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Diet and Food Additives

Ultra-processed food and risk of type 2 diabetes: a systematic review and meta-analysis of longitudinal studies

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Abstract

Background: The consumption of some food groups is associated with the risk of diabetes. However, there is no evidence from meta-analysis which evaluates the consumption of ultra-processed products in the risk of diabetes. This study aimed to review the literature assessing longitudinally the association between consumption of ultra-processed food and the risk of type 2 diabetes and to quantify this risk through a meta-analysis.

Methods: We conducted a systematic review and meta-analysis with records from PubMed, Latin American and Caribbean Literature in Health Sciences (LILACS), Scielo, Scopus, Embase, and Web of Science. We included longitudinal studies assessing ultra-processed foods and the risk of type 2 diabetes. The review process was conducted independently by two reviewers. The Newcastle Ottawa scale assessed the quality of the studies. A meta-analysis was conducted to assess the effect of moderate and high consumption of ultra-processed food on the risk of diabetes.

Results: In total 2272 records were screened, of which 18 studies, including almost 1.1 million individuals, were included in this review and 72% showed a positive association between ultra-processed foods and the risk of diabetes. According to the studies included in the meta-analysis, compared with non-consumption, moderate intake of ultra-processed food increased the risk of diabetes by 12% [relative risk (RR): 1.12;

95% confidence interval (CI): 1.06–1.17, $I^2 = 24\%$], whereas high intake increased risk by 31% (RR: 1.31; 95% CI: 1.21–1.42, $I^2 = 60\%$).

Conclusions: The consumption of ultra-processed foods increased the risk for type 2 diabetes as dose-response effect, with moderate to high credibility of evidence.

Key words: Ultra-processed food, diabetes, meta-analysis, diabetes mellitus

Key Messages

- The moderate consumption of ultra-processed foods was associated with a 12% higher risk of diabetes.
- The high consumption of ultra-processed food increased the risk of diabetes by 31%.
- When stratified by sex, the results were significant in men and women.

Introduction

Type 2 diabetes is a metabolic disease that increases risk for negative outcomes, including renal disease, heart problems and premature mortality.[1,2] A study analyzing data from more than 40 000 deaths found a decrease in years of life due to diabetes in England, reaching 5 years for White men and 6 years for White women.[3] Among older adults, individuals presenting diabetes lost 4.6 years of life, developing disability 6 to 7 years earlier and spending up to 2 more years living with disability compared with non-diabetics.[4]

From 1990 to 2017, a study with data from 195 countries and territories found that the age-standardized rates of type 2 diabetes increased for incidence (from 228.5 per 100 000 population to 279.1), for prevalence (from 4576.7 to 5722.1), for death (from 10.0 to 13.2) and for disability-adjusted life-years (DALYs) (from 553.6 to 709.6).[5] Despite that, the years of life lost due to diabetes have decreased over time.[6] This decline, in combination with an increase in the incidence of diabetes and in life expectancy, is responsible for more years spent with the disease.[6,7] Several studies reported an increase in costs of diabetes treatment, reaching 26% in the USA from 2012 to 2017.[8] Globally, the estimates increased from the US $1.3 trillion in 2015 to $2.1 trillion by 2030.[9]

The diabetes burden is related to metabolic risks and behaviours. In 2017, 30.8% of deaths and 45.8% of DALYs of diabetes were attributable to high body mass index, and 24.7% of deaths and 34.9% of DALYs of diabetes to diet.[5] The accessibility to high-fat, added-sugar and salt-laden foods increased with globalization, and the consumption of ultra-processed foods has been growing for more than a decade.[10,11]

According to the NOVA food classification system, ultra-processed are the foods that undergo industrial processes. Usually, these processes consist of fractionating whole foods into substances, chemical modifications of these substances, sophisticated packaging, cosmetic additives inclusion, and other processes.[12] The intake of ultra-processed products represents a large part of the daily consumption of energy, reaching 42% in a study in Australia and more than 56% in the UK.[3,14] The accessibility and the low cost of high energy-density but low-nutrient food decrease the consumption of whole grains, fruit, and vegetables.[15] Therefore, ultra-processed foods may be an important driver of the obesity and diabetes epidemics worldwide.

A current meta-analysis showed a positive association between ultra-processed food with overweight and obesity.[16] Ultra-processed foods have also been associated with risk of all-cause mortality, cardiovascular diseases, coronary heart diseases, hypertension, metabolic syndrome, depression, irritable bowel syndrome, overall cancer, postmenopausal breast cancer, gestational obesity, adolescent asthma and frailty.[17,18]

Observational studies have reported a positive association between the intake of ultra-processed foods and diabetes.[19–21] In addition, there is evidence from some groups of foods and diabetes risk, including sugar-sweetened beverages and processed meat.[22,23] Although these groups are some of the ultra-processed, there is no evidence from meta-analyses evaluating the risk of diabetes associated with the consumption of all ultra-processed groups. This study aimed to review the literature assessing longitudinally the association between consumption of ultra-processed food and the risk of type 2 diabetes, and to quantify this risk through a meta-analysis.

Methods

Search strategy

We conducted a systematic review and meta-analysis according to the new PRISMA statement and MOOSE guidelines.[24,25] The search was completed in April 2021 and included the following databases: PubMed, Latin American and Caribbean Literature in Health Sciences (LILACS), Scielo, Scopus, Embase and Web of Science (see the Supplementary Material, available as Supplementary data at *IJE* online). We also search non-systematically on Google Scholar. Two groups of keywords were used to locate the articles, based on MeSH and non-MeSH terms. In the first one, we included terms related to ultra-processed food (*ultra-processed, ultraprocessed, fast foods, processed food, ultraprocessed food, ultra-processed food, processed meat, ultra processed food, ham, sausages, hamburger, bacon, luncheon meats, ready-to-eat, ready-to-consume, industrialized, fast-food, fast food, fastfood, junk food, prepared food, candy, ice cream, chocolate, snacks, hot dog, burger, dietary patterns, dietary behaviors, dietary habits*). In the second group, terms related to diabetes (*diabetes, type 2 diabetes, T2DM, diabetes mellitus*) were included. We used the Boolean operator 'OR' within each group, and the Boolean operator 'AND' between groups. When possible, we restricted the results to the terms contained only in the titles or title and abstract, for better results. The systematic review and meta-analysis were registered with PROSPERO (CRD42021246505).

Inclusion criteria

We included studies that met the following criteria: observational study; longitudinal design; ultra-processed food as the main exposure (according to the NOVA food classification system); assessed the association with type 2 diabetes; results reported as odds ratios (ORs), relative risks (RRs) or hazard ratios (HRs), with 95% confidence intervals (CIs). We also included studies that did not use the NOVA food classification system but evaluated foods according to the classification. We have not included restrictions on years or language of publication.

Exclusion criteria

This review did not include studies with animal or i*n vitro*, review articles or studies assessing gestational diabetes. In case of more than one study using the same database, we included the most recent. For studies not reporting data as ORs, RRs or HRs, we tried to contact the author requesting the data before the exclusion. We also excluded studies that assessed only one specific food or including only beverages.

Study selection

Two authors (F.M.D.) and (L.M.F.) independently conducted the study selection based on the previously defined inclusion and exclusion criteria. In case of disagreement, authors resolved this by consensus. Each reviewer selected the article titles independently. The second stage consisted of reading the abstracts previously selected. Then, the full texts of selected articles were read. Finally, the authors checked the reference lists for possible additional articles.

Quality of evidence

Two authors (L.M.F. and F.S.S.) assessed the quality of the manuscripts independently. A third reviewer (F.M.D.) resolved disagreements. We used the Newcastle-Ottawa Scale (NOS) to assess the quality of evidence.[26] The NOS scale is a tool assessing longitudinal studies' quality. This scale consists of eight items related to study selection, comparability and outcome. In NOS, each item receives a star when the study is classified as high-quality in that item, except for the comparability item which can receive two stars. Thus, the total NOS score ranges from 0 to 9. Based on previous publications, we classified studies with less than 5 points as poor-quality, those with 5 or 6 points as medium-quality and articles with more than 7 points as high-quality studies.[27,28] We also performed Egger's regression tests and funnel plot to determine publication bias for analyses with more than 10 studies. Potential sources of between-study variability were tested through meta-regression, including analyses according to NOS score and differences between shorter and long duration of the studies.

The assessment of the credibility of evidence was performed using the NutriGrade scoring system.[29] This instrument considers eight items for meta-analyses of cohort studies: (i) risk of bias, study quality and limitations; (ii) precision; (iii) heterogeneity; (iv) directness; (v) publication bias; (vi) funding bias; (vii) effect size; and (viii) dose-response.[29] The NutriGrade score is summarized as follows: very low (0–3.99), low (4–5.99), moderate (6–7.99), and high (8–10.[29] Separate judgments on credibility of evidence were made for overall ultra-processed foods consumption and for studies that evaluated the exposure using the NOVA food system classification. Details of the NutriGrade tool items are provided in the footnotes for Table 1 (see Results section).

Table 1 Credibility of evidence using NutriGrade tool for association between ultra-processed food consumption type 2 diabetes

	Overall UPF consumption	UPF consumption assessed by NOVA food classification system
NutriGrade items		
Item 1	2	2
Item 2	1	1
Item 3	0.8	0
Item 4	1	1
Item 5	1	0
Item 6	1	1
Item 7	1	1
Item 8	1	0
Total score	8.8	7.0
Credibility of evidence	High	Moderate

Item 1: risk of bias, study quality, and study limitations (0 to 2 points): Newcastle-Ottawa Score (mean) ≥7 = 2 points.

Item 2: precision (0 to 1 point): ≥500 events and the 95% CI excludes the null value; or ≥500 events, but 95% CI overlaps the null value, and 95% CI excludes important harm (RR <1.2) = 1 point.

Item 3: heterogeneity (0 to 1 point): 2 to 5 studies = 0 points; ≥10 studies, heterogeneity measures adequately reported, random-effects models, and subgroups analyses were conducted = 1 point.

Item 4: directness (0 to 1 point): no important differences in the population or intervention; hard clinical outcome = 1 point.

Item 5: publication bias (0 to 1 point): <5 studies = 0 points; no evidence for publication bias with test or plot (≥10 studies) = 1 point.

Item 6: funding bias (0 to 1 point): report from academic or research institution = 1 point.

Item 7: effect size (0 to 2 points): RR >1.20 to 2 and corresponding test statistically significant (highest vs lowest category) = 1 point.

Item 8: dose-response (0 to 1 point): no dose-response analysis = 0 point; significant linear dose-response relation = 1 point.

UPF, ultra-processed foods.

