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REVIEW ARTICLE

Epidemiology and Population Health

Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies

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Abstract

Background Numerous studies have reported the association of ultra-processed foods with excess body weight; however, the nature and extent of this relation has not been clearly established. This systematic review was conducted to analyze the currently documented evidence regarding the association between ultra-processed food with overweight and obesity.
Methods A literature search was performed using multiple literature databases for relevant articles published prior to November 2019. Random effects model, namely the DerSimonian–Laird method, was applied to pool effect sizes. The potential sources of heterogeneity across studies were explored using the Cochrane Q test.
Results Fourteen studies (one cohort study and thirteen cross-sectional studies) were included in this review. A significant association was identified between ultra-processed food intake and overweight (pooled effect size: 1.02; 95% confidence interval (95% CI): 1.01, 1.03, $p < 0.001$) and obesity (pooled effect size: 1.26; 95% CI: 1.13, 1.41, $p < 0.001$).
Conclusion Our findings revealed a positive association between ultra-processed foods and excess body weight. Future studies with longitudinal designs and adequate control for confounding factors are required to clarify whether ultra-processed food intake alters anthropometric parameters and leads to obesity.

Introduction

Obesity and overweight are two prevalent public health problems caused by multifactorial and complex processes that influence countries of various economic conditions [1]. According to the World Health Organization, in 2016, over 1.9 billion adults were overweight, of which, more than 650 million were obese [2]. In 2017, the Global Burden of Disease Project estimated high body mass index (BMI) as the fourth-leading risk factor worldwide for chronic diseases such as cancer, CVD and diabetes, among other health complications [3, 4]. Changes in the global food system, particularly, ultra-food processing performed in the last few decades, are commonly stated to increase incidence and prevalence of excess body weight [5].

In the NOVA food classification system [6], foods and food products are assorted into four categories according to the degree of processing, including unprocessed and minimally processed foods (e.g., fresh fruits and vegetables), processed culinary ingredients (e.g., sugar and honey), processed foods (e.g., fruits in sirup and vegetables in brine), and ultra-processed foods (e.g., pizza and instant noodles) [7]. Ultra-processed foods are often referred to as entirely industrially manufactured, “ready-to-eat”, or “ready-to-heat” preparations created from industrial formulations manufactured from substances derived from foods and additives, with minimal whole foods [7, 8]. Based on this description, ultra-processed foods are commonly high in added sugars, salt, dietary energy density, along with saturated and trans fats; on the other hand, they contain low amounts of fiber, protein, micronutrients, and phytochemicals [8–10].

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The impact of ultra-processed food on several lifestyle-related diseases including diabetes mellitus, metabolic syndrome, heart disease, dyslipidemia, hypertension, and cancer has been previously demonstrated [11–17]. Recently, a possible relationship between ultra-processed food and excess weight is being more widely deliberated. Several studies have suggested that ultra-processed food is associated with excess body weight [18–29], while other studies did not verify such association with any significance [30, 31].

To our best knowledge, no meta-analysis has so far analyzed the association between ultra-processed food and excess body weight. Thus, we conducted a comprehensive systematic review and meta-analysis of descriptive studies, in order to pool available data addressing the association between consumption of ultra-processed foods, and obesity and overweight in adults.

Methodology

Systematic review and meta-analysis were carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines [32].

Information sources and search strategy

A literature search was performed using multiple literature databases, Scopus, PubMed, and ISI (Web of Science), for relevant articles published prior to November 2019. The following keywords, including those from the medical subject headings (MeSH) and non-MeSH terms, were utilized in this search: ("fast foods" OR "Processed food" OR "Ultra-processed food" OR "Processed meat" OR Ham OR Sausages OR Hamburger OR Bacon OR "Luncheon meats") AND ("Body mass index" OR "Bodyweight" OR Obesity OR "Excess weight" OR "Central obesity" OR "Waist circumference" OR "Abdominal obesity" OR "Visceral Obesity" OR Obes* OR Overweight OR Adiposity). No restrictions were set regarding the language and publication date. Moreover, we reviewed references listed by all studies that were revealed in our database searches in order to further collect potentially missed publications. Unpublished data were not included in this meta-analysis. To facilitate the referral process, all publications were stored in the EndNote library (version X9, for Windows, Thomson Reuters, Philadelphia, PA, USA), and duplicate citations were removed. The detailed steps of the literature search are depicted in Fig. 1.

