

Ultra-processed food consumption and the risk of mortality: A Systematic Review

Consumo de alimentos ultraprocessados e o risco de mortalidade: uma revisão sistemática

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Abstract

Introduction and Objectives: Ultra-processed foods are determined by the level of processing. There has been a relationship between their consumption and several risk factors for diseases related to these foods, such as cardiovascular disease. These factors can corroborate the illness and increase the risk of mortality of the adult population. The objective of this systematic review was to verify the contribution of the consumption of ultra-processed foods to the risk of mortality. **Methods:** Through PubMed, Scopus and Web of Science, scientific databases, studies that examine the relationship between the consumption of ultra-processed foods and the risk of mortality up to February 2021 were systematically researched. **Results and Conclusion:** Evidence analysis was performed using robust tools to assess the risk of bias and methodological quality. A total of five studies were included. The consumption of ultra-processed foods was associated with a higher risk of mortality from all causes, proportional to their consumption (in the largest quartiles of consumption, greater risks were found).

Keywords: Ultra-Processed Foods. Food Consumption. Mortality. Systematic Reviews.

Resumo

Introdução e objetivos: Alimentos ultraprocessados são determinados pelo nível de processamento. Existe uma relação entre seu consumo e diversos fatores de risco para doenças relacionadas a esses alimentos, como as cardiovasculares. Esses fatores podem corroborar o adoecimento e aumentar o risco de mortalidade da população adulta. O objetivo desta revisão sistemática foi verificar a contribuição do consumo de alimentos ultraprocessados e o risco de mortalidade. **Métodos:** Por meio do PubMed, Scopus e Web of Science, foram pesquisadas sistematicamente em tais bases de dados científicas, estudos que examinam a relação entre o consumo de alimentos ultraprocessados e o risco de mortalidade até fevereiro de 2021. **Resultados e Conclusão:** A análise de evidências foi realizada por meio de ferramentas robustas para avaliar o risco de viés e a qualidade metodológica. Um total de cinco estudos foram incluídos. O consumo de alimentos ultraprocessados foi associado a um maior risco de

mortalidade por todas as causas, proporcional ao seu consumo (nos maiores quartis de consumo, foram encontrados maiores riscos).

Palavras-chave: Alimentos Ultraprocessados. Consumo de Alimentos. Mortalidade. Revisão Sistemática.

INTRODUCTION

Ultra-processed foods (UPFs) are determined through the level of processing, accordingly the NOVA classification, the UPFs contain predominantly industrial substances and little or no whole foods, being produced by large industries, in which the processing steps and techniques occur by the addition of various ingredients, such as: salt, sugar, oils, fats and in addition to substances whose use is only at the industrial level. This food category includes sweets, sweetened drinks with or without artificial sweeteners, soft drinks powders, sausages and other products derived from meat and animal fat, frozen products ready for heating, dehydrated products (such as cake mixes, powdered soups), Instant “noodles” and “seasoning” ready), and a plethora of new products that hit the market every year^{1,2}.

During the dissemination of these products in society, the relationship between their consumption and human health was perceived, in addition to the relationship with the quality of the diet, associating it to several risk factors for diseases related to food, whose contribution of food consumption is a determining factor for presence or not of these comorbidities, disorders or conditions^{3,4}. The impact of ultra-processed foods on various lifestyle-related diseases has already been studied, including diabetes mellitus, metabolic syndrome, cardiovascular diseases (CVD), dyslipidemia, hypertension and cancer^{5,6,7,8}. However, there are still gaps as to what the effective impact of the consumption of ultra-processed foods and their composition can have on human health, as well as the need to consider that its use is widely disseminated in the routine, due to its impression of practicality, being often allies in the lives of many who resort to these foods because they are often referred to as "ready to eat" or "ready to warm up" ⁹. Preparations created by industrial formulations made from substances derived from food and additives, rich in added sugars, salt, energy density of the diet, together with trans and saturated fats, containing small amounts of fiber, protein, micronutrients, and phytochemicals may indeed be responsible due to several current comorbidities, which contribute to the population's illness and health problems¹⁰.