Meta-analysis

A random-effects model calculated the pooled RR with a 95% confidence interval. Meta-analysis was performed through R language using the Rstudio program and miniMeta package.[30] We pooled the RR across studies through the DerSimonian and Laird random-effects model.[31] We used the Higgins I^2 statistic to estimate statistical heterogeneity among studies.[32] Values above 50% and $P < 0.05$ were classified as high heterogeneity. HR values were considered as RR.[33] Results from ORs were transformed into RRs using the formula: $RR = OR/[(1-P_o) + (P_o \times OR)]$, in which P_o represents the incidence of the outcome of interest in the nonexposed group.[34] We used the fixed-effects model to calculate article-specific RRs for studies assessing values stratified by sex or in subgroups. For the meta-analysis, we considered results from the full adjusted model. For the reference group, we considered the non-consumption or the lowest consumption reported by the studies. In the moderate intake group, after the reference group, we considered the consumption referred to as the first exposure group by the studies. The highest consumption reported by the studies was reported as high intake. Analyses were shown by sex and follow-up time (<9 years and >10 years).

An additional analysis was performed including only studies using the NOVA food classification system. We also conducted a dose-response analysis stratified by frequency of consumption (times per week, quartile and quintile). Moreover a sensitivity analysis, according to the quality of the study (based on NOS scale), race (Western and Eastern) and age at baseline (<50 and ≥50 years) was conducted.

Results

Characteristics of the studies

Figure 1 shows the flowchart of the selection of the articles. After excluding duplicates, 2272 records were located of which 15 met the inclusion criteria and were included. After reading the references of the studies, we found more three studies thus totalling 18 studies included in the present review and almost 1.1 million individuals. In the last step, most studies ($n = 28$) were excluded because they did not show results for ultra-processed food only.

Table 2 shows the main characteristics and results of the included studies. Most studies were conducted in the USA ($n = 4$),[35–38] followed by The Netherlands and the UK with two studies each.[19,39–41] One study used data from eight European countries.[42] The follow-up time ranged from 4.6 to 23 years.[43,44] Sample size ranged from 2001 to more than 340 000 individuals.[38,42] Four studies included only women,[35,36,44,45] one only men[46] and the other 13 both women and men.[19,20,37–43,47–50] Three studies classified the foods as ultra-processed according to the NOVA food classification system,[19,20,50] and the other 15 assessed foods classified in the group of ultra-processed. The most studies ($n = 11$) were published from 2012.

Main findings

A total of 13 (72%) studies showed significant associations between the consumption of ultra-processed foods and risk of diabetes.[19,20,35–37,39–42,44–46,50] In a study, compared with non-consumption, the high consumption of ultra-processed products increased the risk of diabetes by 86.0%.[35] In another study, an increase of 10.0% in the consumption of ultra-processed foods increased the risk of diabetes by 13.0%.[50] Compared with non-consumption of ultra-processed foods, the three studies that used the NOVA food classification system showed a risk of up to 53.0% between ultra-processed foods and diabetes.[19,20,50]

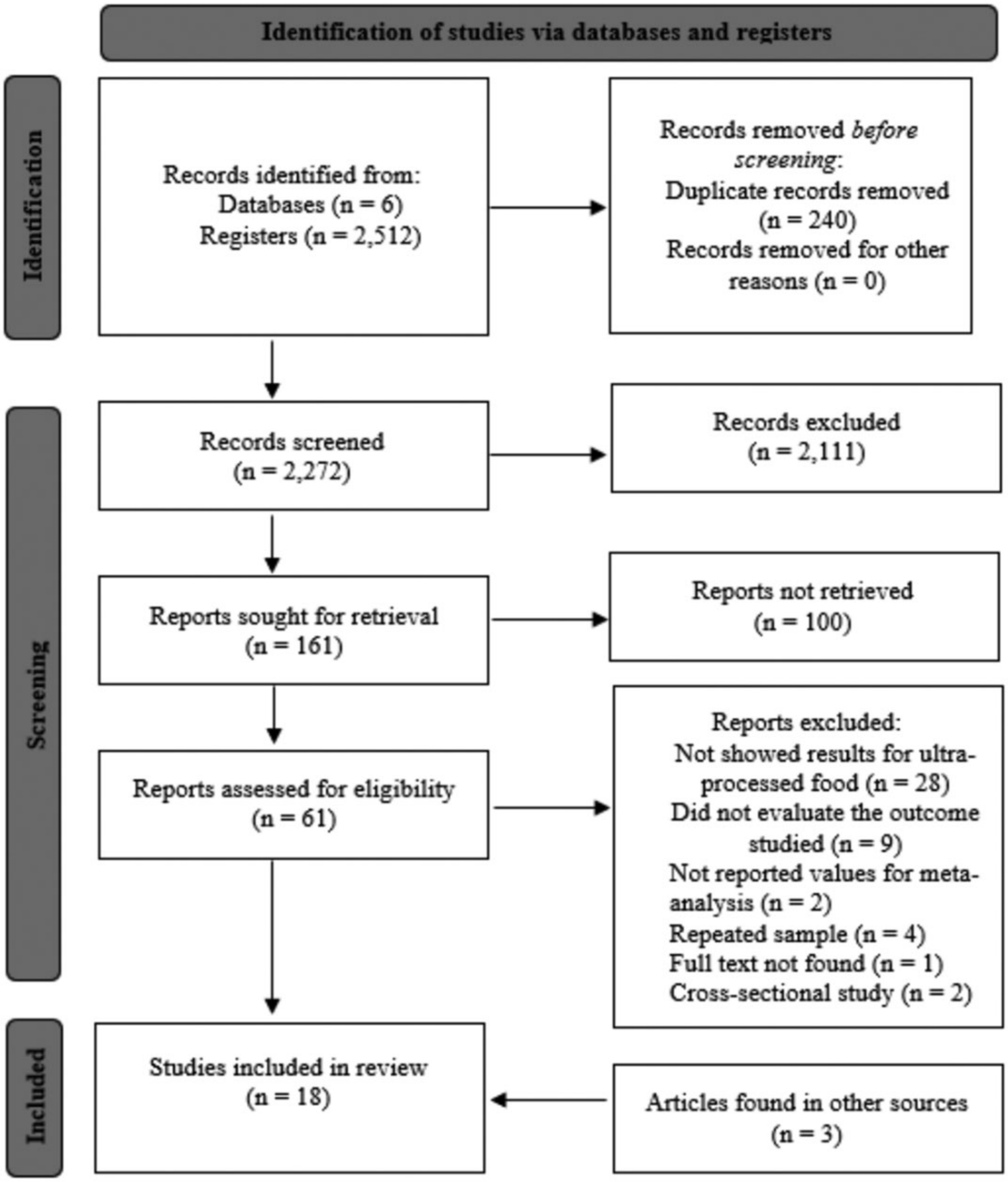

Figure 1 Flow diagram of article selection stages

Quality of evidence

Table 3 shows the Newcastle-Ottawa results. The NOS score varied from 6 to 9 points. None of the included studies scored less than 6 points. Two studies were classified as medium-quality, with 6 points each.[19,36] The other 16 studies were classified as high-quality, among which only five scored 9 points. According to the NutriGrade score, the credibility of evidence was high to overall ultra-processed foods consumption, and moderate considering studies that evaluated the exposure with the NOVA food classification system (Table 1).

Figure 2 shows the funnel plot results. Our Egger's test for moderate and high intake of ultra-processed food was not significant ($P = 0.70$ and $P = 0.83$, respectively). Results from meta-regression suggested that the NOS scale was not a mediator for our results ($P = 0.17$ for moderate intake and $P = 0.61$ for high intake). For differences between shorter and long duration, meta-regression was also not significant ($P = 0.73$ for moderate and $P = 0.92$ for high intake group).

Meta-analysis

Figure 3 shows a 12.0% higher risk of diabetes in people classified with moderate intake of ultra-processed foods (RR: 1.12; 95% CI: 1.06–1.17, $I^2 = 24\%$). A higher risk of diabetes (31%) was found using high intake of ultra-processed as exposure in the pooled analysis (RR: 1.31;

Table 2 Description of studies included in the systematic review. (N = 18)

Identification	Sample	Sample characteristics	Follow-up time in years	Exposure	Adjustment	Main results
Schulze *et al*., 2003 USA	Nurses' Health Study II	91 246 female nurses aged between 24 and 44 years	8	Sausage, salami, bologna, and other processed meats Moderate intake: 1/week High intake: >5/week	Age, body mass index, calories, alcohol, physical activity, family history of diabetes, smoking, history of high blood pressure and high blood cholesterol, post-menopausal hormone use, oral contraceptive use, intake of cereal fibre, magnesium, caffeine, glycaemic index, saturated fat, monounsaturated fat, polyunsaturated fat, trans fat, cholesterol, Western diet pattern	The high intake of ultra-processed food increased risk of diabetes by 86%
Song *et al*., 2004 USA	Women's Health Study	39 876 female health professionals aged > 45 years	8.8	Hot dogs, bacon, sausage, salami, and bologna Moderate intake: 1/week High intake: >5/week	Age, body mass index, total energy intake, smoking, exercise, alcohol use, family history of diabetes, dietary intakes of fibre intake, glycaemic load, magnesium, total fat	The high intake of ultra-processed food increased risk of diabetes by 19%
Montonen *et al*., 2005 Finland	Finnish Mobile Clinic Health Examination Survey	4304 individuals aged between 40 and 69 years	23	Processed meat (not specified) Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, sex, energy intake, body mass index, smoking, family history of diabetes, geographical area	Both moderate and high consumption of ultra-processed food were not associated with a higher risk of diabetes
Villegas *et al*., 2006 China	Shanghai Women's Health Study (SWHS)	81 170 women aged between 40 and 70 years	4.6	Smoked meat/bacon, salted meat/preserved meat, Chinese sausage Moderate intake: <once per month High intake: >once per month	Age, waist to hip ratio, energy intake, body mass index, smoking, alcohol, physical activity, vegetable intake, income, education, occupation status, hypertension, chronic disease	The moderate intake of ultra-processed food increased risk of diabetes, the high intake not increased
McNaughton *et al*., 2008 UK	Whitehall II study	10 308 men and women aged 35–55 years from 20 civil service departments in London	11.6	Low-calorie/diet soft drinks, onions, sugar-sweetened beverages, burgers and sausages, crisps and other snacks, white bread Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, sex, energy misreporting, ethnicity, employment grade, smoking, alcohol, physical activity, blood pressure, body mass index, blood pressure	The high intake of ultra-processed food increased risk of diabetes by 51%

(Continued)

