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To cite this article: Talitha Silva Meneguelli, Jéssica Viana Hinkelmann, Helen Hermana Miranda Hermsdorff, M. Ángeles Zulet, J. Alfredo Martínez & Josefina Bressan (2020): Food consumption by degree of processing and cardiometabolic risk: a systematic review, International Journal of Food Sciences and Nutrition, DOI: [10.1080/09637486.2020.1725961](https://doi.org/10.1080/09637486.2020.1725961)

To link to this article: <https://doi.org/10.1080/09637486.2020.1725961>



Published online: 13 Feb 2020.



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RESEARCH ARTICLE



Food consumption by degree of processing and cardiometabolic risk: a systematic review

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ABSTRACT

Processed and ultra-processed foods (UPF) consumption has been associated with development of noncommunicable chronic diseases (NCD). This systematic review aims to summarise and discuss evidence of the relationship between food consumption according to degree of food processing and cardiometabolic risk. Data search was conducted in databases as PubMed, Bireme and Science Direct until July 2018. Studies have shown a positive association of UPF consumption with excess body weight, hypertension, dyslipidemia and metabolic syndrome features. However, disparities found in the studies analysed regarding dietary assessment, confounding factors and differences in food classifications makes comparisons between studies difficult. In conclusion, current evidences indicate the need to monitor UPF intake in global population. However, more studies are necessary to interpret better these associations with similar methodologies used in the studies. As well as longitudinal analyses can help to improve comparisons between outcomes and establish cause-effect relationship between UPF intake and cardiometabolic risk.

ARTICLE HISTORY

Received 9 December 2019
Revised 28 January 2020
Accepted 2 February 2020

KEYWORDS

Food intake; ultra-processed foods; obesity; cardiovascular disease

Introduction

Food processing consists of a modification in natural and integral form of the food, obtained through physical, thermal and chemical changes, with the aim of improving its palatability, texture, colour, taste, shelf life and nutritional quality (Monteiro et al. 2016). As food processing contributes to the increase in shelf life, also stand out the issues raised by processing in terms of food and nutritional security (Shahidi 2009; Adams and White 2015).

The latest update of the NOVA food classification system divides foods into four groups: unprocessed or minimally processed foods; processed culinary ingredients; processed foods; and ultra-processed foods (Monteiro et al. 2016). Processed foods are those that have addition of sugar, salt, oil or other processed culinary ingredients to a food in unprocessed or minimally processed foods group, and which mostly contain two to three ingredients. In turn, ultra-processed foods (UPF) have been defined as industrial formulations using five or more ingredients that aim to

improve the sensory attributes of foods using additives such as colourants, colour stabilisers, flavourings, and artificial sweeteners (Monteiro et al. 2019). When compared to other groups, UPF had a much higher amount of added sugar, sodium, saturated fat and trans fat (Louzada, Baraldi, et al. 2015; Monteiro, Cannon, et al. 2018; Tseng et al. 2018; Latasa et al. 2018).

UPF consumption has increased in recent years, mainly due to practicality for consumption and low cost (Juul and Hemmingsson 2015; Guo et al. 2017). In this sense, UPF sales increased by 43.7% worldwide and approximately 50% in Latin America in the period between 2000 and 2013 (PAHO 2015). Several studies developed in different countries as Brazil, Chile, Spain, Sweden, Canada and United Kingdom (UK) have shown high UPF consumption lead to nutritionally unbalanced diets and affect the risk for noncommunicable chronic diseases (NCD), such as excess weight, high blood pressure, dyslipidemias, elevated fasting glycaemia and diabetes (Monteiro et al.

2010b; Crovetto and Uauy 2012; Moubarac, Claro, et al. 2013; Martins et al. 2013; Moubarac, Martins, et al. 2013; Moubarac, Batal, et al. 2014; Rauber et al. 2015; Juul and Hemmingsson 2015; Mendonca et al. 2016). Even more worrying, recent studies have shown UPF consumption was associated with all causes mortality (Kim et al. 2019; Schnabel et al. 2019; Rico-Campà et al. 2019).

Given the importance of the theme in recent years, the lack of systematic reviews that addresses a discussion about the relationship between these kinds of foods and cardiometabolic risk factors, and recent evidence from a randomised controlled trial showing association between UPF intake and obesity (Hall et al. 2019); this review introduces an important issue on the topic. A food classification that categorises foods according to the extent and purpose of food processing has become of great scientific relevance specially to facilitate the understanding of the adverse health effects of these food groups (Moubarac, Parra, et al. 2014; Adams and White 2015; PAHO 2015; Monteiro et al. 2016). Overall, the objective of this systematic review was to summarise and discuss evidence of the relationship between food consumption, according to degree of food processing and cardiometabolic risk factors.

Material and methods

For this review, studies were identified by searching electronic databases (PubMed, Bireme and Science Direct) with the MeSH and DeCS terms up to July 2018. The following terms were used: “*minimally processed foods*”, “*processed foods*”, “*ultra-processed foods*”, “*ultraprocessed foods*”, “*obesity*”, “*overweight*”, “*cardiometabolic risk*”, “*hypertension*”, “*insulin resistance*”, “*diabetes*”, “*cholesterol*”, “*triglycerides*”, “*noncommunicable chronic disease*”, “*cardiovascular biomarkers*”. The association between these terms and expressions with the Boolean connectors (AND, OR) has been used.

