectories.	Population size, urbanization and gross national income.	The increase in the per capita volume of sales of ultra-processed foods was significantly and positively associated with the average increase in the countries' BMI (p-value < 0.001).	Mean
Vandevijvere et al. [35] (2019)	Ecological	Countries of the Euromonitor food sales database between 2002-2014 (n = 80).	Total volume, in kg/per capita, of sales of ultra-processed foods.	BMI trajectories.	National income per capita, education, urbanization, average consumption of fruits and vegetables in 2005, GINI index and, indirectly, physical activity.	Increases in the per capita volume of sales of ultra-processed foods were significantly and positively associated with the BMI trajectories in the population (p-value < 0.001).	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Monteiro et al. [36] (2018)	Ecological	European countries between 1991-2008 (n =19).	Participation of ultra-processed foods in the total energy available for consumption in households (national per capita).	Prevalence of obesity in adults.	GDP per capita, GDP^2 per capita, years of difference between the estimates of obesity and availability of ultra-processed foods, obesity measurement method (self-reported or direct measurement), prevalence of physical inactivity and smoking status.	The national household availability of ultra-processed foods was positive and significantly associated with the national prevalence of obesity among adults. The increase of a percentage in the availability of ultra-processed foods at home was associated with an increase of 0.25 percentage points in the prevalence of obesity.	Low
Mendonça et al. [37] (2017)	Cohort	Spanish middle-aged adults with an average follow-up of 9.1 years between 1999-2012 (n = 14,790) (The Sun).	Consumption of ultra-processed foods servings/day.	Hypertension incidence.	Age, sex, physical activity, smoking status, time watching TV, use of analgesics, family history of hypertension and hypercho-lesterolemia, following a special baseline diet, baseline BMI, energy intake, alcohol consumption, oil and fruit and vegetable intake.	Participants in the highest tertile of consumption of ultra-processed foods had a higher risk of hypertension (adjusted HR = 1.21; 95%CI: 1.06; 1.37) when compared to those in the lowest tertile.	High

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Martínez Steele et al. [38] (2019)	Cross-sectional	American adults aged 20 years old or older between 2009-2014 (n = 6,385).	Participation of ultra-processed foods in the food's total energy.	Metabolic syndrome.	Age, sex, race/ ethnicity, socioeconomic status, education, physical activity and smoking status.	Participants in the largest quintile of consumption of ultra-processed foods had a higher prevalence of metabolic syndrome (adjusted PR = 1.28; 95%CI: 1.09; 1.50) when compared to those in the lowest quintile.	Mean
Lavigne-Robichaud et al. [38] (2018)	Cross-sectional	Canadian indigenous people aged 18 years old or older (n = 811).	Participation of ultra-processed foods in the food's total energy, sodium and added sugar.	Metabolic syndrome.	Age, sex, area of residence, smoking status, energy intake and alcohol consumption.	Participants in the largest quintile of consumption of ultra-processed foods were more likely to have metabolic syndrome (adjusted OR = 1.90; 95%CI: 1.14; 3.17) when compared to those in the lowest quintile.	Low
Nasreddine et al. [40] (2018)	Cross-sectional	Lebanese adults aged 18 years old or older (n = 302).	Participation of ultra-processed foods in the food's total energy.	Metabolic syndrome.	Age, sex, income, education, marital status, area of residence, physical activity, smoking status, BMI and energy intake.	The consumption of ultra-processed foods was not significantly associated with metabolic syndrome.	Low

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Lopes et al. [41] (2019)	Cross-sectional	Brazilian adults aged between 35 to 74 years old in 2008-2010 (n = 8,468).	Participation of ultra-processed foods in the food's total energy.	Serum levels of C-reactive protein.	Age, race/color, education, physical activity, smoking status and BMI.	Women in the highest tertile of consumption of ultra-processed foods had higher serum levels of C-reactive protein (adjusted coefficient: 1.14; 95%CI: 1.04; 1.24) when compared to those in the lowest tertile in the model adjusted for age, race/color, education, physical activity, smoking status. The association lost significance when adjusted in the model additionally adjusted for BMI (adjusted coefficient: 1.00; 95%CI: 0.92; 1.08). No association was found between men.	Mean
Montero-Salazar et al. [42] (2020)	Cross-sectional	Spanish adult men aged between 40 to 60 years old (n = 1,876)	Grams of ultra-processed food.	Coronary calcium score.	Age, marital status, education, smoking status, physical activity, sleep duration, serum cholesterol, blood pressure, diabetes, BMI, alcohol intake, fiber intake, cholesterol and total energy.	Men in the highest quartile of consumption of ultra-processed foods had a greater chance of high coronary calcium score (≥ 100) (adjusted OR = 2.0; 95%CI: 1.26; 3.16) when compared to those in the first quartile.	Mean

(continues)

Box 1 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Alonso-Pedrero et al. [43] (2020)	Cross-sectional	Spanish adults aged between 57 and 91 years old (n = 886)	Ultra-processed food portions.	Short telomeres.	Age, sex, education, smoking status, physical activity, television time, family history of diabetes and cardiovascular diseases, prevalence of cancer, diabetes and dyslipidemia, BMI, energy intake.	Participants in the largest quartile of consumption of ultra-processed foods were more likely to have short telomeres (adjusted OR = 1.82; 95%CI: 1.05; 3.22) when compared to those in the lowest quartile.	Low

95%CI: 95% confidence interval; BMI: body mass index; GDP: Gross Domestic Product; HR: harzard ratio; OR: odds ratio; PR: prevalence ratio; RR: relative risk.

a) Obesity and obesity-related indicators

In adults, the association between the consumption of ultra-processed foods and obesity or obesity-related indicators were examined in an randomized clinical trial (high methodological quality) [19], four cohort studies (high quality) [20,21,22,23], seven cross-sectional studies with national representativeness (five with mean [24,25,26,27,28] and two with low quality [29,30]), three local cross-sectional studies (two with mean [31,32] and one with low quality [33]) and three ecological studies (two with mean [34,35] and one with low quality [36]).

After adjusting for confounders, positive associations between the consumption of ultra-processed foods and overweight/obesity or the BMI in adults were demonstrated in the four cohort studies (NutriNet Santé, ELSA-Brasil, The Sun and UK Biobank) [20,21,22,23], in nine out of the ten cross-sectional studies [25,26,27,28,29,30,31,32,33] (five of which were representative samples from Brazil, Canada, United States, Australia and the United Kingdom [25,26,27,28,29]) and in the three ecological studies (which assessed exposure to the consumption of ultra-processed foods based on purchases or sales of these foods in different countries) [34,35,36]. The UK Biobank cohort study demonstrated a direct association between the consumption of ultra-processed foods and the percentage of body fat assessed by bioimpedance [22].