Inclusion criteria

Studies included in the meta-analysis met the following inclusion criteria: (1) were observational studies; (2) considered ultra-processed food as the exposure (as defined by the NOVA classification system in 13 out of 14 studies); (3) examined the association with excess body weight and obesity; (4) reported data as odds ratio (OR), relative risks (RRs), or hazard ratio (HR) with corresponding 95% CIs for the association of ultra-processed food consumption with excess body weight and obesity; and (5) were published in English. Excess body weight was identified as BMI ≥ 25.0 kg/m^2 and obesity as BMI ≥ 30.0 kg/m^2.

Exclusion criteria

Exclusion criteria were as follows: (1) duplicate studies (2) gray literature including book chapters, letters, and comments; (3) animal, in vitro, and cell culture studies; (4) review articles; (5) unrelated publications; and (6) publications that did not meet the inclusion criteria based on the title or abstract. Articles that met the inclusion criteria were reviewed in their entirety. Among the studies that qualified for full-text evaluation, articles were excluded based on the following: (a) non-observational design; (b) review study; (c) irrelevant outcomes reported; (d) data not reported as HRs, RRs or ORs with corresponding 95% CI; and (h) full text published in non-English language. Furthermore, if more than one study used the same dataset, only one study with the largest number of incident cases was entered.

Data extraction

The following data from eligible published articles were extracted: (1) first author's name; (2) year of publication; (3) study design; (4) study location; (5) age range and sex; (6) study sample size; (7) duration of follow-up for cohort studies; (8) ultra-processed food exposure assessment methods; (9) outcome measures, including excess body weight and obesity; and (10) reported risk estimates related to excess bodyweight and obesity (including ORs, RRs, and HRs and 95% confidence intervals). In the present study, reported risk estimates (ORs, RRs, or HRs) for excess bodyweight and obesity among subjects with the highest exposure to the ultra-processed foods were compared to those with the lowest exposure; adjusted effect sizes of covariates were extracted. Several e-mails on multiple occasions were sent to the corresponding authors of the studies, which did not report sufficient data. Each of the above-mentioned steps were assessed by two independent researchers (MA, HSH) and resolved by a third investigator (ED).

Quality of evidence

The Newcastle–Ottawa Scale (NOS) was used to assess the overall quality of studies (Supplementary Table S1). The NOS checklist consists of three sections: selection, comparability, and outcome. Each section was assigned a