The identification and selection of articles in all databases were carried out by two independent researchers. The initial selection was made based on the title and abstract. Then, information about the articles (authors, title, year of publication, study design, sample size, objective and main results) was entered in a spreadsheet so they could be selected by the researchers. To be eligible, articles were original and human studies, evaluating the food intake according to their degree of processing (exposure) and some cardiometabolic risk as obesity, diabetes, dyslipidemia,

hypertension, insulin resistance, cardiometabolic risk and NCD in general (outcome) were included, with no age group, country/region/ethnicity, language nor date restriction. Additionally, editorials, summaries of presentations to meetings, review articles, and studies that did not consider the association between the degree of food processing and some of the cardiometabolic risk factors were excluded. Also, articles using dietary patterns without using as criteria classification for degree of food processing (as exposure variable) were excluded.

Moreover, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to guide the writing of this systematic review. Methodological quality of observational studies included in this systematic review was evaluated using Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement in which consists of a checklist of 22 items (Vandenbroucke et al. 2014). All references were managed by reference manager software Mendeley Desktop Version 1.18.

A total of 3,043 articles were found by electronic database searching, and 2,040 titles and abstracts remained to be analysed after removing duplicates. Thus, reviewer 1 and 2 selected 20 and 21 articles, respectively, and one article was included by manual search. At the end, reviewers agreed to the exclusion of 6 (one of them being the same selected by both reviewers) because they used dietary patterns and did not degree of processing as a criterion for dividing the food groups. Finally, a total of 21 articles were selected for this systematic review, 15 of which had been selected by both reviewers (Figure 1).

Results

Study characteristics are presented in Tables 1–3, including potential confounders. Selected studies were performed in Brazil ($n=10$), Spain ($n=2$), USA ($n=2$), Guatemala ($n=1$), United Kingdom ($n=1$), Norway ($n=1$), Lebanon ($n=1$), Canada ($n=1$), Sweden ($n=1$), and another study that included nineteen European countries as Austria, Belgium, Croatia, Cyprus, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Portugal, Slovakia, Spain and UK ($n=1$). A total of two ecological, six longitudinal and 13 cross-sectional studies were included. The review covered not only different age-groups as children ($n=2$), adolescents ($n=4$), adults ($n=7$), pregnant women ($n=2$) and

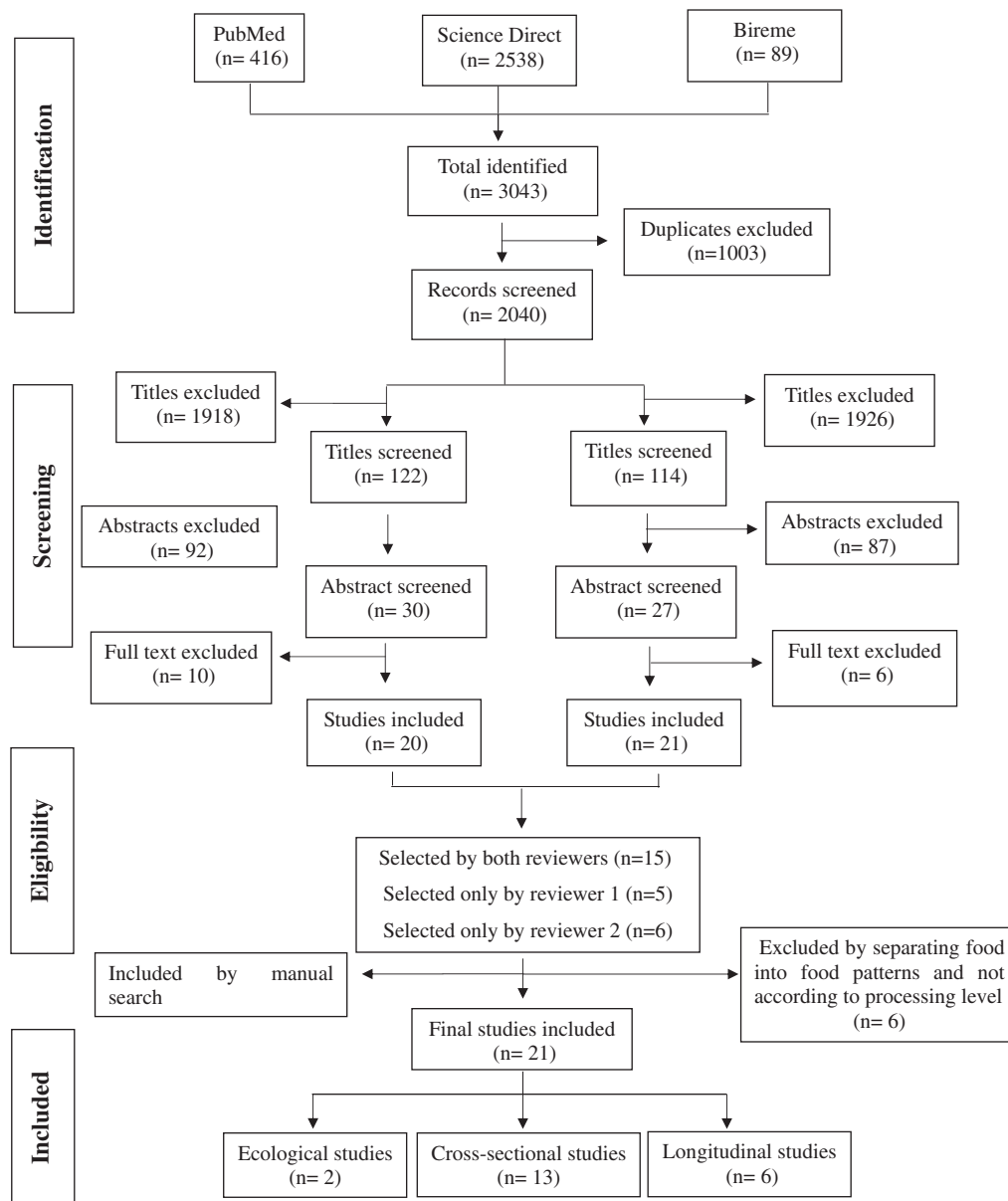


Figure 1. Flowchart of the steps followed to obtain the articles selected for this review.

mixed aged-groups ($n=1$), but also households ($n=5$).