This disease can generate an increased risk of mortality in the adult population. Cross-sectional studies showed a greater chance of obesity with greater consumption of ultra-processed foods¹¹⁻¹³, however it is known that cross-sectional studies do not have the potential to define the incidence of mortality in the population that consumes ultra-processed foods. Then, cohort studies were carried out to seek a possible association between the consumption of these foods and the risks of mortality, since their damage to human health is already known in the literature¹⁴⁻¹⁸. This systematic review aims to verify the consumption of ultra-processed foods in the risk of mortality.

METHODS

Protocol and registration

The systematic review protocol was reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P) protocol¹⁹. The protocol was registered at the international prospective register of systematic reviews (PROSPERO) database under the registration number CRD42020205382.

Search strategy and eligibility criteria

To identify potentially relevant studies to the present review, a systematic literature search of databases (PubMed, Scopus, and Web Of Science) was conducted through February 2021, following terms MeSH (1) "ultra-processed food", researched in combination with (2) "food consumption", for more sensitive research that would encompass all the articles needed for the review. No restrictions or filters were applied.

Our research only included observational articles with human. Inclusion criteria were: (1) Studies that evaluate the consumption of ultra-processed products; (2) Mortality outcome; (3) the articles were published as full papers; (4) Studies in adults (<18 years) and previously healthy.

The exclusion criteria were as follows: (1) In vitro studies; (2) animal model; (3) Studies with children, adolescents, pregnant women or infants; (4) Case reports, meta-analyses, editorials, narrative reviews.

Study selection

The articles were screening in two phases. Firstly, duplicate articles and triplicates articles were removed. In the first phase, two reviewers independently analyzed

titles and abstracts in the electronic database and selected articles to identify potentially eligible articles. In the second phase, two reviewers independently analyzed and performed the full reading of the articles selected in the first phase, excluding all the articles that did not meet the eligibility criteria. At all stages, a third reviewer was consulted in the case of any concerns or disagreements between the other investigators, being, all disputes, resolved by consensus. At the end of the process, five studies were collectively included in the analysis.

Data extraction

Data extraction was completed independently by three authors. The extraction was performed required according to the PRISMA¹⁹ statement for reporting systematic, was reconciled, and recorded on a purpose-designed Microsoft Excel[®] spreadsheet. The data from the articles were extracted: article title, study design, reference, sample size, aim study, population, exposure, control, year of publication, outcome, main findings, and limitation of the included studies. Constant meetings were held to maintain the standard of analysis.

Risk of bias assessment and quality of evidence

The Newcastle-Ottawa Scale (NOS) 20 tool is recommended for observational studies for observational studies²⁰. The tool was used to assess the risk of bias and methodological quality of the cohort articles in this review, examining the following domains: selection, comparability and exposure.

In the selection domain, the representativeness of the exposed cohort is evaluated, selection of the unexposed cohort, verification of the exposure and demonstration that the result of interest was not present at the beginning of the study. For this reason, we consider the cohort that had an adult population and studies with initial data, prior to the study, of comorbidities that could interfere with mortality, in addition to the use of validated tools to verify exposure.

In comparability the measurement would be a comparison of cohorts based on the project or analysis and the score was used when considering comorbidities to avoid potential bias and the consumption of ultra-processed by the sample.

In the exhibition, the tool uses the outcome evaluation, adequate time between the beginning of the cohort and the possible outcome and adequacy of the monitoring of the cohorts. With a higher score when the tools for assessing the frequency of food consumption were carried out by trained professionals, validated, and used other

methods for analyzing the outcome (electronic medical records, biochemical assessments), the work should mention the cohort time and the number of participants lost while driving.