Table 2 Continued

Identification	Sample	Sample characteristics	Follow-up time in years	Exposure	Adjustment	Main results
Mannisto *et al.*, 2010 Finland	Alpha-Tocopherol, BetaCarotene Cancer Prevention study	29 133 male smokers aged 50–69 years and living in Southwestern Finland	12	Processed meat (not specified) Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, intervention groups, body mass index, number of cigarettes smoked daily, smoking years, systolic blood pressure, diastolic blood pressure, serum total cholesterol, serum HDL-cholesterol, leisure-time physical activity, intakes of alcohol and energy, consumption of fruits, vegetables, rye, milk and coffee	The high intake of ultra-processed food increased risk of diabetes by 37%
Steinbrecher *et al.*, 2011 USA	Multiethnic Cohort (MEC) Study	More than 215 000 men and women, aged 45–75 years were recruited between 1993 and 1996	12	Processed meat (not specified) Moderate intake: 2° quintile of intake High intake: 5° quintile of intake	Ethnicity, education, body mass index, physical activity, age, and total energy intake	The high intake of ultra-processed food increased risk of diabetes by 57% for men and 45% for women
Fretts *et al.*, 2012 USA	Strong Heart Family Study (SHFS)	2001 individuals from 13 communities in Arizona, North Dakota, South Dakota, and Oklahoma, aged between 18 and 75 years	5	Spam, breakfast sausage, hot dogs, lunch meat Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, sex, site, total calories/day, education, smoking, alcohol, family history of diabetes, pedometer-determined physical activity, fibre from grains, glycaemic load, body mass index	Both moderate and high consumption of ultra-processed food were not associated with diabetes
Lajous *et al.*, 2012 France	Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale	66 118 disease-free French women	14	Sausage, salami, bacon, ham Moderate intake: 1 or 2/week High intake: >5/week	Age, education, residence in the Mediterranean, body mass index, smoking, parental history of diabetes, physical activity, hormone replacement therapy, hypertension, hypercholesterolaemia, n-3 polyunsaturated fatty acid, carbohydrates, fibre, coffee, and fruits and vegetables	The high intake of ultra-processed food increased risk of diabetes by 30%
van Woudenbergh *et al.*, 2012 The Netherlands	Rotterdam Study	4093 individuals from Rotterdam aged > 55 years	12.4	Meats that were preserved by smoking, curing, salting or addition of preservatives Moderate intake: >0 to <17.4 g daily High intake: >29.8 g daily	Age, body mass index, sex, smoking, diet prescription, family history of diabetes, intake of energy, energy-adjusted carbohydrates, energy-adjusted polyunsaturated fatty acids, energy-adjusted fibre, energy-adjusted milk, energy-adjusted cheese, soya, fish, alcohol, tea, red meat, poultry, and C-reactive protein	The moderate intake of ultra-processed food increased risk of diabetes by 76% and the high intake increased by 73%

(Continued)

Table 2 Continued

Identification	Sample	Sample characteristics	Follow-up time in years	Exposure	Adjustment	Main results
Bauer *et al*., 2013 The Netherlands	European Investigation into Cancer and Nutrition (EPIC-NL) study	20 385 overweight and obese participants in the Dutch	10.1	Soft drinks, other non-alcoholic beverages, French fries, snacks, low-fiberecereal bread Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, sex, total energy intake, education, physical activity, smoking, family history of diabetes, body mass index	The high intake of ultra-processed food increased risk of diabetes by 56%
Bendinelli *et al*., 2013 Multiple European countries	EPIC-InterAct study	340 234 individuals from 26 cohorts in eight European countries aged between 20 and 80 years	11.7	Bacon, ham, liver-containing items and all other processed meats (black pudding, chorizo, sausages, corned beef) Moderate intake: 2° quartile of intake High intake: 5° quartile of intake	Energy intake, sex, smoking, alcohol consumption, physical activity, education level, body mass index	The high intake of ultra-processed food increased risk of diabetes by 16%
Ericson *et al*., 2013 Sweden	Study of men and women from the Malmö Diet and Cancer (MDC)	27 140 women and men born between 1923 and 1945 living in the city of Malmo	12	Sausage and cured meat Moderate intake: 2° quartile of intake High intake: 5° quartile of intake	Age, method version, season, total energy, education, smoking, alcohol intake, physical activity, body mass index	Both moderate and high consumption of ultra-processed food were not associated with a higher risk of diabetes
Kurotani, 2013 Japan	Japan Public Health Center-based Prospective (JPHC)	89 947 individuals from five Japanese public health centre areas aged between 49 and 59 years	5	Ham, sausage or Wiener sausage, bacon, luncheonm eat Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, public health centre area, body mass index, smoking status, alcohol consumption, total physical activity, the history of hypertension, coffee consumption, the family history of diabetes, Mg intake, Ca intake, rice intake, fish intake, vegetable intake, soft drink consumption, energy intake	Both moderate and high consumption of ultra-processed food were not associated with diabetes
Son *et al*., 2019 South Korea	Korean Genome Epidemiology Study (KoGES)	10 030 individuals aged between 40 and 69 years from areas in South Korea	10	Vienna sausages or ham Moderate intake: <11.5 g/week High intake: >11.5 g/week	Age, sex, educational level, monthly household income, residential area, smoking, physical activity, body mass index, alcohol intake, energy intake, consumption levels of dietary fat, crude fibre, sodium, fruit and vegetables, and use of antihypertensive and antihyperlipidemic medication	Both moderate and high consumption of ultra-processed food were not associated with a higher risk of diabetes

(Continued)

Table 2 Continued

Identification	Sample	Sample characteristics	Follow-up time in years	Exposure	Adjustment	Main results
Srour *et al.*, 2020 France	French NutriNet-Santé cohort	104 707 French individuals aged 18 years or older	6	Ultra-processed food according to NOVA food classification system Moderate intake: increment of 10% in the consumption of ultra-processed food	Age, sex, educational level, baseline body mass index, physical activity level, smoking status, alcohol intake, number of 24-h dietary records, energy intake, Food Standard Agency nutrient profiling system dietary index score, family history of type 2 diabetes, weight change	An increment of 10% in the intake of ultra-processed food resulted in a risk by 13% for the development of diabetes
Levy *et al.*, 2021 UK	UK Biobank	21 730 individuals aged between 40 and 69 years	5.4	Ultra-processed food according to NOVA food classification system Moderate intake: 2° quartile of intake High intake: 4° quartile of intake	Age, family history of diabetes, sex, ethnicity, Index of Multiple Deprivation, physical activity, smoking status, total energy intake, body mass index	The high intake of ultra-processed food increased risk of diabetes by 44%
Llavero-Valero *et al.*, 2021 Spain	Seguimiento Universidad de Navarra (SUN)	20 060 individuals from Spain aged from 20 to 90 years	12	Ultra-processed food according to NOVA food classification system Moderate intake: 2° tertile of intake High intake: 3° tertile of intake	Sex, age, tertiles of body mass index, educational status, family history of diabetes, smoking status, snacking between meals, 8-item active + sedentary lifestyle score, following a special diet at baseline	The high intake of ultra-processed food increased risk of diabetes by 53%

Table 3 Quality of evidence in included studies in the systematic review, Newcastle-Ottawa Scale (NOS), ($N = 18$)

	Perspectives								
Study	Selection				Comparability	Outcome			Score
Longitudinal studies	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow up of cohorts	0 to 9
Schulze *et al.*, 2003	C	A*	B*	A*	B*	B*	A*	A*	7
Song *et al.*, 2004	C	A*	B*	A*	A*B*	C	A*	A*	6
Montonen *et al.*, 2005	B*	A*	B*	A*	A*	B*	A*	D	7
Villegas *et al.*, 2006	A*	A*	B*	A*	B*	B*	A*	B*	8
McNaughton *et al.*, 2008	C	A*	B*	A*	A*B*	B*	A*	B*	8
Mannisto *et al.*, 2010	C	A*	B*	A*	B*	B*	A*	B*	7
Steinbrecher *et al.*, 2011	A*	A*	B*	A*	A*B*	B*	A*	B*	9
Fretts *et al.*, 2012	A*	A*	B*	A*	A*B*	B*	A*	B*	9
Lajous *et al.*, 2012	C	A*	B*	A*	B*	B*	A*	A*	7
van Woudenbergh *et al.*, 2012	B*	A*	B*	A*	A*B*	B*	A*	B*	9
Bauer *et al.*, 2013	C	A*	B*	A*	A*B*	B*	A*	B*	8
Bendinelli *et al.*, 2013	C	A*	B*	B	A*B*	B*	A*	A*	7
Ericson *et al.*, 2013	A*	A*	B*	A*	A*B*	B*	A*	A*	9
Kurotani, 2013	B*	A*	B*	A*	A*B*	C	A*	A*	8
Son *et al.*, 2019	A*	A*	B*	A*	A*B*	B*	A*	B*	9
Srour *et al.*, 2020	C	A*	B*	A*	A*B*	B*	A*	B*	8
Levy *et al.*, 2021	D	A*	B*	A*	A*B*	C	A*	D	6
Llavero-Valero *et al.*, 2021	C	A*	B*	A*	A*B*	B*	A*	B*	8

A and B with * means that the study scored in the item. C and D means the article did not score in the item.

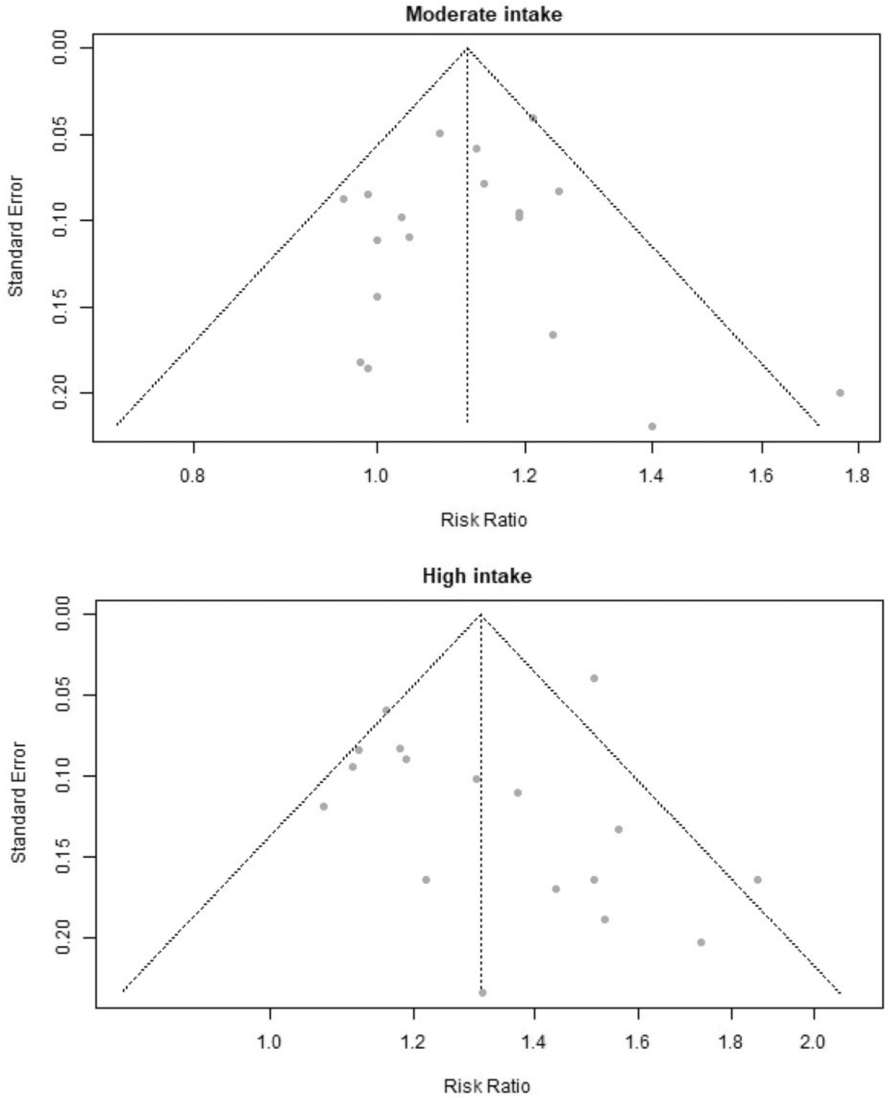

Figure 2 Funnel plot assessing the publication bias for association between ultra-processed food consumption and risk of diabetes

95% CI: 1.21–1.42, $I^2 = 60\%$). The results stratified by sex are shown in Figure 4. For men, moderate intake of ultra-processed food was associated with 12% risk of diabetes (RR: 1.12; 95% CI: 1.04–1.20, $I^2 = 2\%$) and for women, the risk was 11% (RR: 1.11; 95% CI: 1.04–1.19, $I^2 = 22\%$). In comparison with non-consumption of ultra-processed food, high intake increased risk of diabetes by 37% in men (RR: 1.37; 95% CI: 1.23–1.53, $I^2 = 47\%$) and 25% in women (RR: 1.25; 95% CI: 1.12–1.39, $I^2 = 59\%$).