Food consumption was assessed using 24-h dietary recall (R24h) ($n=5$), Food-frequency questionnaire (FFQ) ($n=11$), food diary ($n=1$), and household consumption and expenditure surveys ($n=4$). Regarding the classification of foods, 18 articles have used the NOVA classification proposed by Monteiro (Tavares et al. 2012; Canella et al. 2014; Adams and White 2015; Juul and Hemmingsson 2015; Louzada, Baraldi, et al. 2015; Rauber et al. 2015; Alves-Santos et al. 2016; Mendonca et al. 2016; Melo et al. 2017; D'Avila and Kirsten 2017; Djupegot et al. 2017; Mendonça et al. 2017; Rohatgi et al. 2017; Juul et al. 2018; Monteiro, Moubarac, et al. 2018; Nasreddine

et al. 2018; Silva et al. 2018), while two studies did not use the NOVA classification method (Asfaw 2011; Rinaldi et al. 2016) and another analysed dietary patterns in which the “Western pattern” was composed by processed and UPF according to NOVA classification (Cunha et al. 2018).

Regarding the association with cardiometabolic risk factors, 11 studies presented positive association of UPF with body weight (Asfaw 2011; Canella et al. 2014; Juul and Hemmingsson 2015; Louzada, Baraldi, et al. 2015; Mendonca et al. 2016; Djupegot et al. 2017; Rohatgi et al. 2017; Juul et al. 2018; Cunha et al. 2018; Monteiro, Moubarac, et al. 2018; Silva et al. 2018), other study pointed out a borderline positive association between pre-pregnancy BMI and variation

Table 1. Characteristics of ecological studies that evaluated the relationship between ultra-processed food consumption and cardiometabolic risk factors.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/ Outcome	Results	Authors/Year/ Country
National household budget surveys (1991–2008)	Living Costs and Food Survey / National Household Budget Surveys	NOVA classification Group 1: Unprocessed or minimally processed foods Group 2: Processed culinary ingredients Group 3: Processed foods Group 4: Ultra-processed foods	Countries' GDP per capita, squared GDP per capita, difference in years between the year of the obesity survey and the household food budget survey, measurement method of obesity (self-reported or directly measured), prevalence of physical inactivity and of smoking	Obesity	<ul style="list-style-type: none"> Each percentage point increase in the household availability of UPF increases 0.25 percentage points in obesity prevalence Linear regression coefficient (95% CI): 0.25 (0.05; 0.45) 	Monteiro et al. 2018 19 European countries
Households (n = 4000)	National Household Budget Surveys	NOVA classification Group 1: unprocessed/ minimally processed ingredients Group 2: processed culinary ingredients Group 3: processed food products and ultra-processed products	–	BMI/overweight and obesity	Obesity increased in parallel to UPF consumption from 1960 to 2010	Juul and Hemmingsson et al. 2015 Sweden

GDP: gross domestic product

in ultra-processed food intake ($\beta = 0.449$; p value = 0.06) (Alves-Santos et al. 2016), three studies found association with metabolic syndrome (Tavares et al. 2012; Rinaldi et al. 2016; Lavigne-Robichaud et al. 2018), one with hypertension (Mendonça et al. 2017) and another with lipid profile (Rauber et al. 2015), independently of age-group or country/region. Furthermore, one study showed a higher consumption of UPF in eutrophic adolescents compared to those who are overweight (D'Avila and Kirsten 2017). Besides that, further studies found association with other food groups, minimally processed foods consumption was inversely associated with body weight and with metabolic syndrome (Melo et al. 2017; Nasreddine et al. 2018). Also, one found inverse association with processed culinary ingredients consumption and body weight (Adams and White 2015). Excess body weight was assessed through elevated BMI in most studies that the outcome was excess body weight, only three of these also assessed abdominal obesity by waist circumference (WC) (Melo et al. 2017; Juul et al. 2018; Silva et al. 2018).

The mean STROBE score of all studies was 19.67 (minimum of 15 and maximum of 22), indicating good methodological quality of selected studies for this review. Studies have generally described any efforts to address potential sources of bias and reported the generalisation of the results (Asfaw 2011; Canella et al. 2014; Adams and White 2015; Juul and Hemmingsson 2015; Louzada, Baraldi, et al. 2015; Rinaldi et al. 2016; Alves-Santos et al. 2016; Melo et al. 2017; D'Avila and Kirsten 2017; Djupegot et al. 2017; Lavigne-Robichaud et al. 2018; Nasreddine et al. 2018; Juul et al. 2018; Silva et al. 2018). Although many studies have not calculated the sample size, they have presented many participants ($n = 811$ – $21,803$) (Asfaw 2011; Adams and White 2015; Juul and Hemmingsson 2015; Mendonca et al. 2016; Mendonça et al. 2017; Lavigne-Robichaud et al. 2018; Juul et al. 2018; Silva et al. 2018), unlike other studies where sample size has been smaller ($n = 45$ – 497) (Tavares et al. 2012; Rauber et al. 2015; Alves-Santos et al. 2016; Rinaldi et al. 2016; Djupegot et al. 2017; Melo et al. 2017; Rohatgi et al. 2017). In addition to use potential confounders, some articles also included effect modifiers (Adams and White 2015; Louzada, Martins, et al. 2015; Mendonca et al. 2016; Mendonça et al. 2017; Rohatgi et al. 2017; Cunha et al. 2018; Juul et al. 2018; Lavigne-Robichaud et al. 2018; Monteiro, Moubarac, et al. 2018). Finally, some studies did not mention the source of financing (Asfaw 2011; Tavares