Crossover-type randomized clinical trial in adults conducted by the NIH showed an association between the exposure to a diet based on ultra-processed foods and obesity indicators. Its results showed that, when exposed to ad libitum diets with more than 80% of calories from ultra-processed foods, participants consumed, on average, 508Kcal/day more than when exposed to diets without ultra-processed foods and that, at the end of two weeks, participants increased 0.9kg in weight and 0.4kg in body fat by consuming the ultra-processed diet and decreased 0.9kg in weight and 0.3kg in body fat by consuming the non-ultra-processed diet. The ultra-processed and non-ultra-processed diets offered to the participants were matched in terms of the amount of energy, macronutrients, sugar, sodium and fiber [19].

After adjusting for confounders, there was a positive association between the consumption of ultra-processed foods in adults and the waist circumference in all studies in which this outcome was

assessed, including two cohort studies (ELSA-Brasil and UK Biobank) [20,22] and three cross-sectional studies with national representativeness (United States , United Kingdom and Australia) [26,27,28] and a local cross-sectional [32].

b) Metabolic risk markers

In adults, the association between the consumption of ultra-processed foods and hypertension was examined in a cohort study (high methodological quality) [37], metabolic syndrome in three cross-sectional studies (one with mean [38] and two with low [39,40]), serum levels of C-reactive protein under cross-sectional study (mean quality) [41], subclinical atherosclerosis in a cross-sectional study (mean quality) [42] and telomere length in a cross-sectional study (mean quality) [43].

After adjusting for confounders, The Sun cohort study found, in Spanish middle-aged adults, a positive association between the consumption of ultra-processed foods and the risk of developing hypertension [37].

After adjusting for confounders, a positive association between the consumption of ultra-processed foods and metabolic syndrome in adults was found in two out of three studies that assessed this outcome, those were the cross-sectional study with a sample from the *National Health and Nutrition Examination Survey* (NHANES) [38] and one local study with Canadian indigenous people [39].

A cross-sectional study with middle-aged Brazilian adults showed that, among women, after adjusting for sociodemographic characteristics, smoking status and physical activity, the consumption of ultra-processed foods was associated with higher levels of C-reactive protein; however, this association lost statistical significance with the inclusion of BMI in the model. Among men, there was no association between ingestion of ultra-processed foods and C-reactive protein [41]. A cross-sectional study with Spanish adult men demonstrated, after adjusting for confounders, an association between the consumption of ultra-processed foods and the coronary calcium score, which assesses subclinical atherosclerosis [42]. A cross-sectional study with Spanish adults demonstrated, after adjusting for confounders, an association between the consumption of ultra-processed foods and short telomeres, an aging biomarker [43].

- **Pregnant woman**

Box 2 describes the studies' main characteristics that assessed the association between the consumption of ultra-processed foods and the indicators related to obesity and metabolic risk markers in pregnant women.

a) Obesity and obesity-related indicators

In pregnant women, the association between the consumption of ultra-processed food and the obesity-related indicators was examined in two cohort studies (one with high methodological quality [44] and the other with mean [45]) and two cross-sectional studies (both with low quality [46,47]). After adjusting for confounders, the cohort study demonstrated, in pregnant women from the United States, that the participation of ultra-processed foods in the diet was associated with an increase in gestational weight gain (and higher values of thigh and subscapular folds and percentage of body adiposity of the newborn) [44]. A cohort study with Brazilian pregnant women demonstrated, after adjusting for confounders, that the consumption of ultra-processed foods in the 2nd and 3rd trimesters of pregnancy was positively associated with the average weight gain in the same period [45]. The two cross-sectional studies, both conducted in a medium-sized Brazilian city, demonstrate, after adjusting for confounders, a positive association of the consumption of ultra-processed foods with overweight/obesity in pregnant women [46,47].

Box 2

Characteristics of studies that assessed the association between the consumption of ultra-processed foods and obesity and obesity-related indicators and metabolic risk markers (gestational diabetes) in pregnant women.

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Rohatgi et al. [44] (2017)	Cohort	Pregnant women from the United States and their newborns in 2013/2014 (n = 45) (St. Louis Women's Health Center Study).	Participation of ultra-processed foods in the food's total energy.	Maternal gestational weight gain and thigh skin folds, subscapular skin folds and newborn's body fat.	In maternal outcomes: age, ethnicity, socioeconomic status, physical activity, weight, average energy intake/day and average fat intake/day. In the newborn's outcomes: maternal variables and gestational age at which neonatal measurements were conducted.	The consumption of ultra-processed foods was positively associated with maternal gestational weight (adjusted coefficient for the 1% increase in the consumption of ultra-processed foods: 1.3; 95%CI: 0.3; 2.4) and thigh skin fold (adjusted coefficient for a 1% increase in the consumption of ultra-processed foods: 0.22; 95%CI: 0.005; 0.400), subscapular skin fold (adjusted coefficient for a 1% increase in the consumption of ultra-processed foods: 0.14; 95%CI: 0.02; 0.30) and body fat percentage (adjusted coefficient for the 1% increase in the consumption of ultra-processed foods: 0.62; 95%CI: 0.04; 1.20) of the newborn.	High

(continues)

Box 2 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Gomes et al. [45] (2020)	Cohort	Brazilian pregnant women aged 18 years old or over in 2012/2013 (n = 259)	Participation of ultra-processed foods in the food's total energy.	Gestational weight gain.	Sex, age, education, socioeconomic classification, work situation outside the home, living with a partner, parity, race/color and pre-gestational BMI.	The consumption of ultra-processed foods in the 2nd and 3rd trimesters of gestation was positively associated with the average weight gain in the same period (adjusted coefficient for a 1% increase in the consumption of ultra-processed foods: 4.17; 95%CI: 0.55; 7.79).	Mean
Crivellenti et al. [46] (2019)	Cross-sectional	Brazilian pregnant women aged 20 years old or older in 2011/2012 (n = 754).	Participation of ultra-processed foods in the food's total energy.	Gestational overweight and obesity.	Age, education, physical activity, smoking status, family history of diabetes mellitus, gestational diabetes mellitus, gestational week, parity, BMI and energy intake.	Participants in the highest tertile of consumption of ultra-processed foods were more likely to be overweight (adjusted OR = 1.72; 95%CI: 1.10; 2.94) and obese (adjusted OR = 5.24; 95%CI: 2.80; 9.80) when compared to those in the lower tertile.	Low
Sartorelli et al. [47] (2019)	Cross-sectional	Brazilian pregnant women aged 20 years old or older in 2011/2012 (n = 785).	Participation of ultra-processed foods in the food's total energy.	Overweight, obesity and gestational diabetes mellitus.	Age, education, physical activity, smoking status, family history of diabetes mellitus, history of gestational diabetes mellitus, gestational week, parity, BMI and energy intake.	Participants in the highest tertile of consumption of ultra-processed foods were more likely to present gestational obesity (adjusted OR = 3.06; 95%CI: 1.27; 3.37) when compared to those in the first tertile.	Low

95%CI: 95% confidence interval; BMI: body massa index.

b) Metabolic risk markers

In pregnant women, a small cross-sectional study (low quality) carried out in a medium-sized city in Brazil assessed the association between the consumption of ultra-processed foods and gestational diabetes and found no significant results [47].