Figure 5 presents our results stratified by follow-up duration. For studies with a duration of up to 9 years, moderate intake of ultra-processed food increased the risk of diabetes by 10% (RR: 1.10; 95% CI: 1.01–1.20, $I^2 = 32\%$) and for high intake, the risk was 27% (RR: 1.27; 95% CI: 1.11–1.44, $I^2 = 44\%$). For studies with 10 or more years, the risk of diabetes increased by 13% for moderate intake (RR: 1.13; 95% CI: 1.06–1.20, $I^2 = 2\%$) and by 33% for high intake (RR: 1.33; 95% CI: 1.20–1.47, $I^2 = 64\%$). The results for studies that classified the foods by the NOVA classification (Figure 6) showed no significant association for moderate intake (RR: 1.10; 95% CI: 0.99–1.23, $I^2 = 0\%$). However for high intake, the risk of diabetes increased by 48% (RR: 1.48; 95% CI: 1.16–1.89, $I^2 = 0\%$).

Figures 7, 8 and 9 show the analyses stratified by frequency of intake with dose-response results. A frequency of consumption from two to four times per week showed a risk of 1.20 for diabetes (RR: 1.20; 95% CI: 1.08–1.34, $I^2 = 0\%$) and consumption of five or more times per week increased diabetes risk by 1.44 (RR: 1.44; 95% CI: 1.21–1.172, $I^2 = 41\%$). Stratification by quartile of intake (amount of ultra-processed food consumed divided into four parts, with the first quartile being the lowest consumption) revealed that those in quartile three had a 27% risk of diabetes (RR: 1.27; 95% CI 1.05–1.55, $I^2 = 61\%$)

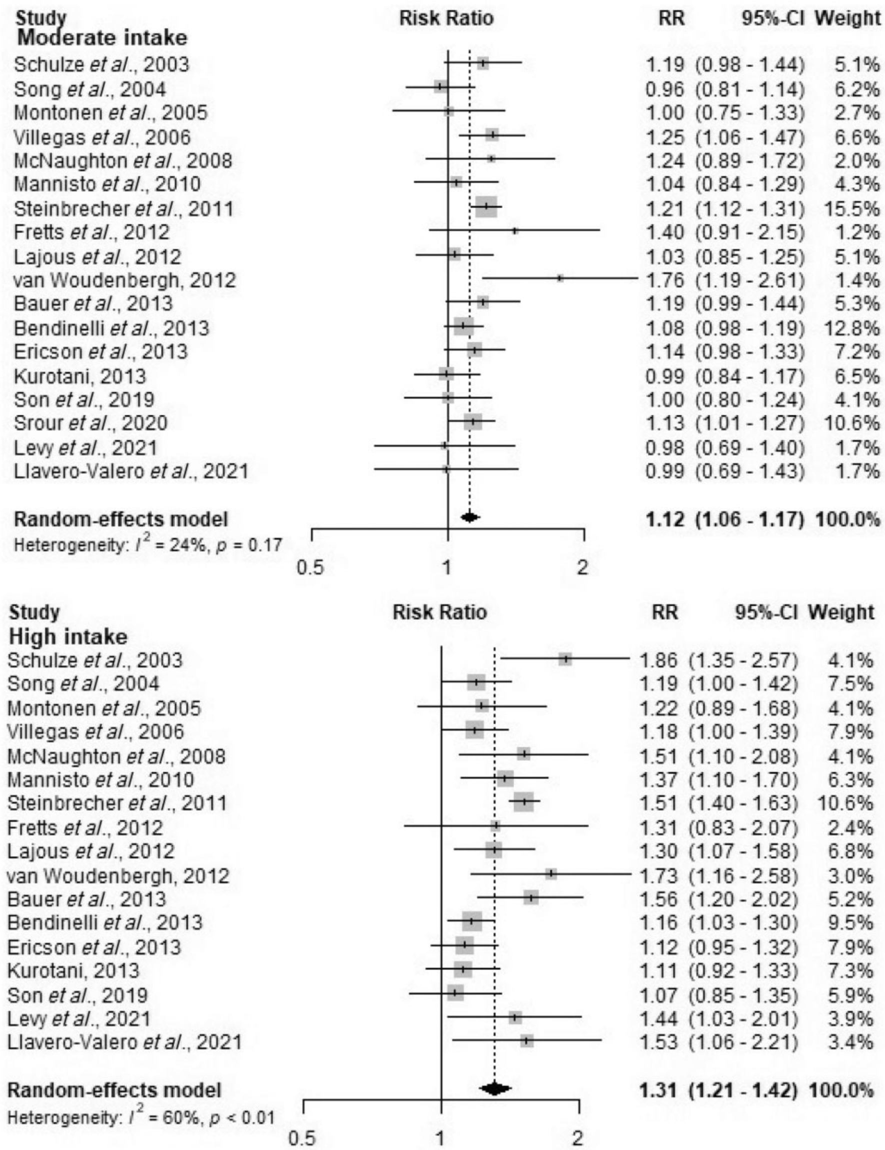

Figure 3 Forest plot of the association between ultra-processed food consumption and risk of diabetes using a random-effects model

and those in the last quartile had a risk of 35% (RR: 1.35; 95% CI: 1.19–1.53, $I^2 = 0\%$). In the analyses by quintile, the amount of ultra-processed food consumed being divided into five parts with the first quartile being the lowest consumption, results showed that the last quintile had a higher risk of diabetes (RR: 1.26; 95% CI: 1.14–1.40, $I^2 = 59\%$). Analysis according to NOS score showed significant results only for high-quality studies for the moderate-intake group (RR: 1.13; 95% CI: 1.08–1.19, $I^2 = 18\%$) and high-intake results were significant for medium- (RR: 1.40; 95% CI: 1.17–1.68, $I^2 = 0\%$) and high-quality studies (RR: 1.31; 95% CI: 1.20 – 1.43, $I^2 = 63\%$) (Figure 10). Results from moderate intake were significant only for the Western population (RR: 1.13; 95% CI 1.08–1.18, $I^2 = 11\%$); both Western (RR: 1.38; 95% CI: 1.26–1.50, $I^2 = 52\%$) and Eastern (RR: 1.13; 95% CI: 1.02 – 1.26, $I^2 = 0\%$) populations presented significant associations among high-intake groups (Figure 11). Figure 12 shows the results stratified by age at baseline. The risk of diabetes was higher in the individuals aged less than 50 years at baseline for the moderate-intake group (RR: 1.18; 95% CI: 1.11–1.26, $I^2 = 0\%$) and the high-intake group (RR: 1.52; 95% CI: 1.42–1.63, $I^2 = 0\%$).

Discussion

To the best of our knowledge, the present study is the first systematic review and meta-analysis to evaluate the consumption of ultra-processed food and risk of type 2 diabetes. Our results showed a positive association between

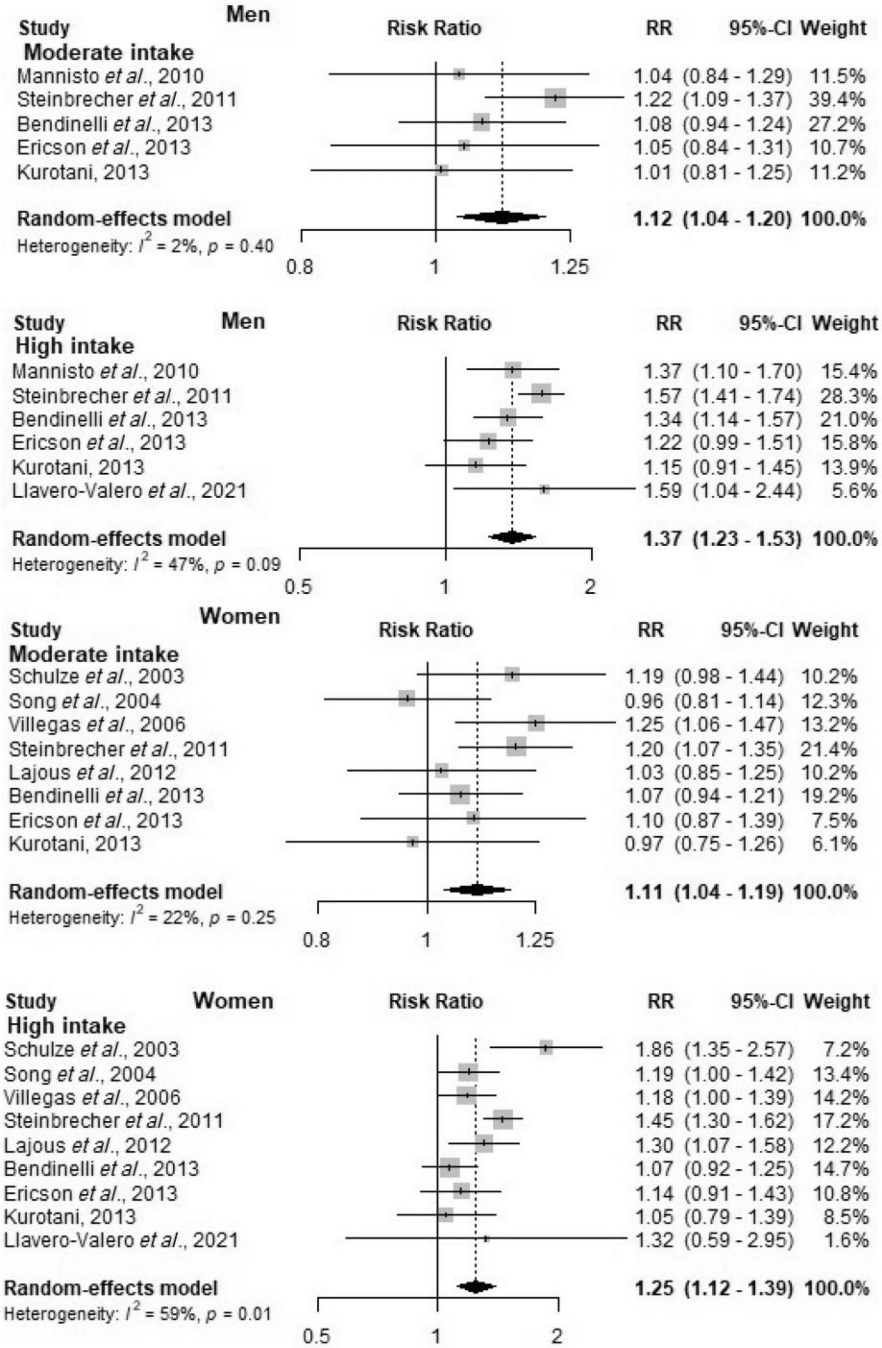

Figure 4 Forest plot of the association between ultra-processed food consumption and risk of diabetes using a random-effects model stratified by sex

moderate and high consumption of ultra-processed foods and diabetes. High consumption showed a higher risk of diabetes than low/moderate consumption. Our stratified analyses by frequency of consumption evidenced a dose-response relationship showing an increased risk of diabetes by consumption times per week and quartiles and quintiles of intake.