Table 2. Characteristics of the cross-sectional studies that evaluated the relationship between ultra-processed food consumption and cardiometabolic risk factors.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/Outcome	Results	Authors/Year/ Country
Households (n = 21,803)	Living Standard Measurement Survey 2-week recall period (100 items)	Group 1: Unprocessed Group 2: Primary processed Group 3: Highly processed	Individual (sex, age, occupation, physical activity), household (income, education level of mothers and fathers, per capita value of meals consumed outside of the home, and per capita total food expenditure) and community level variables (location (urban/rural) and cluster level price of different food items)	BMI/overweight and obesity	<ul style="list-style-type: none"> A 10%-point increase in the share of partially processed foods from the total household food expenditure increases the BMI of family members by 3.95% A 10%-point increase in the share of highly processed food items increases the BMI of individual by 4.25% Regression coefficient (p-value): 0.395 ($p < 0.01$) / 0.425 ($p < 0.001$) 	Asfaw 2011 Guatemala
Adolescents (n = 210)	Semi-quantitative FFQ** (90 items)	NOVA classification Group 1: Unprocessed or minimally processed Foods Group 2: Processed culinary and food industry ingredients Group 3: Ultra-processed foods	Smoking, family hypertriglycerolaemia and energy intake	Metabolic syndrome	<ul style="list-style-type: none"> Higher intake of ultra-processed foods was associated with Mets Prevalence ratio (p-value): 4.50 (0.012) 	Tavares et al. 2012 Brazil
Adolescents (n = 784)	Semi-quantitative FFQ** (90 items)	NOVA classification Group 1: Unprocessed or minimally processed Foods Group 2: Processed foods Group 3: Ultra-processed foods	Daily caloric intake	BMI	<ul style="list-style-type: none"> The eutrophic adolescents present higher consumption of UPF when compared to those who are overweight. Median (p-value): 1,586.2 ($p < 0.001$) eutrophy / 1,213.8 ($p < 0.001$) excess weight 	D'Avila and Kirsten 2017 Brazil
Households (n = 55,970)	Household Budget Survey Records of all foods and drinks – 7 consecutive days	NOVA classification Group 1: Fresh or minimally processed foods Group 2: Processed culinary ingredients Group 3: processed or ultra- processed products	Socio-demographic characteristics, percentage of expenditure on eating out of home, and dietary energy other than that provided by processed and ultra-processed products	BMI/ excess weight and obesity	<ul style="list-style-type: none"> Higher household availability of ultra-processed products increases BMI and the prevalence of excess weight and obesity Linear regression coefficient (95% CI): 0.19 (0.14; 0.25) for BMI; 6.27 (4.15; 8.39) for excess weight; 3.72 (2.50; 4.94) for obesity 	Canella et al. 2014 Brazil
Households (n = 30,243)	Two R24h*	NOVA classification Group 1: Unprocessed, minimally or moderately processed foods Group 2: Processed foods Group 3: Ultra-processed foods	Age, sex, race, region, urban status, education, income, smoking status and physical activity level.	BMI/excess weight and obesity	<ul style="list-style-type: none"> Those in the highest quintile of UPF consumption had higher BMI and higher odds of being obese and excess weight Regression coefficient (95% CI): 0.94 (0.42; 1.47) for BMI / 1.98 (1.26; 3.12) of being obese / 1.26 (0.95; 1.69) excess weight 	Louzada et al. 2015 Brazil

(continued)