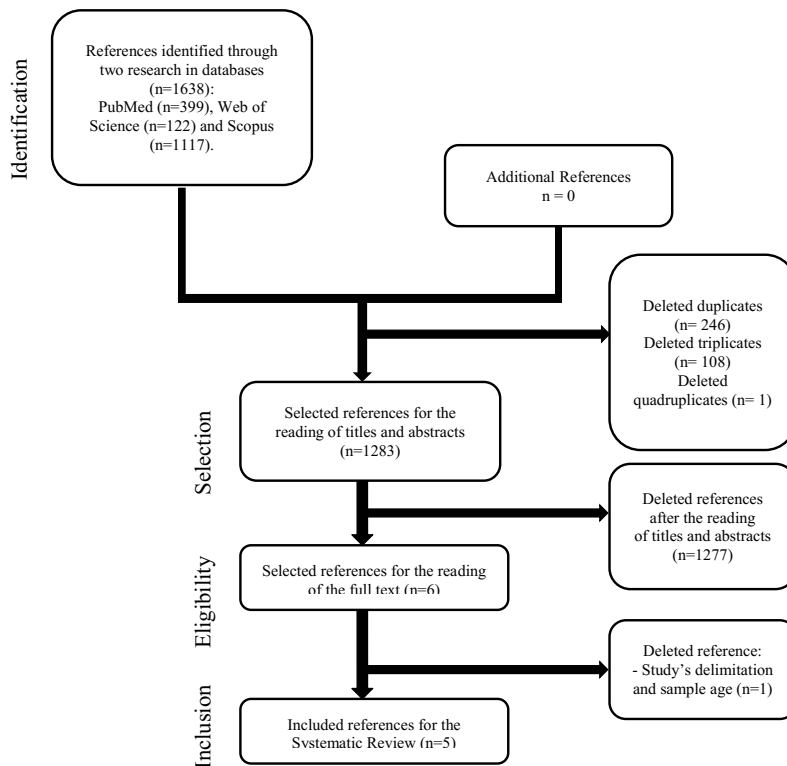
The application of the tool was carried out in duplicate by two independent evaluators and the discrepancies were resolved by a third evaluator, and other doubts were resolved in a scientific meeting of the research. All articles remained in this review because they did not demonstrate low quality or serious risk of bias in their conduct.

RESULTS

There were 1288 potentially relevant studies of the electronic research results identified in the first survey, (259 from PubMed, 950 from Scopus and 79 from Web of Science). After removing duplicates and triplicates, there were 1080 records for reading the title and sorting the abstracts. When updating the database with date filter 2020 until 2021, as the first survey had been carried out without filters in the year 2020, there were 350 potentially relevant studies of the electronic research results identified, (140 from PubMed, 167 from Scopus and 43 from Web of Science). After removing duplicates and triplicates, there were 203 records for reading the title and sorting the abstracts.

Of these, 7 articles were read in their entirety. After excluding 2 articles that did not meet the criteria for inclusion, 5 studies were included (14,15,16,17,18). A flow chart detailing the identification process, screening, eligibility and inclusion of studies is shown in Figure 1.

Figure 1 – Results of studies selection



Study characteristics

As shown in Table 1, the main characteristics of the studies were summarized in the parameters established collectively by the authors: authors, place and year of publication, cohort follow-up time, exposure assessment, outcome, data measurement, objectives, and main findings. The studies are listed in Table 1 according to the year of publication, from the oldest to the most recent.

All articles selected for this review were observational cohort studies.

The samples of the five articles totaled 118,652 individuals, and a follow-up of 64 years. The sample size ranged from 12,948 to 16 to 44,55,115 participants, with a minimum age of 18 years or older¹⁴⁻¹⁸. The form used to measure food consumption of ultra-processed foods was Food Frequency Questionnaires^{14,16,18} and 24-hour Food Recalls in sequential form¹⁵ or the use of both¹⁷. The five included studies were published between 2019 and 2021, all in English. The studies were carried out in the following countries: Spain (Rico-Campà A et al and Blanco-Rojo et al), France (Schnabel L et al), United States (Kim et al) and Italy (Bonaccio M et al).