The analysis for follow-up duration showed that the results were higher in the studies longer than 10 years, for both moderate and high consumption. When we assessed the studies where the authors classified the foods as ultra-processed according to the NOVA food classification system, results showed for high consumption an increase of 48% in the risk of diabetes . Sensitivity analysis showed significant results for high-quality studies for moderate intake, and high-intake results were significant for medium- and high-quality studies. When we stratified by Eastern and Western populations, results from moderate intake

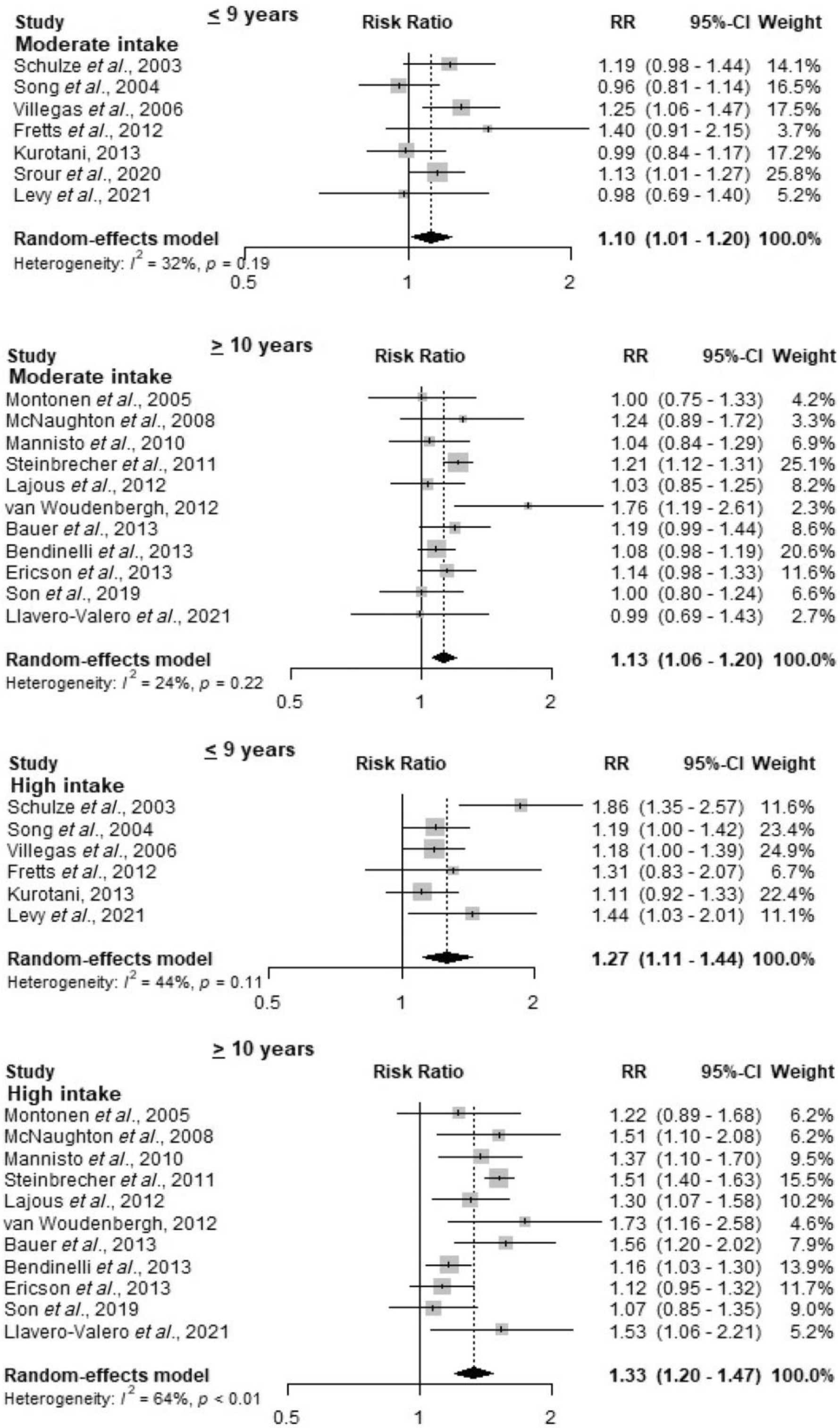

Figure 5 Forest plot of the association between ultra-processed food consumption and risk of diabetes using a random-effects model stratified by duration of follow-up

were null for Eastern populations. However, Western and Eastern showed a high risk of diabetes when consuming a high quantity of ultra-processed foods. Our stratification by age at baseline showed an increased risk among those aged less than 50 for both moderate- and high-intake groups.

In light of our results, a previous meta-analysis including 14 studies (most of them $n = 9$, with follow-up

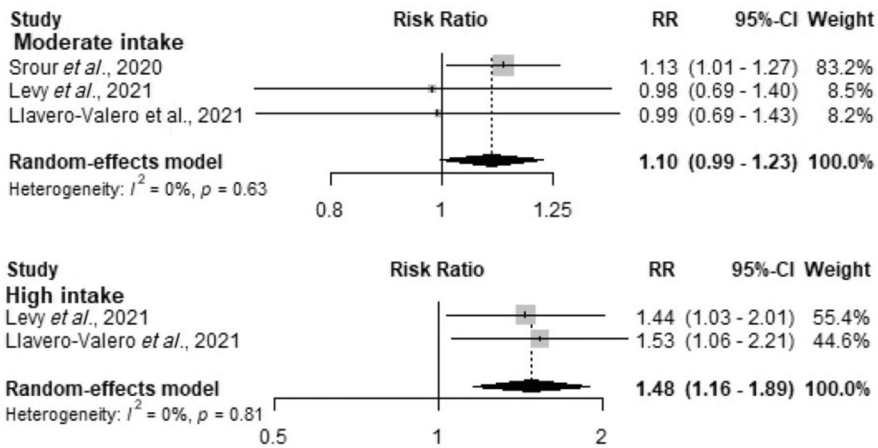

Figure 6 Forest plot of the association between ultra-processed food consumption and risk of diabetes using a random-effects model through the studies that classified foods according to the NOVA food classification system

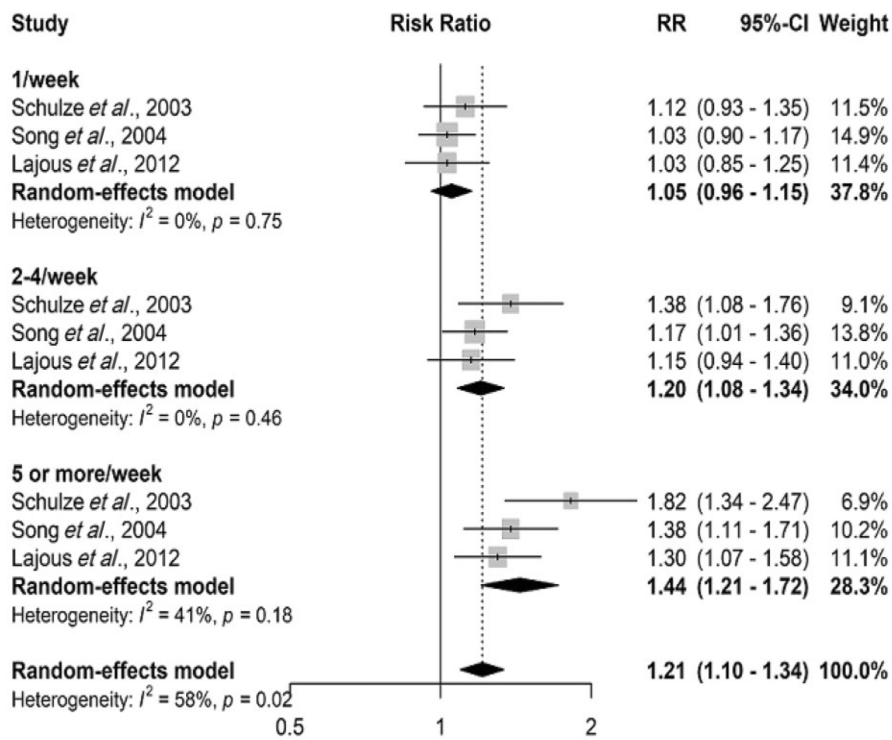

Figure 7 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to frequency of consumption in times per week

longer than 10 years) showed that individuals classified as having high consumption of processed meat (which is mostly part of ultra-processed foods) have statistically an increase in the risk of diabetes by 27%.[22] Each additional daily 50 g of processed meat increased risk by 37%.[22] A recent review showed that the consumption of ultra-processed food was associated with the risk of all-cause mortality and overall cardiovascular diseases.[17] Moreover, ultra-processed food is a risk factor for several conditions, including overweight/obesity, low HDL-cholesterol and metabolic syndrome.[51] According to a recent meta-analysis, both sweetened drinks that are high in calories and artificially sweetened drinks (which have no calories) are associated with a higher risk of diabetes.[23] From these results, it can be hypothesized that calories are not the only

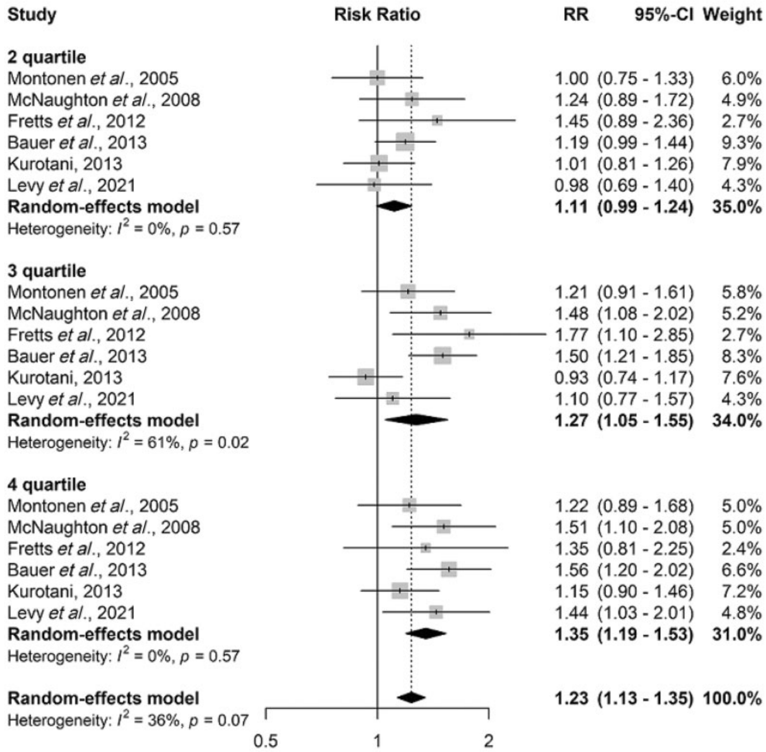

Figure 8 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to frequency of quartiles of intake (amount of ultra-processed food consumed divided into four parts, with the first quartile being the lowest consumption)