- **Children and adolescents**

Box 3 describes the studies' main characteristics that assessed the association of the consumption of ultra-processed foods with the indicators related to obesity and metabolic risk markers in children and adolescents.

a) Obesity and obesity-related indicators

In children and adolescents, the association between the consumption of ultra-processed foods and obesity-related indicators was examined in five cohort studies (three with high methodological quality [48,49,50], one with mean [51] and one with low [52] – the latter making only a cross-sectional analysis at two points of the cohort), in four small local cross-sectional studies [53,54,55,56] (all with low quality) and in a cross-sectional study with national representativeness of the adolescent population in Brazil (mean quality) [25].

After adjusting for confounders, a positive association between the consumption of ultra-processed foods and overweight/obesity or BMI's magnitude was demonstrated in the study with national representativeness of the adolescent population in Brazil [25]. A small cross-sectional study demonstrated, after adjusting for confounders, an association between the consumption of ultra-processed foods and excess weight in Brazilian schoolchildren [56]. A study of the Spanish birth cohort INMA (*Infancia y Medio Ambiente*) demonstrated that low intake of ultra-processed foods at 4 years old was associated with a lower z-score of BMI at 7 years old in a model adjusted for sociodemographic characteristics, but the association became "borderline" (p-value = 0,07) with the addition of the maternal BMI variable in the model [48]. A Pelotas (Rio Grande do Sul State, Brazil) birth cohort study in 2004 found an association between the increase in consumption of ultra-processed foods between 6 and 11 years old and the change in body fat content (assessed by air displacement plethysmography) in the same period [50].

The association between the consumption of ultra-processed foods and waist circumference was demonstrated in one of the two cohorts in which this outcome was assessed. After adjusting for confounders, a 4-year study that followed a cohort of children from 3 to 4 years old of low socioeconomic status demonstrated that the intake of ultra-processed foods at preschool-age was positively associated with an increase in waist circumference values from preschool-age to school-age [49].

b) Metabolic risk markers

In children and adolescents, studies assessed the association between the consumption of ultra-processed foods and blood pressure levels in a cohort study (high methodological quality) [48] and two local cross-sectional studies (both with low quality) [53,55], serum lipids in two cohort studies (high quality) [57,58] and two cross-sectional analysis nested in a cohort study (one with high quality [48] and one with low [52]), blood glucose in a cohort study (high quality) [49], metabolic syndrome in a cross-sectional study (low quality) [59] and urinary levels of 8-OHdG in a cross-sectional study (low quality) [60].

A study of the Spanish birth cohort INMA showed that low intake of ultra-processed foods at 4 years old was associated with lower values of diastolic blood pressure at 7 years old. No associations were found for this outcome in cross-sectional studies [48].

Box 3

Characteristics of studies that assessed the association between the consumption of ultra-processed foods and obesity and obesity-related indicators and metabolic risk markers (high blood pressure, lipid profile/dyslipidemia and blood glucose) in children.

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Bawaked et al. [48] (2020)	Cohort	Spanish children aged 4 to 7 years old between 2003-2008 (n = 1,480) (INMA).	Consumption of ultra-processed foods servings/day.	BMI, waist circumference, blood pressure and lipid profile.	Age, sex, maternal education, maternal age, pre-gestational maternal BMI, follow-up time and INMA sub-cohorts and baseline outcomes.	Participants in the first tertile of consumption of ultra-processed foods at 4 years old had a lower average of standardized diastolic blood pressure at 7 years old, when compared to those in the last tertile (adjusted coefficient: -0.15; 95%CI: -0.29; -0.01). Participants in the first tertile of consumption of ultra-processed foods had a mean BMI-for-age significantly lower than those in the last tertile in the analysis adjusted for the child's age, sex and length of follow-up (-0.12; 95%CI: -0.23; -0.02), but not in the model additionally adjusted for maternal education and BMI (-0.10; 95%CI: -0.20; 0.01).	High

(continues)

Box 3 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Costa et al.[49] (2019)	Cohort	Brazilian children aged 3-4 and 8 years old between 2001/2-2005/6 (n= 307).	Participation of ultra-processed foods in the food's total energy.	BMI-for-age, waist circumference, waist circumference due to height, skin folds (triceps and subscapular) and blood glucose.	Sex, family income, maternal education, birth weight, breastfeeding, screen time and pre-gestational maternal BMI.	The consumption of ultra-processed foods at preschool-age (3-4 years) was positively associated with an increase in waist circumference (adjusted coefficient for a 10% increase in the consumption of ultra-processed foods: 0.70; 95%CI: 0.10; 1.33) between preschool-age and school-age (7-8 years).	High
Costa et al.[50] (2020)	Cohort	Brazilians born in 2004 evaluated between 6 (n = 3,128) and 11 years old (n = 3,454) (Pelotas birth cohort in 2004).	Participation of ultra-processed foods in the total of food grams.	Body fat.	Skin color, age and maternal education, birth weight and sex (perinatal); screen time and energy consumption/ expenditure ratio (6- and 11-year follow-ups). Additional adjustments: other processing groups and total energy consumption (6- and 11-year follow-ups).	In the complete adjusted model, an increase of 100 grams in the contribution from ultra-processed foods to daily intake from 6 to 11 years old was associated with a gain of 0.14kg/m^2 in the fat mass index in the same period. Fifty-eight percent of the total effect of eating ultra-processed foods at 6 years old on the change in fat mass index from 6 to 11 years old was mediated by its caloric content.	High

(continues)

Box 3 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Cunha et al. [51] (2018)	Cohort	Brazilian adolescents enrolled in the first year of high school between 2010-2012 (n = 1,035) (ELANA).	Participation of ultra-processed foods in the food's total energy.	Trajectories of BMI and body fat.	Age, sex, type of school, physical activity and energy intake underreporting.	The consumption of ultra-processed foods was not significantly associated with the outcomes.	Mean
Gadelha et al. [52] (2019)	Cohort	Brazilian adolescents from 11 to 15 years old between 2008/2009-2012/2013 (n = 238).	Frequency score of the consumption of ultra-processed foods.	BMI-for-age, waist circumference, waist circumference due to height and lipid concentrations (total cholesterol, LDL, HDL and triglycerides).	Age, sex, parental education, physical activity, sedentary behavior and score of consumption of fresh and minimally processed foods.	The consumption of ultra-processed foods was not associated with the assessed outcomes.	Low
De Melo et al. [53] (2017)	Cross-sectional	Brazilian adolescents aged between 14 and 19 years old (n = 249).	Frequency score of the consumption of ultra-processed foods.	Overweight, high waist circumference and high blood pressure.	Age and sex.	The consumption of ultra-processed foods was not associated with the studied outcomes.	Low
Enes et al. [54] (2019)	Cross-sectional	Brazilian adolescents aged between 10 to 18 years old (n = 200).	Participation of ultra-processed foods in the food's total energy.	BMI-for-age, overweight, obesity and abdominal obesity.	Sex, age, race/color, socioeconomic status and physical activity.	The consumption of ultra-processed foods was not associated with the studied outcomes.	Low
D'Avilla et al. [55] (2017)	Cross-sectional	Brazilian adolescents aged between 12 and 19 years old in 2013/2014 (n = 784).	Energy consumption of ultra-processed foods.	Excess weight and blood pressure level.	Energy intake.	Adolescents with normal weight had a higher average consumption of ultra-processed foods (p-vale < 0.001) when compared to those with excess weight.	Low