Table 2. Continued.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/Outcome	Results	Authors/Year/ Country
Children (n = 147)	Three R24h*	Processed food (cake mix, chips, frozen food, nuggets, chocolate drinks, pudding mix, noodles, microwave popcorn, sugar-based breakfast cereal cookies) Food with high sugar and fat content (chocolate, milk-based ice cream, sandwich cookies, wafers)	Sex, age and school	Triacylglycerol Glycaemia	<ul style="list-style-type: none"> Positive association of processed foods intake and glycaemia, and of processed food plus high sugar and fat content foods intake and glycaemia and triacylglycerol Linear regression coefficient (p-value): processed and glycaemia: 2.36 (0.045); processed plus high sugar and fat content and glycaemia and triacylglycerol 4.98 ($p \leq 0.05$) / 0.93 ($p \leq 0.05$) 	Rinaldi et al., 2016 Brazil
Adolescents (n = 249)	FFQ** (84 items)	NOVA classification Group 1: minimally processed foods Group 2: processed foods Group 3: ultra-processed foods	Sex and age	Blood pressure WC BMI	<ul style="list-style-type: none"> Consumption of minimally processed foods was inversely associated with excess weight Prevalence ratio (95% CI): 0.61 (0.39–0.96) 	De melo et al. 2017 Brazil
Adults (n = 2174)	Four-day food diary	NOVA classification Group 1: Unprocessed or minimally processed Foods Group 2: Processed ingredients Group 3: Ultra-processed food products	Gender, occupational social class, age and percentage of energy derived from alcohol	BMI/ overweight and obese	<ul style="list-style-type: none"> Processed ingredients consumption was inversely associated with body weight. Linear regression coefficient (95%CI): -0.09 (-0.16 to -0.03) 	Adams and White 2015 United Kingdom
Adults (n = 15 977)	Two R24h*	NOVA classification Ultra-processed foods Non-ultraprocessed foods	Age, sex, educational attainment, race/ethnicity, ratio of family income to poverty, marital status, smoking and physical activity level	BMI and WC/ excess weight and abdominal obesity	<ul style="list-style-type: none"> UPF consumption was positively associated with BMI and WC Linear regression coefficients (95%CI): 1.61 (1.11; 2.10) for BMI / 4.07 (2.94; 5.19) for WC 	Juul et al. 2018 USA
Adults (n = 320)	Semi-quantitative FFQ** (80 items)	NOVA classification Group 1: Unprocessed and minimally processed foods Group 2: Processed culinary ingredients Group 3: Processed foods Group 4: Ultra-processed food and drink products Dietary patterns: Ultra-processed foods Minimally processed/processed	Age, gender, marital status, area of residence, level of education, income, smoking status, physical activity and total energy intake	Metabolic syndrome	<ul style="list-style-type: none"> Minimally processed/processed pattern was inversely associated with metabolic syndrome Odds ratio (95%CI): 0.18 (0.04; 0.77) 	Nasreddine et al. 2018 Lebanon
One R24h*						(continued)

Table 2. Continued.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/Outcome	Results	Authors/Year/ Country
Adults (n = 811)		NOVA classification Group 1: Unprocessed and minimally processed foods Group 2: Processed culinary ingredients Group 3: Processed foods Group 4: Ultra-processed foods NOVA classification Ultra-processed foods: ultra-processed dinner products, sweet/salty snacks & soft drinks and fast foods away from home	Age, sex, area of residence, total daily dietary energy intake, alcohol and smoking status		<ul style="list-style-type: none"> Higher quintiles of energy contribution of UPF showed significant association with MetS (Odds ratio (95%CI): 1.90 (1.14; 3.17)) 	Lavigne-Robichaud et al. 2018 Canada
Adults (n = 497)	FFQ**		Sociodemographic correlates and weight status	BMI/excess weight	<ul style="list-style-type: none"> Overweight/obese participants were more likely to be categorised as high consumers of ultra-processed dinner products and fast foods than normal weight. Odds ratios (95% CI): 1.54 (1.04–2.30) for ultra-processed dinner / 3.40 (2.26–5.11) for fast food 	Djupegot et al. 2017 Norway
Age range 35–74 years (n = 8977)	Semi-quantitative FFQ** (114 items)	NOVA classification Group 1: Unprocessed or minimally processed foods Group 2: Processed culinary ingredients Group 3: Processed foods Group 4: Ultra-processed foods	Age, sex, race/skin colour, per capita family income, physical activity, smoking, hypertension, diabetes, Group 1 + Group 2 energy intake and total energy intake	BMI and WC/ overweight and obese	<ul style="list-style-type: none"> Individuals in the fourth quartile of UPF contribution presented a higher BMI and WC, and higher chances of being overweight, obese and having significantly increased WC, compared with those in the first quartile Linear regression coefficients (95% CI): 0.64 (0.33; 0.95) for BMI / 0.95 (0.17; 1.74) for WC Odds ratio (95% CI): 1.32 (1.15; 1.53) overweight / 1.43 (1.20; 1.72) obesity / 1.21 (1.01; 1.46) WC 	Silva et al. 2018 Brazil

*24-h dietary recall.