Table 1 - Data from the cohort studies included in the systematic review

Authors, Country and Year	Cohort "follow up"	Exposure Assessment	Outcome	Measurement	Objective	Main Findings
Rico-Campà A, Martínez-González MA, Alvarez-Alvarez I, Mendonça RD, de la Fuente-Arrillaga C, Gómez-Donoso C, Bes-Rastrollo M. Spain. (2019)	1999 - 2014	Semiquantitative Food Frequency Questionnaire (136 items, previously validated)	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To evaluate the association between the consumption of ultra-processed foods and all causes of mortality.	The consumption of ultra-processed foods was associated with mortality risk from all causes. Through the participants in the highest quartile of food consumption, they obtained an HR of 1.62 (p = 0.05, 95% CI) compared to the lowest quartile. For each additional portion of consumption, the relative risk of mortality from all causes increased relatively by 18% (adjusted HR of 1.18; p = 0.02). When using the Cox model with repeated measures (all follow-up data), the HR of the highest UPF consumption was 1.44 (p = 0.023). In propensity scores for adjustments of potential residual confounders, the association between UPF consumption and risk and mortality increased the risk ratio to 1.89. The mean age of the study was 37.6 years (SD 2.3). During the average follow-up of 10.4 years, 335 deaths occurred. Analyses by type of mortality or by characteristics of the sample (subgroup analyses) had no statistical significance.
Schnabel L, Kesse-Guyot E, Allès B, Touvier M, Srour B, Hercberg S, Buscaïl C, Julia C. France. (2019)	2009 - 2017	24-hour dietary records, 3 of which are non-consecutive (the records were randomly assigned over a period of 2 weeks) every 6 months and complete all 5 questionnaires each year.	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To analyze the association between the consumption of ultra-processed foods and risk of all-cause mortality.	The highest consumption of ultra-processed foods was associated with younger age, with an average of 45%, SD 0.04% p <0.01. There were 602 deaths (1.4%), after adjusting for the variables, the consumption of ultra-processed foods showed a risk ratio of 1.14 (95% CI, p = 0.008). The relative risk was assessed by a 10% increase in ultra-processed ingested. The associations were statistically significant for the adjustment of the variables, however, when excluding the cases of death in the first two years of study, prevalent cardiovascular diseases, and cases of cancer, the statistical power was reduced, thus generating no significant statistics between the association. consumption of ultra-processed products and mortality.

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Table 1 (continued)

Authors, Country and Year	Cohort "follow up"	Exposure Assessment	Outcome	Measurement	Objective	Main Findings
Blanco-Rojo R, Sandoval-Insausti H, López-García E, Graciani A, Ordovás JM, Banegas JR, Rodríguez-Artalejo F, Guallar-Castillón P. Spain. (2019)	2008 - 2016	Food Frequency Questionnaire - DH-ENRICA- of the study itself was completed by a trained professional on home visits to the study participants.	Mortality from all causes	Cox proportional risk ratios (95% confidence intervals)	To elucidate the association between consumption of ultra-processed foods and all causes of mortality. Also, examine the effect of the theoretical substitution of isocaloric unprocessed foods in this relationship.	The average consumption of ultra-processed foods was 385g / day (24.4% kcal of the daily total). The 7.7-year follow-up resulted in 440 deaths. Participants who were classified in the highest consumption quartile obtained a higher HR of mortality in relation to the lower quartiles, for the model adjusted 4 to HR for mortality obtained a statistical value of 1.44 (95% CI, p = 0.03), when analyzed in relation to the consumption of grams per day per kg of weight, the HR was 1.46 (95% CI, p = 0.03). All associations between consumption and risk of mortality were statistically significant. The analysis of quartile 4 with isocaloric substitution only obtained a statistically significant result when 8.2% of the consumption of ultra-processed foods was substituted for minimally processed or fresh foods (p for non-linearity = 0.04).
Kim H, Hu EA, Rebholz CM. United States. (2019)	1988 - 2011	Food Frequency Questionnaire and 24-hour recalls, applied by the survey interviewers.	Mortality from all Causes and Cardiovascular	Cox proportional risk ratios (95% confidence intervals)	To investigate the association between the consumption of ultra-processed foods and mortality from all causes and mortality from cardiovascular diseases.	The 19-year follow-up resulted in 2451 deaths from all causes and 648 deaths from cardiovascular disease. When analyzing the quality of the diet using tools such as NRF9.3 and HEI-2000, the participants in the highest quartile had low quality of the diet, with statistically significant results with p <0.001 and p = 0.001, respectively. Cox adjustments for model 2, the highest consumption quartile, obtained an HR of 31% (HR 1.31; 95% CI; p = 0.001) for all-cause mortality when related to the other quartiles. Regardless of the adjusted models, the highest quartile of UPF consumption showed higher HR for mortality, with statistically significant values when compared to the lowest quartiles. The risk of mortality from cardiovascular diseases associated with the consumption of UPF did not show significant results for the adjustment models and quartiles of consumption (p > 0.05).