(continues)

Box 3 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Lacerda et al. [56] (2020)	Cross-sectional	Brazilian schoolchildren between 8 and 12 years old (n = 260)	Participation of ultra-processed foods in the food's total energy.	Overweight.	Age, sex, age group, education, guardian's marital status and occupation, per capita income, consumption of school meals, consumption of food in front of the TV, screen time.	Overweight students were 2.05 (95%CI: 1.01; 4.20) times more likely to have higher consumption of ultra-processed foods (last quartile).	Low
Louzada et al. [25] (2015)	Cross-sectional	Brazilians aged 10-19 years old or older in 2008/2009 (n = 7,534).	Participation of ultra-processed foods in the food's total energy.	BMI, overweight and obesity.	Age, sex, race/color, income, education, region, urbanity, physical activity, smoking status, intake of fruits, vegetables and beans.	Participants in the largest quintile of consumption of ultra-processed foods had a higher mean BMI (adjusted coefficient: 0.84; 95%CI: 0.42; 1.42) and a greater chance of being overweight (adjusted OR = 1.52; 95%CI: 0.75; 3.07) and obese (adjusted OR = 2.74; 95%CI: 0.78; 9.60) when compared to those in the lowest quintile.	Mean

(continues)

Box 3 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Rauber et al. [57] (2015)	Cohort	Brazilian children aged 3-4 and 7-8 years old between 2001/2002-2005/2006 (n = 345).	Participation of ultra-processed foods in the food's total energy.	Changes in lipid concentrations (total cholesterol, LDL, HDL and triglycerides).	Sex, family income, maternal education, birth weight, BMI-for-age and energy intake at 7-8 years old.	The consumption of ultra-processed foods at preschool-age (3-4 years) was positively associated with an increase in total cholesterol (adjusted coefficient for a 1% increase in the consumption of ultra-processed foods: 0.430; 95%CI: 0.008; 0.853) and LDL (adjusted coefficient for a 1% increase in the consumption of ultra-processed foods: 0.369; 95%CI: 0.005; 0.733) between preschool-age and school-age (7-8 years).	High
Leffa et al. [58] (2020)	Cohort	Brazilian children at 3 and 6 years old between 2011/2002 and 2014/2005 (n = 308).	Participation of ultra-processed foods in the total of food grams.	Lipid concentrations (total cholesterol, LDL, HDL and triglycerides).	Sex, family income, birth weight, pre-gestational BMI, BMI-for-age at 3 years old, energy and fat intake at 3 years old.	Children in the last tertile of consumption of ultra-processed foods at 3 years old had higher levels of total cholesterol (adjusted β: 0.22mmol/L; 95%CI: 0.04; 0.39) and serum triglycerides at 6 years old (adjusted β: 0.11mmol/L; 95%CI: 0.01; 0.20) when compared to those in the lowest tertile.	High

(continues)

Box 3 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Tavares et al. [59] (2012)	Cross-sectional	Brazilian adolescents aged between 12 to 19 years old in 2006/2007 (n = 210).	Participation of ultra-processed foods in the total of food grams.	Metabolic syndrome.	Smoking status, family history of hypertriacyl-glycerolemia and energy intake.	Participants in the last tertile of consumption of ultra-processed foods had a higher prevalence of metabolic syndrome (adjusted PR: 2.48, p-value = 0.012).	Low
Edalati et al. [60] (2020)	Cross-sectional	Iranian adolescents aged between 13 to 19 years old from the Karaj city, Iran (n = 139)	Daily grams of ultra-processed foods.	Urinary levels of 8-hydroxy-2'-deoxygua-nosine (8-OHdG).	Sex, age, physical activity, BMI, energy intake, consumption of whole grains, nuts and legumes, ratio between the ingestion of unsaturated and saturated fatty acids and Mediterranean dietary score.	Adolescents in the highest tertile of consumption of ultra-processed foods had higher urinary levels of 8OHdG when compared to those in the lowest tertile (trend p-value = 0.004).	Mean
Canella et al. [61] (2014) *	Ecological	Brazilian population of all ages 2008/2009 (n = 190,159).	Participation of ultra-processed foods in the total energy available for consumption at home.	BMI and prevalence of overweight and obesity.	Proportion of women, elderly people and children in the stratum, income, region, family configuration, out-of-home expenses and complementary calories, including calories from processed foods.	The ultra-processed foods availability in the household was positively and significantly associated with the mean BMI and the prevalence of overweight and obesity in the households. Participants in the largest quartile of consumption of ultra-processed foods were 37% more likely to have obesity than those in the lower quartile.	Mean

95%CI: 95% confidence interval; BMI: body mass indez; ELANA: *Longitudinal Study of Adolescent Nutritional Assessment*; INMA: *Infancia y Medio Ambiente*; OR: odds ratio; PR: prevalence ratio.

* Study with adults and children.

After adjusting for confounders, a 4-year study that followed a cohort of children from 3 to 4 years old of low socioeconomic status demonstrated that the intake of ultra-processed foods at preschool-age was associated with increases in serum cholesterol and LDL-cholesterol in preschool-age to school-age. After adjusting for confounders, a cohort study showed that the intake of ultra-processed foods at 3 years old was positively associated with serum levels of total cholesterol and triglycerides at 6 years old [58]. No associations were found for this outcome in cross-sectional studies [57]. No association was found between the consumption of ultra-processed foods and blood glucose [49].

A study with adolescents between 12 and 19 years old in the city of Rio de Janeiro, Brazil, found a positive cross-sectional association between the consumption of ultra-processed foods and the metabolic syndrome [59].

A study with Iranian adolescents between 13 to 19 years old found, after adjusting for confounders, a cross-sectional association between the consumption of ultra-processed foods and urinary levels of 8-OHdG, an oxidative DNA damage marker [60].

Finally, an ecological study conducted with a survey of Brazilian family budgets showed, after adjusting for confounders, that the availability of ultra-processed foods at home was positively associated with the mean BMI value and the prevalence of overweight and obesity among its residents of all ages [61].

Cardiovascular diseases, type 2 diabetes, cancer, asthma and mortality

Box 4 describes the studies' main characteristics that assessed the association between the consumption of ultra-processed foods, cardiovascular diseases, type diabetes, cancer and mortality in adults and asthma in children.

- **Adults**

a) Cardiovascular diseases

The association between the consumption of ultra-processed foods and cardiovascular diseases was examined in a NutriNet Santé cohort study of French adults (high methodological quality). After adjusting for confounders, the consumption of ultra-processed foods was associated with a higher incidence of cardiovascular disease in general and for the subgroups of coronary heart disease and cerebrovascular diseases [62].

b) Type 2 diabetes

The association between the consumption of ultra-processed foods and type 2 diabetes in adults was examined in two cohort studies (high methodological quality). Analysis of the NutriNet Santé [63] and UK Biobank [64] cohorts demonstrated associations (after adjusting for confounders) between the consumption of ultra-processed foods and the incidence of type 2 diabetes.

c) Cancer

The association between the consumption of ultra-processed foods and general, prostate, colorectal and breast cancer in adults was examined in a cohort study (high methodological quality) [65] and breast and prostate cancer also in two case-control studies (mean and low quality, respectively) [66,67].