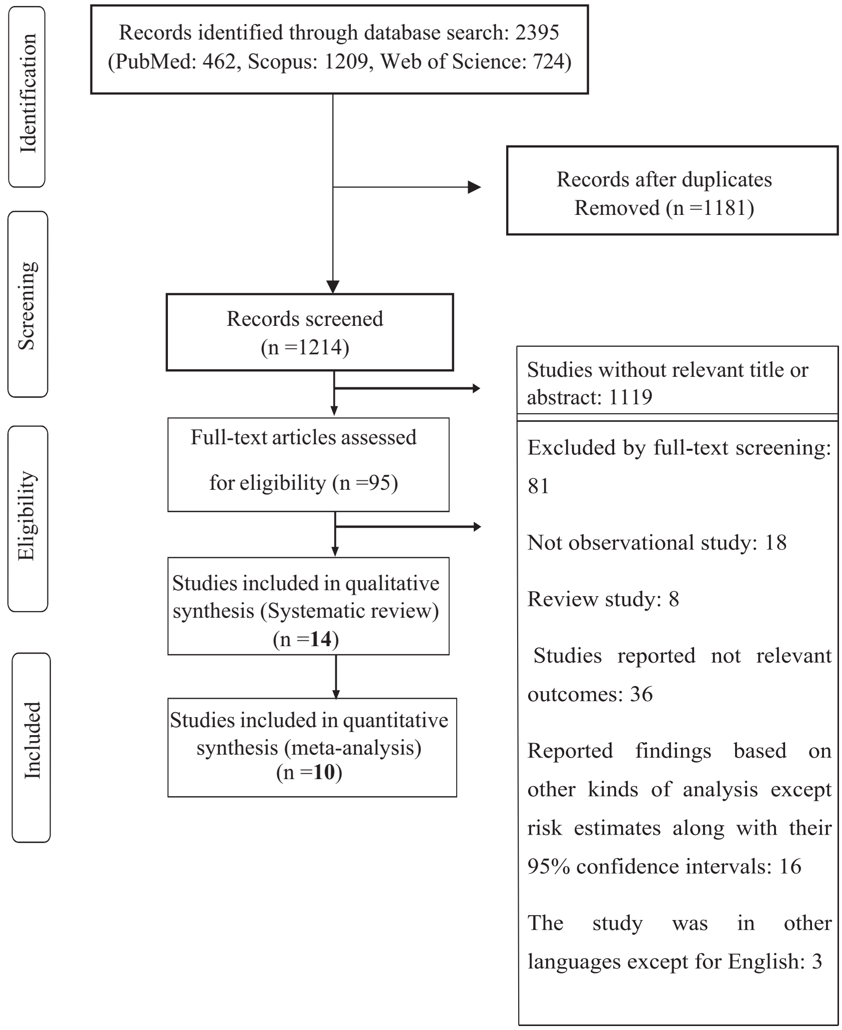

Fig. 1 Literature search flow chart. Flow diagram of study selection for systematic review and meta-analysis.

maximum of four, two and three points, respectively. According to NOS thresholds, 1–3 points indicated poor quality, 4–6 points indicated fair quality, and 7–9 points indicated high quality [33].

Statistical method

All data were measured as log RR with standard errors (SEs) by using the odds ratio, relative risks (and their 95% CI). Fixed-effect model was employed in order to pool effect sizes. The potential sources of heterogeneity across studies were explored using Q Cochrane test and I^2 statistics [34]. I^2 scores of 50% or higher determined the heterogeneity status. Heterogeneity, when evident, was reduced with reanalysis of our data with a random-effects model. Subgroup analysis with the fixed-effect model was conducted on the following factors: study design (cohort or cross-sectional), sample size (be low or above 8000), continent (Europe or North America or South America), study quality (good or fair), exposure assessment tool (food record or food frequency questionnaire), energy adjusted (yes or no), BMI adjusted (yes or no), and outcome measures (excess body weight and obesity). In addition, potential for publication bias was explored visually by the funnel plot and confirmed statistically with Egger's weighted regression test. If publication bias was observed, the trim and fill method was utilized to re-estimate the effect size [35]. Moreover, sensitivity analysis was performed by omitting one or several studies at each stage to assess whether a single study or several publications affected the overall effect size. All statistical analyses were accomplished using STATA software, version 14.0 (Stata Corp LP, College Station, TX). *P* values lower than 0.05 were considered statistically significant.

Results

We initially obtained a total of 2395 potential articles, including the publications identified via screening of references cited with in encountered articles, of which 462 were from PubMed, 1209 were from Scopus, and 724 were from the Web of Science. We retained 95 articles after excluding 1181 duplicate and 1119 irrelevant articles based on the title or abstract. Following the revision of the full texts, 81 articles were excluded. Of these 81 publications, 18 were non-observational studies, 8 were review articles, 36 reported irrelevant outcomes, 16 did not report findings as risk estimates with 95% confidence intervals, and 3 were published in non-English languages. Ultimately, 14 articles were included in this study. The flow diagram of the literature search and exclusion process is depicted in Fig. 1.