**Food-frequency questionnaire.

Table 3. Characteristics of the longitudinal studies that evaluated the relationship between ultra-processed food consumption and cardiometabolic risk factors.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/ Outcome	Results	Authors/Year/ Country
Pregnant women (n = 189)	Semi-quantitative FFQ** (82 items)	NOVA classification Group 1: Unprocessed or minimally processed food Group 2: Food industry ingredients Group 3: Processed food products Group 4: Ultra-processed food products	Age and BMI	Pre-pregnancy BMI	<ul style="list-style-type: none"> • Borderline positive association between pre-pregnancy BMI and the variation in UPF intake • Linear regression coefficient (95%CI): 0.449 (−0.019 to 0.918) 	Alves-Santos et al., 2016 Brazil
Pregnant women and neonate (n = 45)	One-month FFQ**	NOVA classification Group 1: Unprocessed or minimally processed food Group 2: Processed culinary ingredient Group 3: Processed food Group 4: Ultra-processed food	Maternal age, race, socioeconomic status, weight status, average daily energy and fat intake, and time spent in moderate physical activity. Gestational age at time of measurement was also used to evaluate the relationship with newborn body composition	Gestational weight Neonatal Thigh and Subscapular skinfold thickness	<ul style="list-style-type: none"> • A 1%-point increase in PEI-UPF*** increase 1.33 kg gestational weight and 0.22 mm in thigh skinfold, 0.14mm in subscapular skinfold and 0.62 percentage points of total body adiposity • Linear regression coefficient (95% CI): 1.3 (0.3; 2.4) for gestational weight gain / 0.2 (0.005; 0.4) for thigh skinfold / 0.1 (0.02; 0.3) for subscapular skinfold / 0.6 (0.04; 1.2) for body fat • Higher UPF consumption increases total cholesterol and LDL-C • Linear regression coefficient (95% CI): 0.430 (0.008; 0.853) for total cholesterol / 0.369 (0.005; 0.733) for LDL-C • At-home "Western pattern" (processed and ultra-processed) was positively associated with BMI. • Linear regression coefficient (p-value): 0.0006 (p < 0.0001) • Higher UPF consumption increase risk of developing overweight or obesity • Cox proportional hazard ratios (95% CI): 1.26 (1.10; 1.45) 	Rohatgi et al. 2017 USA
Children (n = 345)	Two R24h*	NOVA classification Group 1: unprocessed and minimally processed foods Group 2: processed culinary ingredients Group 3: processed and ultra-processed products Group 4: ultra-processed foods	Sex, group status in the early phase, birth weight, family income, maternal schooling, and BMIz score and total energy intake at age 7–8	Total cholesterol LDL-C	<ul style="list-style-type: none"> • Higher UPF consumption increases total cholesterol and LDL-C • Linear regression coefficient (95% CI): 0.430 (0.008; 0.853) for total cholesterol / 0.369 (0.005; 0.733) for LDL-C • At-home "Western pattern" (processed and ultra-processed) was positively associated with BMI. • Linear regression coefficient (p-value): 0.0006 (p < 0.0001) • Higher UPF consumption increase risk of developing overweight or obesity • Cox proportional hazard ratios (95% CI): 1.26 (1.10; 1.45) 	Rauber et al. 2015 Brazil
Adolescents (n = 1035)	FFQ** (72 items)	NOVA classification Group 1: unprocessed and minimally processed foods Group 2: processed culinary ingredients Group 3: processed food Group 4: ultra-processed food and drink products	Age, sex, education, race and at-home, mean <i>per capita</i> income of the sector and at-home dietary patterns.	BMI	<ul style="list-style-type: none"> • At-home "Western pattern" (processed and ultra-processed) was positively associated with BMI. • Linear regression coefficient (p-value): 0.0006 (p < 0.0001) • Higher UPF consumption increase risk of developing overweight or obesity • Cox proportional hazard ratios (95% CI): 1.26 (1.10; 1.45) 	Cunha et al. 2018 Brazil
Adults (n = 8451)	Semi-quantitative FFQ** (136 items)	NOVA classification Group 1: unprocessed and minimally processed foods Group 2: processed culinary ingredients Group 3: processed food Group 4: ultra-processed food and drink products	Age, sex, marital status, educational status, baseline BMI, physical activity, television watching, siesta sleep, smoking status, snacking between meals, following a special diet at baseline, and consumption of fruit and vegetables.	overweight and obesity	<ul style="list-style-type: none"> • Higher UPF consumption increase risk of developing overweight or obesity • Cox proportional hazard ratios (95% CI): 1.26 (1.10; 1.45) 	Mendonça et al. 2017 Spain

(continued)

Table 3. Continued.

Study population	Dietary assessment	Food classification	Confounding variables	Variables/ Outcome	Results	Authors/Year/ Country
Adults (n = 14790)	Semiquantitative FFQ** (136 items)	NOVA classification Group 1: unprocessed and minimally processed foods Group 2: processed culinary ingredients Group 3: processed food Group 4: ultra-processed food and drink products	Age, sex, physical activity, hours of television watching, baseline body mass index, smoking status, use of analgesics, following a special diet at baseline, family history of hypertension, hypercholesterolaemia, and alcohol consumption, total energy intake, olive oil intake, and fruits and vegetables consumption	Hypertension	<ul style="list-style-type: none"> Higher UPF consumption increases risk of developing hypertension Cox proportional hazard ratios (95% CI): 1.21 (1.06; 1.37) 	Mendonça et al. 2016 Spain

*24-h dietary recall.

**Food-frequency questionnaire.

***Percent of energy intake from ultra-processed foods.

et al. 2012; Rinaldi et al. 2016) and only one did not indicate the limitations (Asfaw 2011).

Discussion

Degree of food processing and cardiometabolic risk factors

Most studies showed a positive association of UPF consumption with excess body weight, hypertension, total cholesterol and low-density lipoprotein-cholesterol (LDL-C), and metabolic syndrome; all recognised cardiometabolic risk factors, regardless of age or ethnicity/nationality. UPF have traditionally high content of *trans* fats, saturated fats, sodium, sugars as well as low fibre and mono and polyunsaturated fats (Monteiro et al. 2010a; Monteiro et al. 2012; Moubarac, Martins, et al. 2013; PAHO 2015). In addition, this food group has higher energy density and glycemic response as well as lower satiety, compared to non-processed foods (Fardet 2016).

Both *trans* and saturated fats are commonly used by the food industry to improve the palatability and texture of the product, as well as prolong shelf life (Simplicio et al. 2017). However, they result in health damage, mainly due to the increase in LDL-C and the reduction of high-density lipoprotein-cholesterol (HDL-C) (Kennedy et al. 2009). Excessive saturated fat intake also may result in hypertrophy of adipocytes and general white adipose tissue enlargement (Muir et al. 2018). These fatty acids have important role on pro-inflammatory condition (Rocha et al. 2016; Rocha et al. 2017). All these outcomes may contribute to a higher cardiometabolic risk.