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Table 1 (continued)

Authors, Country and Year	Cohort "follow up"	Exposure Assessment	Outcome	Measurement	Objective	Main Findings
Bonaccio M, Di Castelnuovo A, Costanzo S, De Curtis A, Persichillo M, Sofi F, Cerletti C, Donati MB, de Gaetano G, Iacoviello L. Italy. (2021)	2005 - 2015	Semiquantitative Food Frequency Questionnaire validated and adapted for the Italian population, administered by the interviewer.	Mortality from all Causes, Cardiovascular and from Cancer	Cox proportional risk ratios (95% confidence intervals)	To estimate the association between the consumption of ultra-processed products and mortality risk.	During an average follow-up of 8.2 years, 1216 deaths from all causes occurred, 439 from cardiovascular disease, 255 from cerebrovascular disease, 477 from cancer, and 300 from other causes. The relative risks were analyzed according to the causes of mortality in a stratified way and the quartiles of consumption. All-cause mortality (1216) when adjusted to the models showed higher HR in the highest consumption quartile (HR 1.28; 1.32; 1.26; respectively to the adjusted models), similar results were found when stratified analysis for mortality from cardiovascular, cerebrovascular diseases, and other causes. When the consumption of ultra-processed products was associated with cancer mortality, they did not obtain significant results for the association, regardless of the adjusted models. The p values have not been demonstrated, only HR.

Bias risk assessment

Most of the studies included in this review had a low risk of bias, with few concerns for most items, as shown in Table 2. Two studies showed a low risk of bias^{14,18} while the others scored between 7 and 6 stars¹⁵⁻¹⁷ raised some concerns in the domains. Schnabel et al had a higher risk of potential biases regarding the selection domain, since their sample was obtained through volunteering by the population, in addition to the important data that would be about previous diseases and dietary records were self-reported, increasing the potential bias of underreporting¹⁵. Self-reported dietary data were considered potential biases and found in the work of Schnabel et al¹⁵. No study scored two stars in the comparability domain, due to the purpose of the domain, in which the reduction of biases that could result in mortality outcomes, such as the presence of diseases that are potential mortality risks were assessed only at the first moment of the study and not reassessed during the follow-up of the cohorts¹⁴⁻¹⁸. The works by Kim et al and Blanco-Rojo et al did not present data on the number of individuals lost during the follow-up of the cohort, and for this reason they scored only with two stars in the exposure domain^{16,17} Table 2.