After adjusting for confounders, a study carried out in the NutriNet Santé cohort showed direct associations for general and breast cancer (but not for prostate and colorectal cancer) [65]. A hospital-based case-control study conducted in Brazil showed that participants with breast cancer had a higher intake of ultra-processed foods when compared to those in the control group (non-cancer patients from the same hospital) [66].

Box 4

Characteristics of studies that assessed the association between the consumption of ultra-processed foods and cardiovascular diseases, type 2 diabetes, cancer, asthma and all-cause mortality in children and adults.

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Srour et al. [62] (2019)	Cohort	French adults aged 18 years old or older with a mean follow-up of 5.2 years between 2009-2018 (n = 105,159) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	Incidence of cardiovascular diseases and coronary heart disease.	Age, sex, education, physical activity, smoking status, family history of cardiovascular diseases and type 2 diabetes at baseline, dyslipidemia, hypertension, hyper-triglyceridemia and treatment for these conditions, BMI, energy intake, alcohol consumption, intake of sugar, fat, saturated fatty acid and sodium, consumption of sugary products, processed red meat, drinks and sauces and number of 24-hour dietary records.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of cardiovascular disease (adjusted HR = 1.23; 95%CI: 1.04; 1.45) when compared to those in the lowest quartile.	High
Srour et al. [63] (2020)	Cohort	French adults aged 18 years old or older with a mean follow-up of 6 years between 2009-2019 (n = 104,707) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	Incidence of type 2 diabetes.	Age, sex, education, physical activity, smoking status, family history of cardiovascular disease, dyslipidemia, hypertension and hyper-triglyceridemia and treatment for these conditions, weight change during the follow-up BMI, energy intake, alcohol consumption and number of 24-hour dietary records.	The consumption of ultra-processed foods was associated with a higher risk of developing type 2 diabetes (adjusted HR associated with a 10% increase in the consumption of ultra-processed foods = 1.13; 95%CI: 1.01; 1.27).	High

(continues)

Box 4 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Levy et al. [64] (2021)	Cohort	British adults aged 40 to 69 years old with a mean follow-up of 5.4 years between 2007-2019 (n = 21,730) (UK Biobank).	Participation of ultra-processed foods in the total of food grams.	Incidence of type 2 diabetes.	Age, sex, ethnicity, socioeconomic index, physical activity, smoking status, family history of type 2 diabetes, overweight at baseline and energy intake.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of type 2 diabetes (adjusted HR = 1.44; 95%CI: 1.04; 2.02) when compared to those in the lowest quartile.	High
Fiolet et al. [65] (2018)	Cohort	French adults aged 18 years old or older with a mean follow-up of 5 years between 2009-2013 (n = 104,980) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	Incidence of all types of cancer and breast, prostate and colorectal cancer.	Age, sex, education, physical activity, smoking status, family history of cancer, number of children, menopause, hormonal treatment for menopause and use of baseline oral contraception, height, BMI, energy intake (without alcohol), alcohol consumption, intake of lipids, sodium and carbohydrates, western dietary pattern and number of 24-hour dietary records.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of all types of cancer (adjusted HR = 1.23; 95%CI 1.08; 1.40) and post-menopausal breast cancer (adjusted HR = 1.38, 95%CI: 1.05; 1.81) when compared to those in the lowest quartile.	High
Queiroz et al. [66] (2018)	Case-control	Brazilian women with an average age of 53.1 years old in 2015 (n = 118).	Regular consumption of ultra-processed foods (five or more times a week).	Breast cancer.	BMI and energy intake.	Participants with cancer had a higher regular consumption of ultra-processed foods compared to those in the control group (adjusted OR = 2.35; 95%CI: 1.08; 5.12).	Mean

(continues)

Box 4 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Trudeau et al. [67] (2020)	Case-control	Canadian men under the age of 76 years old between 2005 and 2009 (n = 1,919).	Consumption frequency of ultra-processed foods.	Prostate cancer.	Age, education, ethnicity, marital status, family history of prostate cancer and time since the last screening for prostate cancer.	No significant association was found between the consumption of ultra-processed foods and prostate cancer.	Low
Kim et al. [68] (2019)	Cohort	Adults from the United States aged 20 years old or older with a mean follow-up of 19 years between 1988-1994 (n = 11,898) (NHANES III).	Consumption of ultra-processed foods servings/day.	Mortality from cardiovascular disease and all-causes.	Age, sex, ethnicity, poverty level, education, physical activity, smoking status, high blood pressure, total cholesterol, glomerular filtration rate, BMI, energy intake and alcohol consumption.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of all-cause mortality (adjusted HR = 1.30; 95%CI: 1.08; 1.57) when compared to those in the lowest quartile. No association was found with deaths from cardiovascular disease (adjusted HR = 1.13; 95%CI: 0.74; 1.71).	High

(continues)

Box 4 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Rico-Campà et al. [69] (2019)	Cohort	Spanish adults aged 20 years old or older with a mean follow-up of 10.4 years between 1999-2014 (n = 19,899) (The Sun).	Consumption of ultra-processed foods servings/ day (adjusted for energy).	All-cause mortality.	Age, sex, education, marital status, physical activity, smoking status, family history of cardiovascular disease, presence of cardiovascular disease, cancer or diabetes, hypertension, hyper-cholesterolemia or depression at baseline, cumulative exposure to smoking throughout life, following a special diet at baseline, BMI at baseline, energy intake, alcohol consumption and snacks consumption between meals.	Participants in the highest quartile of consumption of ultra-processed foods had a higher risk of all-cause mortality (adjusted HR = 1.62; 95%CI: 1.13; 2.33) when compared to those in the lowest quartile.	High
Schnabel et al. [70] (2019)	Cohort	French adults aged 45 years old or older with a mean follow-up of 7.1 years between 2009-2017 (n = 44,551) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	All-cause mortality.	Age, sex, income, education, marital status, place of residence, physical activity, smoking status, first degree family history of cancer or cardiovascular diseases, BMI, energy intake, alcohol consumption, period of dietary record and number of dietary records.	The consumption of ultra-processed foods was associated with a higher risk of all-cause mortality (adjusted HR associated with a 10% increase in the consumption of ultra-processed foods = 1.14; 95%CI: 1.04; 1.27).	High

(continues)