In relation to sodium, salt is widely used as a way of food conservation, aiming to extend the “shelf life” and improve taste. Thus, UPF and processed foods are manufactured by adding salt. According to the World Health Organisation (WHO), the average of salt intake is 9 to 12 grams/day, much higher than recommended (5 grams/day). The WHO still stands that 2.5 million of deaths could be prevented each year if global salt consumption was reduced to the recommended level. A study by Micha et al. (2017) in the United States showed 45.4% of deaths from cardiometabolic diseases in 2012 were related to diet, and among these, the highest number of deaths occurred due to high sodium intake (9.5%).

Finally, added sugars are commonly found in UPF and have gained prominence, since high intake increases the risk of obesity, type 2 diabetes mellitus, hypertriglyceridaemia and cancer (Fiolet et al. 2018; Juul et al. 2018; Silva et al. 2018). In fact, excess of

dietary fructose has resulted in impaired very low-density lipoprotein cholesterol (VLDL-C) catabolism and increased VLDL-C synthesis, with subsequent increase in triglycerides, LPL inactivation and high accumulation in visceral adipose tissue (Zakim 2009). In this context, high fructose corn syrup is of great utility in the food industry as sweetener of UPF, becoming a major source of added sugars. A study in the USA showed added sugars represented 21.1% of calories from UPF, values greatly than that found in processed foods (2.4%) and in unprocessed foods or minimally processed and processed culinary ingredients, all three together (3.7%) (Martinez Steele et al. 2016). In addition, enriched sugar food provides empty calories, without nutritional benefits, being associated with obesity when consumed in excess (Malik et al. 2006).

Furthermore, the present review found few studies have used WC as a cardiometabolic risk factor, considering those who used this marker for metabolic syndrome. Although BMI is a recognised adiposity indicator, extensively applied in epidemiological studies (Wellens et al. 1996; World Health Organization 2000), it does not consider body fat distribution (total vs central adiposity). In turn, WC is also an anthropometrical measurement of easy application, which presents stronger relation to cardiovascular risk and is also strongly related to the low-grade pro-inflammatory state (Klein et al. 2007; Hermsdorff et al. 2010; Hermsdorff et al. 2011; De Oliveira et al. 2014; Martínez-González et al. 2014; Pereira et al. 2015).

Moreover, the studies showed positive association of the processed and UPF consumption with cardiometabolic risk factors in children, adolescents and pregnant women, with an impact on the newborns, which means in the early stages of life. This situation is worrying, since the consumption of UPF is increasing among children and adolescents (Mallarino et al. 2013; Diethelm et al. 2014; Longo-Silva et al. 2017; Costa et al. 2018; Machado et al. 2019; Relvas et al. 2019; Vandevijvere et al. 2019) and childhood is a critical period for creating eating habits and promoting lifelong health (Ramos and Stein 2000; Stein et al. 2012). At this stage learning is an important factor in the acceptance of new foods and there is a direct relationship between the frequency of exposures and food preference (Beauchamp and Moran 1984). Sensory properties of foods with a higher energy content are preferred, indicating that higher energy content is sufficient to establish a preference (Birch and Davison 2001). However, excessive consumption of high-calorie foods may limit the intake of a varied diet as it

quickly quenches the child by preventing them from eating other foods (Giugliani and Victoria 2000). Consumption of UPF at this stage of life is already associated with an increase in lipid profile that can lead to lipogenesis, low density lipoprotein secretion and fatty acid accumulation in tissues and blood (Rauber et al. 2015). In addition, high sodium intake during childhood may lead to increased blood pressure in adulthood, as sodium excretion does not yet occur efficiently during this period (Fleischer Michaelsen et al. 2000).

Among those studies that did not observed association between UPF consumption and cardiometabolic risk, Adams and White (2015) and De Melo et al. (2017) presented inverse association of processed ingredients and minimally processed foods with body weight, respectively. In fact, the use of processed culinary ingredients is accompanied by the consumption of unprocessed or minimally processed foods, as they are used in home-made preparations, considered healthier. In addition, the last one found a relationship in the consumption of sausage and prevalence of overweight when analysing each food separately.

All these factors discussed lead us to reinforce the stimulus to reduce the consumption of UPF since the traditional dietary patterns of many countries are nutritionally superior to these products.

Dietary assessment, confounding variables and food classification

Despite the associations found some concerns are needed since different methodologies were used by the articles. We need to take this into consideration to compare associations among food consumption according to the degree of processing and cardiometabolic risk factors between studies. First, different dietary assessments used may make comparisons between studies difficult. Dietary assessment can be categorised as direct (e.g. R24h, food record and FFQ) or indirect (i.e. household consumption) methods. The first one collects primary dietary data from individuals and it is used to evaluate diet-disease associations. While the second one utilises secondary data for assessing diets and so, it cannot be directly obtained by primary dietary data from individuals to evaluate dietary intake or food consumption on an individual basis.

Both R24h and FFQ are retrospective methods which means it measures food intake from the past, while food record is a prospective method. Although R24h and food record are open methods which allows the inclusion of all reported foods (which is a positive

point when evaluating food consumption by degree of processing), more than one is required to represent a habitual intake. Already the FFQ allows to evaluate a habitual intake but presents a predefined list of foods, which cannot cover all the foods consumed by the respondent and may lead to underreporting, as well as does not give precise information on the estimated portion size consumed. As observed in the tables, food items from FFQ between studies ranged from 72 to 136 items. On the other hand, household consumption (indirect method) may be less precise than individual dietary assessment methods because it does not collect information about the distribution of foods among household members and also because it does not include food eaten away from home and foods wasted or given away.