Table 2 - Methodological quality assessment of observational studies included in the systematic review using the Newcastle–Ottawa Scale (NOS)

First author, year	Study design	Selection	Comparability	Exposure/ Outcome	Total scores
Rico-Campà A et al (2019)	Cohort	★★★★	★	★★★	8
Schnabel L et al (2019)	Cohort	★★★	★	★★	6
Blanco-Rojo R et al (2019)	Cohort	★★★★	★	★★	7
Kim H et al (2019)	Cohort	★★★★	★	★★	7
Bonaccio M et al (2021)	Cohort	★★★★	★	★★★	8

NOS - Newcastle–Ottawa Scale tool

Selection - NOS tool selection domain

Comparability - comparability domain between the observed groups of the NOS tool

Exposure/Outcome - exposure domain and outcome

★ - point assigned to the article according to the questions in each domain of the NOS tool

The selection section has four questions and can score up to four points. Comparability has only one question that can score up to two points. In the outcome section are three questions which can score three points. The score depends on the methodological quality of the observational articles and possible risks of bias, where the higher the score, the better the quality and the lower the risk of bias.

Consumption of Ultra-processed Products and Mortality for All Causes

The cohorts evaluated in this review, the risk of mortality from all causes included all the causes-deaths of the population, ascertained through reports from family

members or from the register of the country of origin of the cohort. In general, causes of mortality were recorded, such as cardiovascular, cancer, cerebrovascular diseases, as well as unknown causes.

In the work of Rico-Campà et al 335 deaths occurred during the cohort of 19899 participants.

The consumption of ultra-processed foods was associated with the risk of mortality from all causes when in the highest quartile of these foods, obtaining a risk ratio (HR) of 1.62 ($p = 0.05$, 95% CI). An additional analysis of consumption for each additional portion the relative risk of mortality from all causes increased relatively 18% (adjusted HR of 1.18; $p = 0.02$). For the Cox model adjustments, the HR of the highest UPF consumption was 1.44 ($p = 0.023$). Adjustments for potential residual confounders, the association between UPF consumption and risk and mortality increased the risk ratio to 1.89¹⁴.

During the follow-up of the Schnabel et al cohort, 602 deaths (1.4%) occurred, including 219 deaths from cancer and 34 from CVD. After adjusting for variables, the consumption of ultra-processed foods showed a risk ratio of 1.14 (95% CI, $p = 0.008$). When the cases of death in the first two years of study, mortality from cardiovascular diseases and cancer were excluded, the statistical power was reduced, and no significant statistic was found between the association of ultra-processed consumption and mortality¹⁵.

Blanco-Rojo et al demonstrated that the increase in the intake of ultra-processed foods was associated with higher mortality after 7.7 years of follow-up of the cohort, in which 440 deaths of 11,898 individuals were incidents. Participants who were classified in the highest consumption quartile obtained a higher HR of mortality compared to the lowest quartiles, for the adjusted model 4 (the intake of ultra-processed foods contributed more than 33% of the total energy intake) to HR for mortality obtained a statistical value of 1.44 (95% CI, $p = 0.03$), whereas when analyzed in relation to the consumption of grams per day per kg of weight, the HR was 1.46 (95% CI, $p = 0, 03$). In view of the isocaloric substitution of these foods, when quartile 4 was analyzed, it only obtained a statistically significant result when 8.2% of the consumption of ultra-processed foods was replaced with minimally processed or fresh foods (p for non-linearity = 0.04)¹⁶.

Kim et al contemplated a sample number of $n = 18,779$ and during the average follow-up of 19 years 2,451 deaths from all causes occurred, 648 deaths were due to

cardiovascular diseases. The highest quartile of frequency of ingestion of ultra-processed foods generated a 31% higher risk of mortality from all causes, with Cox's adjustments for model 2 (HR 1.31; 95% CI; $p = 0.001$), however, the analysis of adjusted models was independent for the results of the highest quartile of UPF consumption, which demonstrated higher HR for mortality, all values being statistically significant when compared with the lowest quartiles. In addition, participants in the highest quartile had significantly higher intake of total energy, total fat, saturated fat, monounsaturated fat and added sugar, and lower protein intake ($p < 0.001$ for all comparisons)¹⁷.