Box 4 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Blanco-Rojo et al. [71] (2019)	Cohort	Spanish adults aged 18 years old or older with a mean follow-up of 7.7 years between 2008-2016 (n = 11,898) (ENRICA).	Participation of ultra-processed foods in the food's total energy.	All-cause mortality.	Age, sex, education, living by themselves, physical activity, smoking status, time watching TV, time performing other sedentary activities, number of medications/day, presence of chronic conditions and alcohol consumption.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of all-cause mortality (adjusted HR = 1.44; 95%CI: 1.01; 2.07) when compared to those in the lowest quartile.	High
Zhong et al. [72] (2021)	Cohort	Adults from the United States aged between 55 and 74 years old with a mean follow-up of 13.5 years between 1993 and 2015 (n = 91,891) (*PLCO Cancer Screening Trial*).	Consumption of ultra-processed foods servings/day.	Mortality from cardiovascular disease.	Age, sex, race, education, marital status, aspirin use, smoking status, history of hypertension, diabetes, physical activity, BMI, alcohol consumption and total energy consumption.	Participants in the largest quintile of consumption of ultra-processed foods had a higher risk of mortality from cardiovascular diseases (adjusted HR = 1.52; 95%CI: 1.39; 1.67), heart diseases (adjusted HR = 1.70; 95%CI: 1.52; 1.89). No association was found with deaths from cerebrovascular diseases (adjusted HR = 1.00; 95%CI: 0.80; 1.23).	High

(continues)

Box 4 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Azeredo et al. [73] (2020)	Cohort	Brazilian adolescents born in 2004 assessed between 6 and 11 years old (n = 2,190) (Pelotas birth cohort 2004).	Participation of ultra-processed foods in the food's total energy.	Incidence of wheezing, asthma and severe asthma.	Sex, family income, parental smoking up to the age of 6 years old, maternal variables (age, race/color, education, parity, smoking during pregnancy, perinatal asthma), energy requirement estimates, energy consumption.	The consumption of ultra-processed foods at 6 years old was not associated with asthma (adjusted OR = 0.84, 95%CI: 0.58; 1.21), severe asthma (adjusted OR = 1.12; 95%CI: 0.62; 2.03) or wheezing in the chest (adjusted OR = 0.85; 95%CI: 0.54; 1.34) at 11 years old.	High
Melo et al. [74] (2018)	Cross-sectional	Ninth grade students from Brazilian public and private schools in 2012 (n = 109,104).	Frequency score of the consumption of ultra-processed foods.	Asthma and wheezing.	Age, sex, maternal education, type, region and urban area of the school, physical activity, parental smoking, smoking in the last 30 days and alcohol consumption in the last 30 days.	Participants in the largest quintile of consumption of ultra-processed foods were more likely to have asthma (OR = 1.27; 95%CI: 1.15; 1.41) or wheezing (OR = 1.42; 95%CI: 1.35; 1.50) when compared to those in the smallest quintile.	Mean
Elias et al. [75] (2019)	Cross-sectional	Ninth grade students from Brazilian public and private schools in 2012 (n = 106,983).	Frequency score of the consumption of ultra-processed foods.	Active asthma.	Region of residence and diagnosis of past asthma.	Participants with higher consumption of ultra-processed foods were more likely to experience wheezing (adjusted OR = 1.16; 95%CI: 1.11; 1.19) when compared to those with lower consumption.	Mean

95%CI: 95% confidence interval; BMI: body mass index; ENRICA: *Study on Nutrition and Cardiovascular Risk in Spain*; HR: harzard ratio; NANHES: *National Health and Nutrition Examination Survey*; OR: odds ratio.

d) Mortality

The association between the consumption of ultra-processed foods and all-cause mortality was assessed in four cohort studies (high methodological quality) [68,69,70,71] and mortality from cardiovascular diseases was studied in two cohort studies (high methodological quality) [68,72]. After adjusting for possible confounders, analysis of the NHANES III [68] follow-up study, and of The Sun study [69], NutriNet Santé [70] and *Study on Nutrition and Cardiovascular Risk in Spain* (ENRICA) [71] cohorts found dose-response associations between the consumption of ultra-processed foods and the risk of all-cause death. After adjusting for possible confounders, association and dose-response between the consumption of ultra-processed foods and the risk of death from cardiovascular diseases was found in the *PLCO Cancer Screening Trial* [72] study, but not in the NHANES III [68] follow-up study.

- **Children**

a) Asthma or wheezing

The association between the consumption of ultra-processed foods and asthma or wheezing was assessed in adolescents in a cohort study (high methodological quality) [73] and two cross-sectional studies with national representativeness samples (both with medium quality) [74,75].

A Pelotas birth cohort study in 2004 found no association between the consumption of ultra-processed foods at 6 years old and the occurrence of wheezing or asthma at 11 years old [73]. The two cross-sectional studies were carried out with a representative sample of Brazilian adolescents from the 9th grade. After adjusting for possible confounders, they found dose-response associations between an ultra-processed food consumption score and the occurrence of asthma and wheezing [74, 75].

Frailty, gastrointestinal diseases and depression

Box 5 describes the studies' main characteristics that assessed the association between the consumption of ultra-processed foods and frailty and gastrointestinal diseases in adults and depression in adults and pregnant women.

- **Adults**

a) Frailty

The association between the consumption of ultra-processed foods and frailty was examined in a cohort study of Spaniards with 60 years old (high methodological quality). After adjusting for confounders, the consumption of ultra-processed foods was associated with a higher incidence of frailty [76].

b) Gastrointestinal diseases

The association between the consumption of ultra-processed foods and gastrointestinal disorders in adults was examined in a cohort study (high methodological quality) [77] and a cross-sectional study (mean quality) [78].

A study carried out with the French cohort NutriNet Santé showed no association between the consumption of ultra-processed foods and the incidence of inflammatory bowel diseases after adjusting for confounders (only in the gross analysis) [77]. A cross-sectional study demonstrated, after adjusting for confounders, the association with the occurrence of irritable bowel syndrome and functional dyspepsia [78].

Box 5

Characteristics of studies that assessed the association between the consumption of ultra-processed foods and depression, frailty and gastrointestinal diseases in adults and pregnant women.

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Sandoval-Insausti et al. [76] (2019)	Cohort	Spanish elderly people aged 60 years old or older with a mean follow-up of 3.5 years between 2008-2012 (n = 1,822) (ENRICA).	Participation of ultra-processed foods in the food's total energy.	Incidence of frailty.	Age, sex, education, marital status, smoking status, diagnosis of chronic respiratory disease, coronary heart disease, stroke, osteoarthritis/ arthritis, cancer and depression with treatment, number of medications used and previous consumption of alcohol.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of frailty (adjusted OR = 3.67; 95%CI: 2.00; 6.73) when compared to those in the lowest quartile.	High
Vasseur et al. [77] (2020)	Cohort	French adults aged 18 years old or older with a mean follow-up of 2.3 years between 2009-2016 (n = 105,832) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	Incidence of inflammatory bowel diseases.	Age, sex, income, education, marital status, place of residence, physical activity, smoking status, use of hormonal contraception, BMI, energy intake, dietary pattern derived from the analysis of main components and number of 24-hour dietary records.	Participants in the highest tertile of consumption of ultra-processed foods had a higher risk of having inflammatory bowel disease (gross RR = 1.81; 95%CI: 1.05; 3.12) when compared to those in the lowest tertile in the gross analysis. The trend did not remain significant after adjusting for possible confounding factors.	High