The second point is the studies have adjusted for different confounding factors, which makes comparisons difficult. Several studies have not adjusted for total caloric intake which is associated with overweight and obesity. So, if those who eat more UPF also eat more calories, then the association reported for UPF is actually confounded for an established association between calories and obesity. Also, it is known that physical activity is a protective factor for the cardiovascular diseases' development. However, some studies did not use physical activity as a confounding factor, which may have attenuated the association between UPF consumption and cardiovascular risk factors. Finally, some studies included alcoholic drinks in the adjusted model, thus alcoholic drinks were excluded from the food processing framework.

Lastly, food consumption by degree of processing is a worldwide concern, as several organisations have already included in their food guide directions on reducing consumption of these kinds of food. Canada's Food Guide recommends people to limit consumption of highly processed foods and to prepare meals that contain little or no ingredients like sodium, sugar or saturated fat (Health Canada 2019). As well as World Cancer Research Fund, with its cancer prevention recommendations, advises population to reduce UPF. The consumption of these foods, high in calorie, increases the risk of weight gain or being overweight/obese. According to their report, body fatness and weight gain affects the risk of developing several cancers. (World Cancer Research Fund/American Institute for Cancer Research 2018). In Brazil, a new food classification called NOVA emerged in 2010, resulting in 3 different food groups: unprocessed and minimally processed foods (group 1); processed culinary or food industry ingredients

(group 2); ultra-processed foods (group 3) (Monteiro et al. 2010a). In 2014, this classification was updated and inserted in the dietary guidelines for the Brazilian population, containing 4 groups: unprocessed and minimally processed foods (group 1); oils, fats, salt and sugars (group 2); processed foods (group 3); ultra-processed foods (group 4) (Martins et al. 2014). In 2016, it was updated again (Monteiro et al. 2016). Finally, an article has been published to facilitate the understanding of what UPF are (Monteiro et al. 2019).

Due to the modifications and updates made over the years, although most studies in this review have used the NOVA classification, caution is required in interpreting some associations because some foods are included or excluded from UPF-group what make association analysis difficult. It is worth highlighting some foods and in which groups they were included. In the study by Alves-Santos et al. (2016) flour was classified in the unprocessed or minimally processed food, while alcoholic beverages were classified in the ultra-processed food group. In another study by D'Avila and Kirsten (2017), foods like oils, fats, flours, pasta, starch, and sugars were grouped within processed foods used as ingredients of culinary preparations. De Melo et al. (2017) included olive oil and butter/margarine in processed foods, while cassava flour in the ultra-processed group. In another study alcoholic beverages were analysed separately (Juul and Hemmingsson 2015). In the Adams and White (2015)'s study foods such as vegetable oils, margarine, butter, gums, flours and "raw" pastas and noodles (made from flour with the addition only of water) were placed in processed ingredients group. In the studies by Canella et al. (2014) and Lavigne-Robichaud et al. (2018) margarine was included in the ultra-processed group. In Silva et al. (2018)'s study as presented in the [Supplementary material](#) from their paper, they considered for the UPF group in addition to the margarine, distilled beverages (whiskey, vodka, cachaça). So, caution is required when analysing associations between the food groups according to the degree of processing and the outcomes between studies.

Moreover, the study by Nasreddine et al. (2018) besides having used the NOVA classification, and classified nuts and seeds in the group of processed, and fish and low-fat dairy products in the group of minimally processed, they also evaluated dietary patterns and nuts, seeds, fish, low-fat milk and dairy products were grouped in ultra-processed, because they were considered foods ready-to-eat, being

necessary caution in the interpretation of this result. Also, Cunha et al. (2018) evaluated dietary patterns and observed “Western pattern” consisted of processed and ultra-processed foods according with the NOVA classification. However, they associated foods from these two groups together with the outcome.

In addition, some studies used classifications other than NOVA. One study separated foods into two processing groups, processed foods in which they included foods as nuggets, chocolate drinks and microwave popcorn, and another group classified foods into high sugar and fat content (Rinaldi et al. 2016). While other used the classification developed in Guatemala in which it divided the food into unprocessed, partially processed and highly processed foods and according to the evaluation made has the limitation for not distinguishing domestic processing methods of industrial methods (Moubarac, Parra, et al. 2014).

This systematic review presents some limitations. Most of the studies had a cross-sectional design, which does not allow a cause-effect relationship, and the studies presented different methodologies, which was discussed in this review. In turn, a strong point was no restriction for age-groups and nationalities, reinforcing external validity of our discussion and worrying about the health consequences of UPF consumption in global population.

In conclusion, despite the positive associations found between UPF consumption with cardiometabolic risk-related outcomes, further studies are still needed to better compare these associations since the studies used different confounding factors, adopted distinct methods to assess food intake, and different food classifications between groups. In addition, further longitudinal studies are needed to establish a cause effect relationship between UPF intake and cardiometabolic risk.

Disclosure statement


No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the CAPES Foundation (Ministry of Education, Brazil, Financial code 001) and CNPq/CGAN/MS [process n° 408279-2017-6]. HHM Hermsdorff and J Bressan are CNPq Research Productivity Fellows. M. Ángeles Zulet and J. Alfredo Martínez for the Spanish Biomedical Research Centre in Physiopathology of Obesity and Nutrition (CIBEROBN) by the financial support.

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