Ultra-processed consumption and the stratified mortality analysis

Mortality when assessed in a stratified way was presented by two articles included in the present review.

The results by Kim et al did not demonstrate a statistically significant relationship regarding the risk of mortality from cardiovascular diseases when associated with the consumption of UPFs for the adjustment models and quartiles of consumption ($p > 0.05$)¹⁷.

The Bonaccio et al cohort, on the other hand, assessed the risk of mortality during the mean follow-up of 8.2 years, with 1216 deaths from all causes, 439 from cardiovascular diseases, 255 from cerebrovascular diseases, 477 from cancer and 300 from other causes, in a sample of 22,475 individuals. Mortality from all causes ($n = 1216$) when adjusted to the Cox models showed higher HR in the highest consumption quartile (HR 1.28; 1.32; 1.26; respectively to the adjusted models), similar results were found when stratified analysis for mortality from: cardiovascular, cerebrovascular diseases and other causes. The consumption of ultra-processed products, when associated with cancer mortality, did not show significant results to the association, regardless of the adjusted models¹⁸.

DISCUSSION

Bearing in mind that all the studies included¹⁴⁻¹⁸ in this systematic review presented the classification of UPF by the NOVA category of foods, this categorization is determined through the composition of the foods, indicating levels of industrial processing of these: fresh or minimally processed foods; processed culinary

ingredients; processed foods with salt, sugar or oil and the UPFs containing predominantly industrial substances and little or no complete food¹.

The nutritional composition of ultra-processed foods and the industrial processes to which they have been subjected, such as the use of contaminants and food additives, can potentially increase the consequences for human health²¹⁻²³.

The randomized study by Hall et al. reinforces that the intake of UPFs can cause factors harmful to human health, since it presented a higher intake of energy and carbohydrates in the group where the diet was predominantly of UPFs, in addition, there were changes in weight that were correlated with the intake of energy ($p < 0.0001$), participants who gained weight (0.9 ± 0.3 kg; $p = 0.009$) were consuming the ultra-processed diet and losing weight during the unprocessed diet (0.9 ± 0.3 kg; $p = 0.007$)²⁴.

Gibney *et al* brought an important counterpoint in his work when he mentions the NOVA classification and its wide range of interpretations, since it can be very imprecise and incomplete to form an adequate basis for making diet recommendations^{25,26}. In addition, there are several attributes of these foods that make them more accessible and practical for consumption, being they the cost, the long useful life, they are relatively safe from the microbiological point of view and their high convenience, as they are often ready for eat or ready to warm up²⁷.

Consumption of Ultra-processed Products and Mortality

In the work by Rico-Campá et al, the risk of mortality from all causes was assessed according to the daily consumption of ultra-processed foods, the significant findings represented the consumption of > 4 servings of ultra-processed foods associated with the mortality risk of 62% higher than when consumed in fewer servings. In addition, with each additional portion of consumption, an 18% increase in mortality risk was found¹⁴. Bearing in mind that the consumption and feeding of these foods entails nutritional and health risks, the work of the GBD 2017 DIET COLABORATORS¹⁰ group showed that, in 2017, 11 million deaths (95% CI) were associated with diet and decreased quality of life. life, and 3 million deaths associated with cardiovascular diseases, it is worth mentioning that ultra-processed foods are rich in sodium.

During the follow-up of the Schnabel et al cohort, 602 deaths were recorded, among them 219 from cancer and 34 from cardiovascular diseases¹⁵, considering these

causes is related to data from the World Health Organization in the year 2012²⁵, in which 71% of causes of death worldwide were due to cardiovascular diseases, cancer and diabetes mellitus²⁸, in addition, the data show the increased risk of death associated with chronic non-communicable diseases and the diet. When the prevalent cardiovascular diseases and cancer cases were excluded in the research by Schnabel et al, the statistical power was reduced and no significant value was found¹⁵, corroborating the idea that the chronic non-communicable diseases so prevalent are related to the quality of the diet, as well as in the nutritional profile of those who consume them²⁹.