(continues)

Box 5 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Schnabel et al.[78] (2018)	Cross-sectional	French adults aged 18 years old or older in 2009 (n = 33,343).	Participation of ultra-processed foods in the total of food grams.	Functional gastrointestinal disorders (irritable bowel syndrome, functional constipation, constipation, functional diarrhea and functional dyspepsia).	Age, sex, income, education, marital status, area of residence, physical activity, smoking status, BMI, time of dietary records, time between dietary questionnaires' adherence to national nutritional recommendations, energy intake.	Participants in the largest quartile of consumption of ultra-processed foods were more likely to have irritable bowel syndrome (adjusted OR = 1.25; 95%CI: 1.12; 1.39) and functional dyspepsia (adjusted OR = 1.25; 95%CI; 1.05; 1.47) when compared to those in the lowest quartile.	Mean
Adjibade et al.[79] (2019)	Cohort	French adults aged 18 years old or older with a mean follow-up of 5.4 years between 2009-2018 (n = 26,730) (NutriNet Santé).	Participation of ultra-processed foods in the total of food grams.	Incidence of depressive symptoms.	Age, sex, monthly family income, education, marital status, occupation, area of residence, physical activity, BMI, energy intake (without alcohol), alcohol consumption and number of 24-hour dietary records.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of presenting depressive symptoms (adjusted HR = 1.30; 95%CI: 1.15; 1.47) when compared to those in the lowest quartile.	High

(continues)

Box 5 (continued)

AUTHOR (YEAR)	STUDY DESIGN	STUDY PARTICIPANTS	EXPOSURE	HEALTH OUTCOME	CONTROL VARIABLES	KEY FINDINGS	QUALITY
Gómez-Donoso et al. [80] (2019)	Cohort	Spanish middle-aged adults with a mean follow-up of 10.3 years between 1999-2014 (n = 14,907) (The Sun).	Participation of ultra-processed foods in the total of food grams.	Incidence of depression.	Age, sex, education, marital status, physical activity, smoking status, living by themselves, employment status, health care career, weekly working hours, self-perceived levels of competitiveness, anxiety and dependence at baseline, BMI at baseline, energy intake, adherence to the Mediterranean dietary.	Participants in the largest quartile of consumption of ultra-processed foods had a higher risk of depression (adjusted HR = 1.33; 95%CI 1.07; 1.64) when compared to those in the lowest quartile.	High
Badanai et al. [81] (2019)	Cross-sectional	Brazilian pregnant women aged 20 years old or older in 2011/2012 (n = 784).	Participation of ultra-processed foods in the food's total energy.	Depressive symptoms or sadness in pregnancy.	Age, education, marital status, physical activity, smoking status, hours of sleep, gestational week at the time of the interview, pre-gestational BMI, energy intake and alcohol consumption.	Participants in the highest tertile of consumption of ultra-processed foods were more likely to experience depression or sadness (adjusted OR = 2.39; 95%CI: 1.29; 4.41) when compared to those in the lowest tertile.	Low

95%CI: 95% confidence interval; BMI: body mass index; ENRICA: *Study on Nutrition and Cardiovascular Risk in Spain*; HR: harzard ratio; OR: *odds ratio*; RR: relative risk.

c) Depression

The association between the consumption of ultra-processed foods and depression/depressive symptoms in adults was examined in two cohort studies (high methodological quality). Results of studies carried out in the NutriNet Santé [79] and The Sun [80] cohort showed associations (after adjusting for confounders) between the consumption of ultra-processed foods and the incidence of depression.

The overall evidence quality was assessed as high for the association between the consumption of ultra-processed foods and obesity and mortality indicators, moderate for type 2 diabetes and depression and low for the other outcomes.

- **Pregnant woman**

a) Depression

In pregnant women, a cross-sectional study (low methodological quality) carried out in a medium-sized city in Brazil showed, after adjusting for confounders, a positive association between the consumption of ultra-processed foods and symptoms of depression [81].

Discussion

This review described the results of several studies that showed the association between the consumption of ultra-processed foods and some non-communicable diseases and their risk factors. The evidence seems particularly consistent with regard to obesity in adults, whose association with the consumption of ultra-processed foods has been demonstrated, with dose-response effect, in cross-sectional studies with representative samples from five countries (United States, United Kingdom, Australia, Canada and Brazil), in four large cohort studies and in a randomized clinical trial. Large cohort studies have also shown an association between the consumption of ultra-processed foods and the risk of cardiovascular diseases, type 2 diabetes and breast cancer – even after adjusting for obesity. Two cohort studies also demonstrated an association between the consumption of ultra-processed foods and the incidence of depression. Additionally, four large cohort studies have described the association between the consumption of ultra-processed foods and all-cause mortality, the most important indicator of disease burden. Most of these studies were carried out in high-income countries and in adults. In children, studies are limited in number and methodological quality, although the available evidence suggests associations in the same direction. No studies that evaluated outcomes of non-chronic diseases were found.

Although several mechanisms are not completely elucidated, numerous characteristics of ultra-processed foods, determined by the highly processed nature of these foods, contribute to their role in disease risk.

Ultra-processed foods are convenient, practical and portable. They are generally developed to be consumed anywhere. Most of the time, they are sold as snacks, drinks or dishes ready or semi-ready for consumption and promoted by aggressive marketing strategies. Therefore, they are easily associated with ways of eating that induce excessive and "unnoticed" consumption of calories, in addition to replacing freshly made meals, based on fresh or minimally processed foods. Forde et al. [14] showed that people exposed to ultra-processed foods ate meals 50% faster than those exposed to non-ultra-processed foods and suggested that this would be an important mechanism to explain differences in energy consumption. Large portion sizes, a frequent feature in many ultra-processed foods, have also been associated with weight gain [82,83].

Ultra-processed foods have a higher energy density, more free sugar and saturated and trans fats, and less dietary fiber, protein, micronutrients and bioactive compounds, than non-ultra-processed foods, and its consumption is systematically associated with the deterioration of the nutritional quality of food [3,4,5,6,7,8,11,12]. It also induces high glycemic responses and have low satiety potential [13]. Its ingredients, which are mainly characterized by sugars and fats, added to cosmetic additives and processing techniques that use the destruction of the food matrix and the withdrawal of water, prevent its nutritional content from being transmitted accurately to the brain, affecting satiety control systems. Many of these additives, in particular thickeners and dyes, in addition to artificial sweeteners, have also been associated with metabolic changes [84,85,86,87]. Increasing evidence indicates that a large part of this mechanism may be associated with disturbances in intestinal microbiota homeostasis caused by the consumption of ultra-processed foods [17,88].

Finally, chemical compounds formed during manufacturing processes or released from the packaging materials of ultra-processed foods are also other mechanisms that explain the association between the consumption of ultra-processed foods and the occurrence of diseases. Acrylamide, acrolein and nitrosamine, contaminants present in thermal-treated processed foods, have been associated with an increased risk of cardiovascular diseases [89,90], neoplasia [91] and insulin resistance [92,93].