Study characteristics

The 14 included studies were published between 2014 and 2019, and comprised a total of 189,966 participants with an age range between 10 and 64 years [18–31]. All studies reported clear descriptions of the inclusion criteria. Summary of all available information about the included studies are presented in Table 1. Seven studies were conducted in South America, Brazil [18, 23–26, 29, 30] while the remaining were performed in Canada [22], U.S.A. [20], UK [31], Guatemala [28], Spain [21], and Norway [19]; finally, one multinational study incorporated nineteen European countries [27]. Thirteen were cross-sectional studies [18–20, 22–31], while one was a cohort study [21]. All studies except Sartorelli et al. [23] examined both sexes. Five papers utilized FFQ [19, 21, 24, 25, 30], six studies applied 24-h food recall or records [20, 22, 23, 26, 29, 31], one study analyzed food purchasing data [28], and others referenced household availability [18, 27] for assessment of UPF intake. All papers evaluated excess body weight [18–26, 29–31], and seven studies also evaluated obesity [20, 22–24, 27, 29, 31].

Quality of studies

According to the Newcastle-Ottawa Quality Assessment Scale [33] scores, we classified seven studies as high-quality [18, 20, 22, 24, 29–31], and six studies as fair quality [19, 21, 23, 26–28]. Table 1 summarizes the total points allocated for all quality domains for each study. In the selection domain, six studies scored three [18, 21, 23, 24, 27, 28], two studies scored two [19, 26], and six studies scored four out of four quality score points [20, 22, 24, 29–31]. In the comparability domain, seven studies scored one [19–21, 23, 24, 27, 28], and remaining seven studies scored two out of two points [18, 22, 24, 26, 29–31]. Likewise, in the exposure domain, five studies scored one [19, 21, 23, 24, 29], and nine scored two out of four quality score points [18, 20, 22, 24, 26–28, 30, 31].

Systematic review

The only cohort study in this review evaluated the association between ultra-processed food consumption and the risk of overweight and obesity in Spanish participants [21]. A total of 1939 incident cases of overweight and obesity were identified during follow-up. After adjustment for potential confounders, participants in the highest quartile of ultra-processed food consumption were recognized to be at a higher risk of developing overweight or obesity (adjusted HR: 1.26; 95% CI: 1.10, 1.45; P-trend = 0.001) than those in the lowest quartile of consumption [21].

Among 13 cross-sectional studies, ten studies suggested an association of overweight and obesity with the consumption of ultra-processed food [18–20, 22–28]. Six studies identified higher odds of obesity among those with higher intake of ultra-processed food [20, 22–24, 29, 31]. Asfaw et al. demonstrated that households with 10% increase in ultra-processed food purchases were associated with higher individual-level BMI, overweight, and obesity among adults and children [28]. Canella et al. indicated that people in the upper quartile of household consumption of ultra-processed products, compared with those in the lower quartile, were 37% more likely to be obese [18]. Sparrenberger et al. observed that the mean dietary contribution of UPF among eutrophic individuals was not statistically different from the mean among overweight (48.2% vs. 49.0% respectively, $p = 0.73$) [26]. Louzada et al. presented that those in the highest quintile of ultra-processed food consumption experienced significantly greater odds of obesity (OR = 1.98; 95% CI: 1.26, 3.12) compared to those in the lowest quintile [29]. Mendonca et al. revealed a direct correlation between consumption of ultra-processed food and gain weight (OR = 1.26; 95% CI = 1.10–1.45) [21]. Djupegot et al. reported greater odds of weight gain with higher consumption of ultra-processed foods (OR = 1.54; 95% CI = 1.04–2.30) [19]. Silveira et al. associated excessive consumption of sugar-sweetened beverages and ultra-processed food with overweight (OR = 2.33; 95% CI = 1.36–4.03) [25]. The study by Monteiroet al. clarified a direct relationship between household availability of ultra-processed foods and the prevalence of obesity (Mean = 0.25; 95% CI = 0.05–0.45) [27]. Juul et al. mentioned 48%, 53% and 62% greater odds of BMI ≥ 25 kg/m^2, BMI ≥ 30 kg/m^2 and abdominal obesity, respectively, with high UPF consumption (OR 1.48; 95% CI 1.25, 1.76; OR 1.53; 95% CI 1.29, 1.81; OR 1.62; 95% CI 1.39, 1.89, respectively) [20]. This association was more pronounced among women [20]. Nardocci et al. showed that ultra-processed food consumption, with adjustment for confounding factors, is positively associated with obesity; individuals in the highest quintile of ultra-processed food consumption were 32% more likely to experience obesity compared to

Table 1 Characteristics of studies that reported the relationship between ultra-processed food consumption and excess weight.