In view of the quality of the diet, the study Kim et al analyzed that the consumption of ultra-processed foods when higher, presented a lower quality index for the diet using the NRF 9.3 and HEI-2000 tools, with statistically significant results of $p < 0.01$ and $p = 0.01$, respectively. In their analysis, the consumption of ultra-processed products and the risk of mortality from all causes showed results like other studies, with significant measures for the Cox adjustments of model 2 when in the largest consumption quartile, the relative risk of 31% (HR 1, 31; 95% CI; $p = 0.001$). In the evaluation of mortality from cardiovascular diseases, no result was statistically significant¹⁷.

The research by Bonaccio et al also presented a stratified analysis of the risk of mortality, such as mortality from CVD, cancer, cerebrovascular diseases, and other causes. when the risk of mortality from CVD associated with the consumption of ultra-processed foods was evaluated, it presented HR from 1.5 to 1.58, adjusted to Cox's models, there was no presentation of p value¹⁸, the values disagree with the study by Kim et al, as it was demonstrated lower HR values (1.04; 1.10; 1.13) and did not obtain statistical significance. In the analysis of mortality data when stratified, no study in the present review showed statistical significance.

Blanco-Rojo et al in their cohort study, demonstrated that participants whose consumption had the highest level of quartiles obtained a risk ratio of 44% (HR 1.44; 95% CI; $p = 0.03$), the highest rate of mortality from all causes than the others, which in fact reinforces the values found in the studies included in the review¹⁶. Mortality data may be associated with increased changes in eating habits, added to the increased incidence of chronic diseases at younger ages, as shown by the study by Lin et al³⁰, in addition, there is a prospect of increased consumption of these foods by the younger population³¹, making the analysis of the risks of this consumption to

human health essential. The meta-analysis study by Pagliai et al verified such associations, in addition to reaffirming that mortality from all causes is associated with the consumption of ultra-processed foods, which is statistically significant at a risk ratio of 1.25 ($p < 0.00001$; $I^2\% 2$)³².

Limitations

This systematic review has limitations inherent to the studies included. The included observational cohort studies should be analyzed as measurement potentials and biases, however, they have been minimized by the sensitivity analysis in some articles. Another bias is in relation to the instruments of investigation of food consumption, whether they are food frequency questionnaires or 24-hour reminders, which may be interfered with the interviewee's own memory. In addition, most of the cohorts in the present review obtained the answers to the questionnaires and other variables only at the baseline, making no new assessments during the follow-up, which are also potential limitations for data analysis.

The use of only two descriptors for the manual search of articles may be cause for doubts in relation to the methodology carried out in this review, however we reiterate that this proposal was determined through the construction of a database whose use will be for other systematic reviews, and, in addition furthermore, the use of two descriptors can minimize the risk of losses since the search becomes more sensitive and less specific, covering greater themes and content for later choice, which is also manual by researchers.

The same for of the PROSPERO record, which was recorded more broadly, but it was decided to make use of only one outcome so that such a systematic review is more focused and consequently highlights in detail only one outcome.

CONCLUSION

By investigating the contribution of the consumption of ultra-processed foods and the risk of mortality, it can be concluded that there is research in the literature that demonstrates a statistically positive association between consumption and the increased risk of mortality. The studies included in the present review reinforce this close relationship between the consumption of UPFs and mortality by presenting statistical measures of HR of at least 14%⁴⁵ more mortality to those who consume this food category in a greater frequency or quantity. It is even observed in one of the cohorts that, with each additional portion of UPF consumption, the risk of mortality

increases approximately 18%¹⁴, thus refuting the interaction between the consumption of foods with a high degree of industrialization and the risk of mortality.

CONFLICT OF INTERESTS

The authors have no conflicts of interest.

TRANSPARENCY DECLARATION

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained. The protocol was registered at the international prospective register of systematic reviews (PROSPERO) database under the registration number CRD42020205382.

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