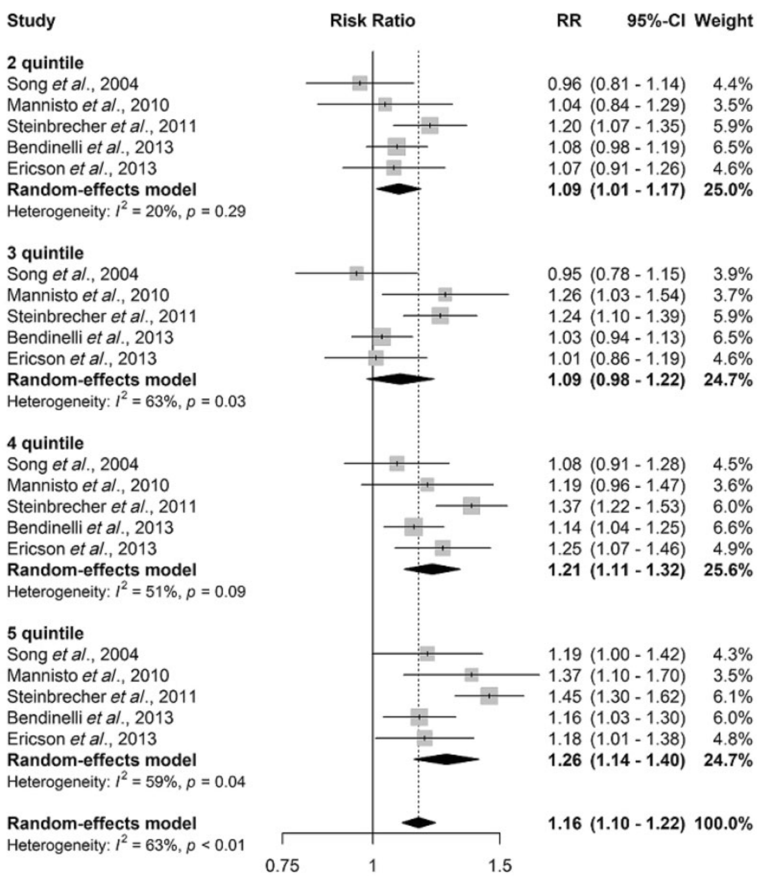

Figure 9 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to frequency of quintiles of intake (amount of ultra-processed food consumed divided into five parts, with the first quartile being the lowest consumption)

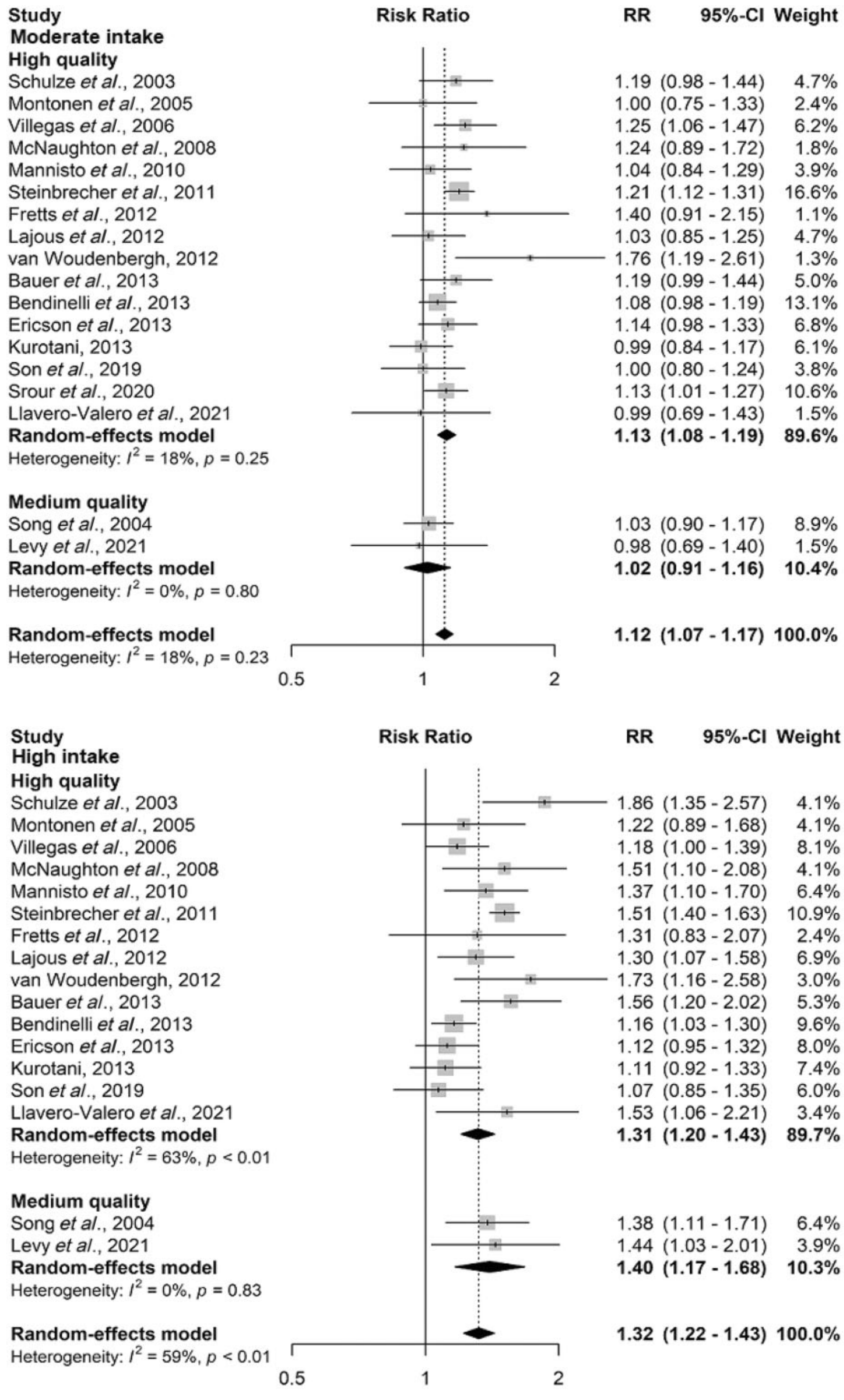

Figure 10 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to the Newcastle-Ottawa Scale (NOS)

problem that leads to diabetes in ultra-processed foods, but the additives they contain also seem to have an influence [52].

In children of low socioeconomic status, the consumption of ultra-processed food was associated with an increase in waist circumference, but not affecting glucose metabolism.[53] In adolescents, high consumption of ultra-processed foods increased the prevalence of metabolic syndrome.[54] A review from 2017 showed evidence that ultra-processed food is associated with a high risk of elevated fasting glucose, obesity and metabolic syndrome.[55] The authors conclude that it is unclear if the association

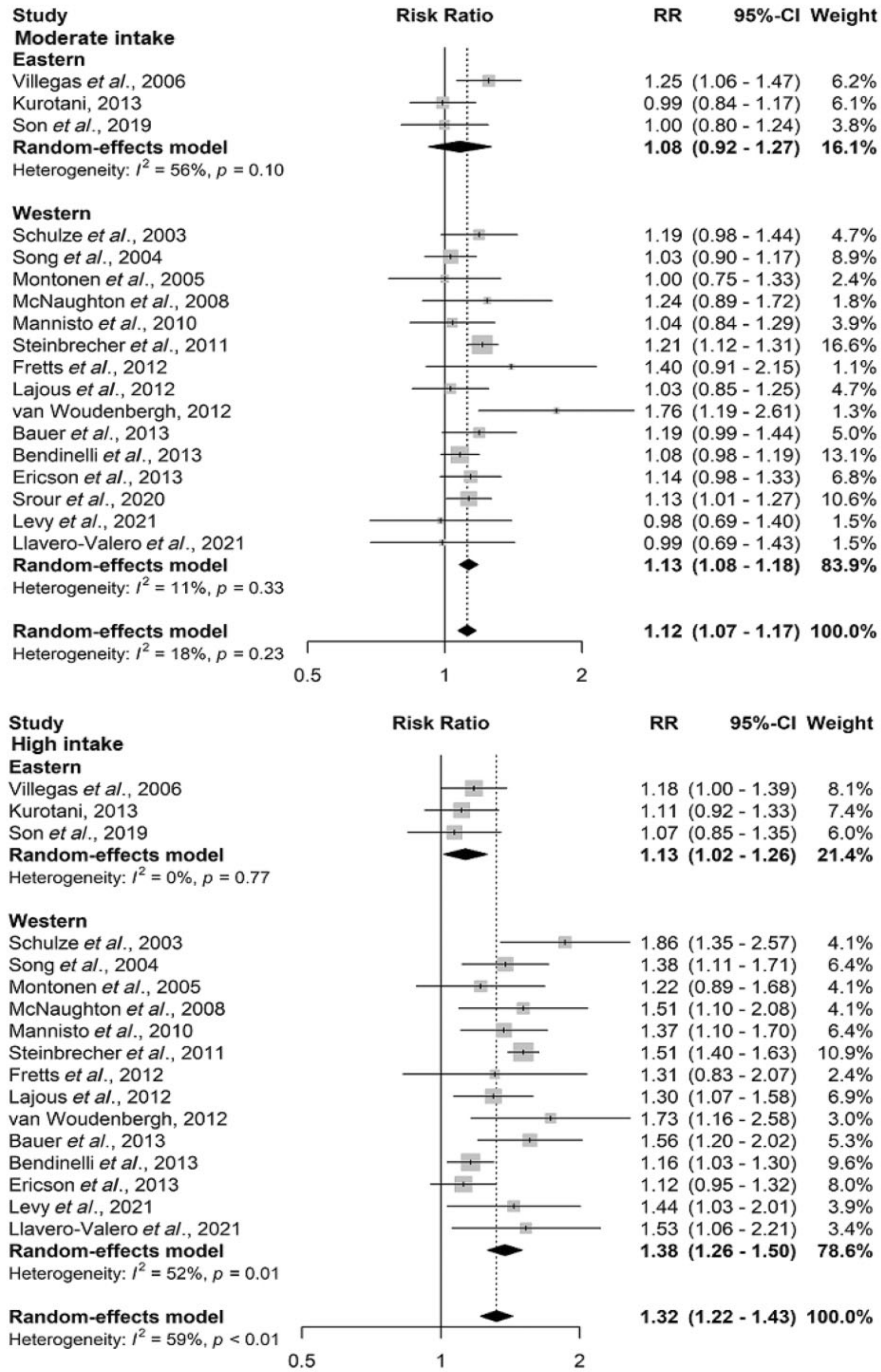

Figure 11 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to race (Western and Eastern)

happens through food processing or the content of ultra-processed foods.[55]