Authors (year)	Kind of study	Country	Age (years)	Sex	Sample size	Follow-up (year)	Exposure assessment	Outcome	Measurements	Adjustment*	NOS
Afsaw et al. (2011)	Cross-sectional	Guatemala	>10	M + F	21,803		2-week food purchasing data	Overweight; obesity; BMI	β: 1.61 ± 0.29[a] β: 0.98 ± 0.18[a] β: 0.027 ± 0.002[a]	Age, sex, education, household expenditure, occupation, time spent in high physical activity, urban/rural, region, food prices, food away-from-home expenditure	6
Canella et al. (2014)	Cross-sectional	Brazil	>18	M + F	55,970		Household availability of ultra-processed foods	Overweight; obesity	β: 6.27 (4.15–8.39)[b] β: 3.72 (2.50, 4.94)[b]	Income, proportion of women in stratum, proportion of elderly in stratum, proportion of children in stratum, setting, region, and percentage of expenditure on eating out of home, complementary calories, including calories of processed food products	7
Adams et al. (2015)	Cross-sectional	UK	> 18	M + F	2174		4-day food record	Overweight; obesity; BMI	OR: 1.01 (1.00, 1.02)[c] OR: 1.01(1.00, 1.02)[c] β: 0.02 (−0.02, 0.07)[b]	Age, sex, occupation social class, alcohol intake	8
Sparrenberger et al. (2015)	Cross-sectional	Brazil	5.9 ± 2.5	M + F	204		24-h food record	Overweight	Mean: 0.8 ± 0.01[d]	–	6
Louzada et al. (2015)	Cross-sectional	Brazil	>10	M + F	30,243		24-h food records	Overweight; obesity; BMI	OR: 1.27 (0.95,1.69)[c] OR: 1.97 (1.26,3.09) [c] Mean: 0.95 (0.43, 1.48)[e]	Age, sex, race, education, income, interaction of sex and income, smoking status, physical activity, urban status, region; intake of fruit, vegetables, or beans	7
Mendonca et al. (2016)	Cohort	Spain	37.6 ± 11.0	M + F	8451	8.9	FFQ	Overweight	HR: 1.26 (1.10, 1.45)[c]	Age, sex, education, smoking, physical activity, siesta sleep, TV time, marital status, snacking, fruit/vegetable intake, following special diet, baseline BMI	5
Djupegot et al. (2017)	Cross-sectional	Norway	32.2	M + F	497		FFQ	Overweight	OR: 1.54 (1.04, 2.30)[c]	–	4
da Silveira et al. (2017)	Cross-sectional	Brazil	29.8 ± 8.5	M + F	503		FFQ	Overweight	OR: 2.33 (1.36, 4.03)[c]	Time as vegetarian	5
Melo et al. (2017)	Cross-sectional	Brazil	16	M + F	249		FFQ	Overweight	OR: 0.76 (0.47, 1.22)[c]	Age and sex	8
			>18	M + F	46,573			Obesity			6

Table 1 (continued)