Bisphenol A – an industrial chemical used in some plastic packaging for ultra-processed foods – interferes with cellular pathways related to weight and glucose homeostasis and its intake has already been associated with an increased risk of obesity [94] and a number of chronic diseases [95]. Recent studies conducted with data from the population in the United States assessed at NHANES have shown that the consumption of ultra-processed foods was associated with a higher urinary concentration of bisphenols, phthalates and organophosphates, all endocrine disruptors used in industrial plastic packaging [15,16].

The findings of this study are even more relevant when we consider that, in the last decades, the consumption of ultra-processed foods has increased significantly and accelerated in several countries driven by recent changes in the food system [2]. Since the 1980s, economic policies enacted by global organizations supported by the most powerful governments have favored the phenomenal rise of ultra-processed food transnationals. These policies deregulated the industry, promoted the flow of capital, opened countries to foreign investment, allowed transnational companies to take over national companies and restricted national governments from introducing statutory policies to limit their consumption. Meanwhile, economic growth and the increase in the average income of some populations have made ultra-processed foods accessible to more people [96].

This study has limitations. It was observed that some original studies were more susceptible to bias, such as those that used food consumption data collection instruments subject to memory bias, or self-reported weight and height. The use of the quality assessment tool, however, was important to take into account these possible biases in the presentation of the results. Our study limited the search to articles available in the literature (without accessing "gray literature", conference proceedings or studies in progress). Thus, for many outcomes, for populations in low- and middle-income countries and for children and adolescents, we find few studies and of low methodological quality. Therefore, some results must be interpreted as not conclusive. On the other hand, this study used a comprehensive and rigorous research and selection strategy that identified studies from different designs carried out in different population subgroups. Although cross-sectional studies contribute less weight in the evaluation of the evidence totality, they are important in a scenario of few studies or in the absence of other available evidence. Thus, we believe that our results summarize the best current data on the association between the consumption of ultra-processed foods and health, also highlighting the gaps in knowledge that need further investigation.

The relevance of the NOVA classification is increasingly recognized, and, in recent years, it has been addressed in the recommendations of several international entities, such as the Food and Agriculture Organization of the United Nations (FAO) [97], the Pan American Health Organization (PAHO) [98] and the Lancet Commission on Obesity [99], in addition to national food guides [100]. The *Dietary Guidelines for the Brazilian Population*, published in 2014, was a pioneer in using this classification as the basis for its recommendations and brings as a golden rule that "*it is preferred fresh or minimally processed foods and their culinary preparations to ultra-processed foods*" [100].

In conclusion, our study described the results of several studies that demonstrated the impact of the consumption of ultra-processed foods on health, with particularly consistent evidence for obesity and other chronic non-communicable diseases and all-cause mortality in adults. Additionally, the review made it possible to identify gaps in the literature, namely studies with outcomes of non-chronic diseases (such as nutritional deficiencies), with children and adolescents and in populations from low- and middle-income countries. Despite this, these results have important implications, considering that the reduction in the consumption of ultra-processed foods by the populations can be reverted in important benefits.

Contributors

M. L. C. Louzada and C. S. Costa participated in the conception, analysis and interpretation of data and writing of the manuscript. T. N. Souza and G. L. Cruz were literature reviewers and contributed to the writing of the article. R. B. Levy e C. A. Monteiro contributed to the data interpretation and carried out a relevant critical review of the intellectual content.

Additional informations

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Resumo

O objetivo deste trabalho foi realizar uma revisão de escopo da literatura acerca da associação entre o consumo de alimentos ultraprocessados e desfechos em saúde. A busca foi realizada nas bases PubMed, Web of Science e LILACS. Foram elegíveis os estudos que avaliaram a associação entre o consumo de alimentos ultraprocessados identificados com base na classificação NOVA e os desfechos em saúde. O processo de revisão resultou na seleção de 63 estudos, os quais foram analisados em termos de qualidade com base em ferramenta do Instituto Nacional de Saúde dos Estados Unidos. Os desfechos encontrados incluíram indicadores de obesidade, marcadores de risco metabólico, diabetes, doenças cardiovasculares, câncer, asma, depressão, fragilidade, doenças gastrointestinais e mortalidade. A evidência foi particularmente consistente para obesidade (ou indicadores relacionados a ela) em adultos, cuja associação com o consumo de ultraprocessados foi demonstrada, com efeito dose-resposta, em estudos transversais com amostras representativas de cinco países, em quatro grandes estudos de coorte e em um ensaio clínico randomizado. Grandes estudos de coorte também encontraram associação significativa entre o consumo de alimentos ultraprocessados e o risco de doenças cardiovasculares, diabetes e câncer, mesmo após ajuste para obesidade. Dois estudos de coorte demonstraram associação do consumo de alimentos ultraprocessados com depressão e quatro estudos de coorte com mortalidade por todas as causas. Esta revisão sumarizou os resultados de trabalhos que descreveram a associação entre o consumo de alimentos ultraprocessados e as diversas doenças crônicas não transmissíveis e seus fatores de risco, o que traz importantes implicações para a saúde pública.

Alimentos Industrializados; Consumo de Alimentos; Doença Crônica; Revisão

Resumen

El objetivo de este estudio fue realizar una revisión de alcance de la literatura sobre la asociación entre el consumo de alimentos ultraprocesados y los resultados de salud. La búsqueda se realizó en las bases de datos PubMed, Web of Science y LILACS. Fueron elegibles los estudios que evaluaron la asociación entre el consumo de alimentos ultraprocesados identificados según la clasificación NOVA y los resultados de salud. El proceso de revisión resultó en la selección de 63 estudios, cuya calidad se analizó con base en una herramienta delo Instituto Nacional de Salud de Estados Unidos Los resultados encontrados incluyeron indicadores de obesidad, marcadores de riesgo metabólico, diabetes, enfermedad cardiovascular, cáncer, asma, depresión, fragilidad, enfermedad gastrointestinal y mortalidad. La evidencia fue particularmente consistente para la obesidad (o indicadores relacionados con ella) en adultos, cuya asociación con el consumo de alimentos ultraprocesados se demostró, con un efecto dosis-respuesta, en estudios transversales con muestras representativas de cinco países, en cuatro grandes estudios de cohortes y en un ensayo clínico aleatorizado. Grandes estudios de cohortes también encontraron una asociación significativa entre el consumo de alimentos ultraprocesados y el riesgo de enfermedades cardiovasculares, diabetes y cáncer, incluso después de ajustar la obesidad. Dos estudios de cohortes mostraron una asociación entre el consumo de alimentos ultraprocesados y la depresión y cuatro estudios de cohortes con mortalidad por todas las causas. Esta revisión resumió los resultados de estudios que describieron la asociación entre el consumo de alimentos ultraprocesados y las diversas enfermedades crónicas no transmisibles y sus factores de riesgo, lo que tiene importantes implicaciones para la salud pública.

Alimentos Industrializados; Consumo de Alimentos; Enfermedad Crónica; Revisión

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