The process that ultra-processed products go through involves different aspects, including fractionating whole foods into smaller parts, chemical modifications, different cosmetic additives and sophisticated packaging.[12] Each of these processes can be a significant risk factor in the development of diabetes. For example, bisphenol (a common component in plastic packaging) increased the risk of diabetes by 28% in a meta-analysis with 41 320 individuals.[56] Furthermore, a study showed that exposition to carrageenan, an additive commonly used in processed food, elevated fasting blood glucose and insulin resistance in mice.[57,58] Also, ultra-processed foods represent an increase in energy intake, since among its characteristics is the fact that it contains large amounts of calories in small portions.[59–61] It is known the higher-energy intake of these foods that present high in sodium, added sugar, trans fats

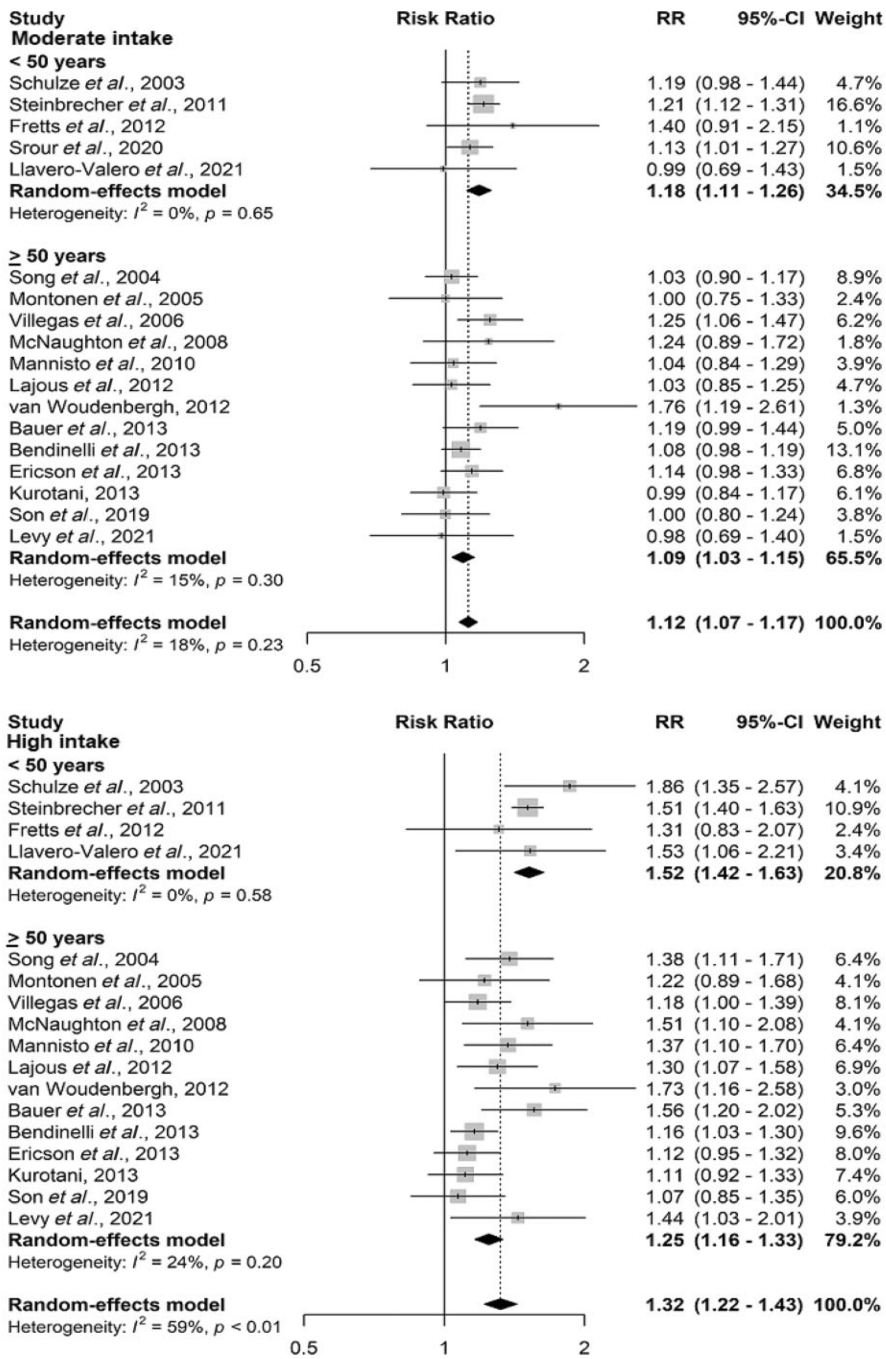

Figure 12 Forest plot of the association between ultra-processed food consumption and risk of diabetes according to age at baseline

and saturated fat is associated with a higher chance of overweight and obesity, which are risk factors for diabetes.[62]

Several alternatives may be helpful for diabetes treatment or prevention, in addition to non-consumption of ultra-processed foods. The exchange of these foods for fruits and vegetables can be a practical and healthy option. According to previous meta-analysis, increase in consumption of fruits and vegetables is associated with reduction in the risk of diabetes.[63,64] The practice of physical activity and some alternative treatments may also be helpful in the prevention of diabetes.[65–67]

The literature has evidenced strategies to decrease the consumption of ultra-processed foods and increase less processed foods consumption. Some authors have proposed the taxation of ultra-processed foods and a decrease in the price of more natural foods.[68,69] However, such a proposal must be made with special attention to low-income countries, as it can limit access to food for people with few resources to buy food. On the other hand, if in consonance with these strategies, the governments increase access to healthier foods, facilitate their acquisition and encourage production, such strategies may be viable. In Brazil, a study estimated the increase in the price of ultra-processed foods and obesity. Authors showed that a 1% increase in the price of ultra-processed foods might represent a decrease of 0.33 and 0.59% in the prevalence of overweight and obesity, respectively.[70] In addition to the taxation, change is expected by companies reformulating their products to fit the new regulations.[71]

This meta-analysis has several strengths. First, to our knowledge it is the first meta-analysis of longitudinal studies that assessed the risk from ultra-processed foods in the development of diabetes. With our results, we are adding new knowledge to the literature from 18 included studies. Second, we included a high number of databases, in addition to a non-systematic search on Google Scholar in order to find all studies on the topic. Third, we expanded the keywords to find any study that has evaluated foods that fit as ultra-processed. Fourth, our analysis included only longitudinal studies, which are mostly represented by large samples.

However, we need to point out some limitations. There were significant variations in the measures to assess food consumption, the number of subjects included in each cohort and the follow-up duration. Also, many studies evaluated only processed meats (which are in the ultra-processed category), and only three studies categorized their foods according to the NOVA food system classification. However, our stratified analysis showed that, from these three studies, the risk of diabetes was statistically significant higher in the group classified as high-consumption of ultra-processed food compared with those in the lowest-consumption group. Despite the strengths and limitations, our results were consistent and may be important for public policies to be undertaken in the face of the risk of ultra-processed foods in the development of diabetes.

In conclusion, our results showed that the consumption of ultra-processed foods substantially increased the risk for type 2 diabetes, with a dose-response effect and moderate to high credibility of evidence. Strategies such as exchange for fresh or minimally processed foods and physical activity, in addition to alternative therapies, can be effective in preventing or treating diabetes, as long as they are accompanied by a reduction in the consumption of ultra-processed foods.

Supplementary Data

Supplementary data are available at *IJE* online.

Ethics approval

The present manuscript does not require institutional ethics approval since we did not collect personal or confidential information from participants and all evidence collected is publicly accessible.

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Data availability

No new data were generated or analyzed in support of this research.

Author Contributions

F.M.D. designed, wrote and was the first reviewer of the manuscript. L.M.F. was the second reviewer and contributed to the writing of the manuscript. F.S.S. was a reviewer and contributed to the writing of the manuscript. B.G.C.S., R.M.B., G.C.M., T.R.M., R.A.A. and BPN reviewed and contributed part of the writing of the manuscript. All authors reviewed and approved the final version of the manuscript.

Conflict of Interest

None declared.

References

1. Yang JJ, Yu D, Wen W *et al.* Association of diabetes with all-cause and cause-specific mortality in Asia: a pooled analysis of more than 1 million participants. *JAMA Netw Open* 2019;**2**:e192696.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;**33(Suppl 1)**:S62–69.
3. Wright AK, Kontopantelis E, Emsley R *et al.* Life expectancy and cause-specific mortality in type 2 diabetes: a population-based cohort study quantifying relationships in ethnic subgroups. *Diabetes Care* 2017;**40**:338–45.
4. Bardenheier BH, Lin J, Zhuo X *et al.* Disability-free life-years lost among adults aged ≥50 years with and without diabetes. *Diabetes Care* 2016;**39**:1222–29.
5. Lin X, Xu Y, Pan X *et al.* Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. *Sci Rep* 2020;**10**:14790.
6. Gregg EW, Zhuo X, Cheng YJ, Albright AL, Narayan KMV, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985-2011: a modelling study. *Lancet Diabetes Endocrinol* 2014;**2**:867–74.
7. Kontis V, Bennett JE, Mathers CD, Li G, Foreman K, Ezzati M. Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble. *Lancet* 2017;**389**:1323–35.
8. Yang W, Dall TM, Beronjia K *et al.* Economic costs of diabetes in the U.S. in 2017. *Diabetes Care* 2018;**41**:917–28.
9. Bommer C, Sagalova V, Heesemann E *et al.* Global economic burden of diabetes in adults: projections from 2015 to 2030. *Diabetes Care* 2018;**41**:963–70.