Authors (year)	Kind of study	Country	Age (years)	Sex	Sample size	Follow-up (year)	Exposure assessment	Outcome	Measurements	Adjustment*	NOS
Monteiro et al. (2017)	Cross-sectional	19 European countries*					Household availability of ultra-processed foods		Mean: 0.25 (0.05, 0.45)[e]	Method of obesity measurement, physical inactivity and smoking, countries' per capita gross domestic product, time lag in years between the estimates on obesity and availability of ultra-processed foods	
Juul et al. (2018)	Cross-sectional	US	20–64	M + F	15,977		24-h food record	Overweight; obesity; BMI; WC	OR:1.48 (1.25, 1.76)[c] OR: 1.53 (1.29, 1.81)[c] β: 1.61(1.11, 2.10)[b] β: 4.07 (2.94, 5.19)[b]	Age, sex, educational attainment, race/ethnicity, ratio of family income to poverty, marital status, smoking, physical activity level	7
Nardocci et al. (2018)	Cross-sectional	Canada	45.99 ± 0.13	M + F	19,363		24-h food record	Overweight; obesity	OR: 1.03 (1.02, 1.09)[c] OR: 1.05 (1.02, 1.10)[c]	Sociodemographic characteristics, lifestyle habits, cultural background, environment, measurement type	8
Silva et al. (2018)	Cross-sectional	Brazil	35–64	M + F	8977		FFQ	Overweight; obesity; BMI; WC	OR: 1.32 (1.15, 1.53)[c] OR: 1.43 (1.20, 1.72)[c] β: 0.64 (0.33, 0.95)[b] OR: 1.21 (1.01, 1.46)[c]	Age, sex, race/skin color, per capita family income, physical activity, smoking, hypertension, diabetes, energy intake, total energy intake	8
Sartorelli et al. (2019)	Cross-sectional	Brazil	22–35	F	785		24-h food record	Overweight; obesity	OR: 1.17 (0.85, 1.82)[c] OR: 3.06 (1.27, 3.37)[c]	Age, gestational week at the time of the interview, schooling, smoking, physical activity, and total energy intake	5

NOS Newcastle–Ottawa Scale, *F* female, *M* male, *FFQ* food frequency questionnaire, *BMI* body mass index, *UK* United Kingdom, *WC* waist circumference.

[a]$\beta \pm$ SE.

[b]β (95% CI).

[c]OR, RR or HR (95% CI).

[d]Mean ± S.D.

[e]Mean (95% CI.)

*Included Austria, Belgium, Croatia, Cyprus, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Portugal, Slovakia, Spain and the UK.

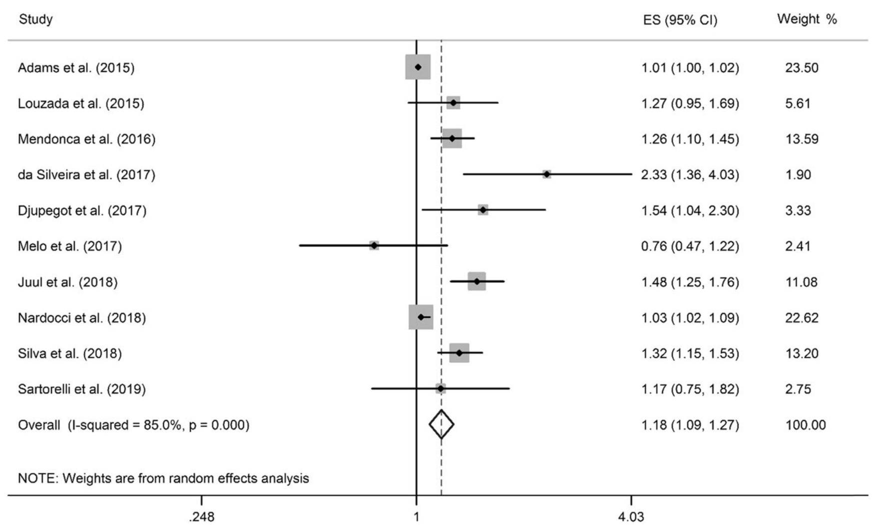

Fig. 2 Forest plot of the association between Ultra-processed food consumption and overweight using a random-effects model. Forest plot demonstrating meta-analysis of studies investigating the association between ultra-processed food consumption and overweight (ES and 95% CIs) using a random-effects model. ES, effect size; CI, confidence interval.