10. Martins APB, Levy RB, Claro RM, Moubarac JC, Monteiro CA. Increased contribution of ultra-processed food products in the Brazilian diet (1987-2009). *Rev Saude Publica* 2013;**47**: 656–65.
11. Monteiro CA, Levy RB, Claro RM, De Castro IRR, Cannon G. Increasing consumption of ultra-processed foods and likely impact on human health: Evidence from Brazil. *Public Health Nutr* 2011;**14**:5–13.
12. Monteiro CA, Cannon G, Levy RB *et al.* Ultra-processed foods: what they are and how to identify them. *Public Health Nutr* 2019;**22**:936–41.
13. MacHado PP, Steele EM, Levy RB *et al.* Ultra-processed foods and recommended intake levels of nutrients linked to non-communicable diseases in Australia: Evidence from a nationally representative cross-sectional study. *BMJ Open* 2019;**9**: e029544.
14. Rauber F, Louzada MLDC, Martinez Steele E *et al.* Ultra-processed foods and excessive free sugar intake in the UK: A nationally representative cross-sectional study. *BMJ Open* 2019;**9**: e027546.
15. Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev* 2012**70**:3–21.
16. Askari M, Heshmati J, Shahinfar H, Tripathi N, Daneshzad E. Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies. *Int J Obes (Lond))* 2020;**44**:2080–91.
17. Chen X, Zhang Z, Yang H *et al.* Consumption of ultra-processed foods and health outcomes: a systematic review of epidemiological studies. *Nutr J* 2020;**19**:86.
18. Lane MM, Davis JA, Beattie S *et al.* Ultraprocessed food and chronic noncommunicable diseases: a systematic review and meta-analysis of 43 observational studies. *Obes Rev* 2021;**22**: e13146.
19. Levy RB, Rauber F, Chang K *et al.* Ultra-processed food consumption and type 2 diabetes incidence: a prospective cohort study. *Clin Nutr* 2021;**40**:3608–14.
20. Llavero-Valero M, Escalada San Martín J, Martínez-González MA, Basterra-Gortari FJ, de la Fuente-Arrillaga C, Bes-Rastrollo M. Ultra-processed foods and type-2 diabetes risk in the SUN project: a prospective cohort study. *Clin Nutr* 2021;**40**:2817–24.
21. Nardocci M, Polsky JY, Moubarac JC. Consumption of ultra-processed foods is associated with obesity, diabetes and hypertension in Canadian adults. *Can J Public Heal* 2021;**112**: 421–29.
22. Schwingshackl L, Hoffmann G, Lampousi AM *et al.* Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* 2017; **32**:363–75.
23. Qin P, Li Q, Zhao Y *et al.* Sugar and artificially sweetened beverages and risk of obesity, type 2 diabetes mellitus, hypertension, and all-cause mortality: a dose–response meta-analysis of prospective cohort studies. *Eur J Epidemiol* 2020;**35**:655–71.
24. Stroup DF, Berlin JA, Morton SC *et al.* Meta-analysis of observational studies in epidemiology: A proposal for reporting. *JAMA* 2000;**283**:2008–12.
25. Matthew P, Joanne M, Patrick B *et al. PRISMA 2020 Statement: Updated Guidelines for Reporting Systematic Reviews and Meta Analyses*. 2019. https://linkinghub.elsevier.com/retrieve/pii/S0895435621000731 (1 April 2021, date last accessed).
26. Wells G, Shea B, O'Connell D, Peterson J. *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses*. 2000. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (10 November 2019, date last accessed)
27. Jenkins RH, Vamos EP, Taylor-Robinson D, Millett C, Laverty AA. Impacts of the 2008 Great Recession on dietary intake: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act* 2021;**18**:1–20.
28. Jawad M, Vamos EP, Najim M, Roberts B, Millett C. Impact of armed conflict on cardiovascular disease risk: a systematic review. *Heart* 2019;**105**:1388–94.
29. Schwingshackl L, Knüppel S, Schwedhelm C *et al.* Perspective: NutriGrade: A scoring system to assess and judge the meta-evidence of randomized controlled trials and cohort studies in nutrition research. *Adv Nutr* 2016;**7**:994–1004.
30. Lytras T. Web Application to Run Meta-Analyses [R package miniMeta version 0.2]. Comprehensive R Archive Network (CRAN). 2020. https://cran.r-project.org/package=miniMeta (15 April 2021, date last accessed).
31. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;**7**:177–88.
32. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539–58.
33. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2007;**298**:2654–64.
34. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA* 1998;**280**:1690–91.
35. Schulze MB, Manson JE, Willett WC, Hu FB. Processed meat intake and incidence of Type 2 diabetes in younger and middle-aged women. *Diabetologia* 2003;**46**:1465–73.
36. Song Y, Manson JE, Buring JE, Liu S. A prospective study of red meat consumption and type 2 diabetes in middle-aged and elderly women: The women's health study. *Diabetes Care* 2004; **27**:2108–15.
37. Steinbrecher A, Erber E, Grandinetti A, Kolonel LN, Maskarinec G. Meat consumption and risk of type 2 diabetes: the multiethnic cohort. *Public Health Nutr* 2011;**14**:568–74.
38. Fretts AM, Howard BV, McKnight B *et al.* Associations of processed meat and unprocessed red meat intake with incident diabetes: the Strong Heart Family Study. *Am J Clin Nutr* 2012;**95**: 752–58.
39. McNaughton SA, Mishra GD, Brunner EJ. Dietary patterns, insulin resistance, and incidence of type 2 diabetes in the Whitehall II study. *Diabetes Care* 2008;**31**:1343–48.
40. Van Woudenbergh GJ, Kuijsten A, Tigcheler B *et al.* Meat consumption and its association with C-reactive protein and incident type 2 diabetes: the Rotterdam study. *Diabetes Care* 2012; **35**:1499–505.
41. Bauer F, Beulens JWJ, Van Der A DL *et al.* Dietary patterns and the risk of type 2 diabetes in overweight and obese individuals. *Eur J Nutr* 2013;**52**:1127–34.
42. Bendinelli B, Palli D, Masala G *et al.*; InterAct Consortium. Association between dietary meat consumption and incident

type 2 diabetes: the EPIC-InterAct study. *Diabetologia* 2013;**56**:47–59.

43. Montonen J, Järvinen R, Heliövaara M, Reunanen A, Aromaa A, Knekt P. Food consumption and the incidence of type II diabetes mellitus. *Eur J Clin Nutr* 2005;**59**:441–48.
44. Villegas R, Xiao OS, Gao YT *et al.* The association of meat intake and the risk of type 2 diabetes may be modified by body weight. *Int J Med Sci* 2006;**3**:152–59.
45. Lajous M, Tondeur L, Fagherazzi G, De Lauzon-Guillain B, Boutron-Ruaualt MC, Clavel-Chapelon F. Processed and unprocessed red meat consumption and incident type 2 diabetes among French women. *Diabetes Care* 2012;**35**:128–30.
46. Männistö S, Kontto J, Kataja-Tuomola M, Albanes D, Virtamo J. High processed meat consumption is a risk factor of type 2 diabetes in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study. *Br J Nutr* 2010;**103**:1817–22.
47. Ericson U, Sonestedt E, Gullberg B *et al.* High intakes of protein and processed meat associate with increased incidence of type 2 diabetes. *Br J Nutr* 2013;**109**:1143–53.
48. Kurotani K, Nanri A, Goto A *et al.*; Japan Public Health Center-based Prospective Study Group. Red meat consumption is associated with the risk of type 2 diabetes in men but not in women: a Japan public health center-based prospective study. *Br J Nutr* 2013;**110**:1910–18.
49. Son J, Lee Y, Park K. Effects of processed red meat consumption on the risk of type 2 diabetes and cardiovascular diseases among Korean adults: the Korean Genome and Epidemiology Study. *Eur J Nutr* 2019;**58**:2477–84.
50. Srour B, Fezeu LK, Kesse-Guyot E *et al.* Ultraprocessed food consumption and risk of type 2 diabetes among participants of the NutriNet-santé prospective cohort. *JAMA Intern Med* 2020;**180**:283–91.
51. Pagliai G, Dinu M, Madarena MP, Bonaccio M, Iacoviello L, Sofi F. Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. *Br J Nutr*. 2021;**125**:308–18.
52. Juul F, Vaidean G, Parekh N. Ultra-processed foods and cardiovascular diseases: potential mechanisms of action. *Adv Nutr* 2021;**12**:1673–80.
53. Costa CS, Rauber F, Leffa PS, Sangalli CN, Campagnolo PDB, Vitolo MR. Ultra-processed food consumption and its effects on anthropometric and glucose profile: A longitudinal study during childhood. *Nutr Metab Cardiovasc Dis* 2019;**29**:177–84.
54. Tavares LF, Fonseca SC, Garcia Rosa ML, Yokoo EM. Relationship between ultra-processed foods and metabolic syndrome in adolescents from a Brazilian Family Doctor Program. *Public Health Nutr* 2012;**15**:82–87.
55. Poti JM, Braga B, Qin B. Ultra-processed food intake and obesity: what really matters for health-processing or nutrient content? *Curr Obes Rep* 2017;**6**:420–31.
56. Hwang S, Lim JE, Choi Y, Jee SH. Bisphenol A exposure and type 2 diabetes mellitus risk: a meta-analysis. *BMC Endocr Disord* 2018;**18**:81.
57. Bhattacharyya S, Feferman L, Unterman T, Tobacman JK. Exposure to common food additive carrageenan alone leads to fasting hyperglycemia and in combination with high fat diet exacerbates glucose intolerance and hyperlipidemia without effect on weight. *J Diabetes Res* 2015;**2015**:1.
58. Bhattacharyya S, O-Sullivan I, Katyal S, Unterman T, Tobacman JK. Exposure to the common food additive carrageenan leads to glucose intolerance, insulin resistance and inhibition of insulin signalling in HepG2 cells and C57BL/6J mice. *Diabetologia* 2012;**55**:194–203.
59. Pérez-Escamilla R, Obbagy JE, Altman JM *et al.* Dietary energy density and body weight in adults and children: a systematic review. *J Acad Nutr Diet* 2012;**112**:671–84.
60. Hall KD, Ayuketah A, Brychta R *et al.* Erratum: Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. *Cell Metab* 2019;**30**:67–77.e3.
61. Rouhani MH, Haghighatdoost F, Surkan PJ, Azadbakht L. Associations between dietary energy density and obesity: a systematic review and meta-analysis of observational studies. *Nutrition* 2016;**32**:1037–47.
62. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: A meta-analysis of prospective cohort studies. *Diabetes Res Clin Pract* 2010;**89**:309–19.
63. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: Systematic review and meta-analysis. *BMJ* 2010;**341**:c4229.
64. Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open* 2014;**4**:e005497.
65. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis. *Eur J Epidemiol* 2015;**30**:529–42.
66. Delpino FM, Figueiredo LM, da Silva BGC *et al.* Omega-3 supplementation and diabetes: a systematic review and meta-analysis. *Crit Rev Food Sci Nutr* 2021. PMID: 33480268.
67. Delpino FM, Figueiredo LM. Resveratrol supplementation and type 2 diabetes: a systematic review and meta-analysis. *Crit Rev Food Sci Nutr* 2021. PMID: 33480264.
68. Boysen O, Boysen-Urban K, Bradford H, Balié J. Taxing highly processed foods: what could be the impacts on obesity and underweight in sub-Saharan Africa? *World Dev* 2019;**119**:55–67.
69. Caro JC, Ng SW, Taillie LS, Popkin BM. Designing a tax to discourage unhealthy food and beverage purchases: the case of Chile. *Food Policy* 2017;**71**:86–100.
70. dos Passos CM, Maia EG, Levy RB, Martins APB, Claro RM. Association between the price of ultra-processed foods and obesity in Brazil. *Nutr Metab Cardiovasc Dis* 2020;**30**:589–98.
71. Scarpelli DQ, Fernandes ACP, Osiac LR, Quevedo TP. Changes in nutrient declaration after the food labeling and advertising law in Chile: a longitudinal approach. *Nutrients* 2020;**12**:1–13.