individuals in the first quintile (OR = 1.32; 95% CI = 1.05–1.57) [22]. Silva et al. demonstrated that individuals in the fourth quartile of percentage energy contribution from ultra-processed foods, after controlling for potential confounders, presented higher chances (OR; 95% CI) of being overweight (1.32; 1.15, 1.53), and obese (1.43; 1.20, 1.72) [24]. Sartorelli et al. found a positive association between the highest tertile of energy contribution from ultra-processed food intake (OR = 3.06; 95% CI = 1.27–3.37) and obesity [23]. Three studies reported no association between intake of ultra-processed food and excess body weight [29–31]. First study, Louzada et al. identified no relationship between consumption of ultra-processed foods and excess body weight (OR = 1.26; 95% CI: 0.95, 1.69) [29]. Likewise, Melo et al. documented that the consumption of ultra-processed foods was not associated with excess body weight [30]. Finally, Adams et al. recognized no association between consumption of ultra-processed food and weight gain (OR = 1.01; 95% CI = 1.00–1.02) [31].

Meta-analysis

Ten observational studies met the inclusion criteria for the current meta-analysis. Nine cross-sectional and one cohort studies were assessed to evaluate the relationship between ultra-processed food, and excess body weight, and obesity. Four studies were excluded as they did not include risk estimates [18, 26–28]. In this meta-analysis, the consequences of ultra-processed food consumption was compared between adult men and women. When the heterogeneity was deemed significant, its source was determined by employing subgroup analysis based on study design (cohort or cross-sectional), sample size (below or above 8000), continent (Europe or North America or South America), study quality (good or fair), exposure assessment tool (food record or FFQ), energy adjustment (yes or no), BMI adjustment (yes or no), and outcome measures (excess body weight and obesity).

Association between consumption of ultra-processed foods and overweight

We first pooled the odds ratio for all ten studies evaluating the association between consumption of ultra-processed foods and overweight. We found that participants with higher intake of ultra-processed foods experienced two percent higher odds of excess body weight (pooled effect size: 1.02; 95% CI: 1.01, 1.03, $p < 0.001$), with significant heterogeneity ($I^2 = 85.0\%$, $p_{heterogeneity} < 0.001$) (Fig. 2). We also repeated the analysis by excluding the study by Sartorelli et al. which was performed solely in pregnant women [23]. The association between consumption of ultra-processed foods and excess body weight remained statistically significant (pooled effect size: 1.18; 95% CI: 1.09, 1.27, $p < 0.001$) ($I^2 = 86.6\%$, $p_{heterogeneity} < 0.001$)

The quality of studies, energy, and BMI adjustment were identified as the potential sources of heterogeneity, following subgroup analysis (Table 2). Sensitivity analysis indicated that two studies, authored by Adams et al. [31] and Nardocci et al. [22], were outside the limit (Supplementary Fig. S1). Therefore, the analysis was repeated with studies within the limit; the significant association remained following the exclusion of both studies (pooled effect size: 1.33; 95% CI: 1.18, 1.49, $p < 0.001$) ($I^2 = 43.6\%$, $p_{heterogeneity}$: 0.088).

Association between consumption of ultra-processed foods and obesity

The results of the meta-analysis illustrated that ultra-processed food consumption carried, a statistically significant, 26 percent

Table 2 Subgroup analysis based on fixed effects models for the association between Ultra-processed food consumption and overweight (Odds ratios and 95% confidence intervals).

Subgroup	Effect sizes (*n*)	Effect sizes (95% CI)	I^2 (%)	*P* heterogeneity	*P* within	*P* between
Overall	10	1.02 (1.01, 1.03)	85.0%	<0.0001	<0.0001	–
Design						
Cohort	1	1.26 (1.10, 1.45)	–	–	0.001	0.002
Cross-sectional	9	1.01 (1.01, 1.02)	84.2%	<0.0001	0.002	
Sample size						
<8000	5	1.01 (1.00, 1.02)	73.7%	0.004	0.039	0.001
>8000	5	1.07 (1.04, 1.10)	88.2%	<0.0001	<0.0001	
Continent						
Europa	3	1.01 (1.00, 1.02)	85.8%	0.001	0.024	<0.0001
North America	5	1.29 (1.15, 1.53)	58.2%	0.048	<0.0001	
South America	2	1.04 (1.01, 1.08)	94.0%	<0.0001	0.010	
Study quality						
Good	6	1.01 (1.00, 1.02)	86.5%	<0.0001	0.004	<0.0001
Fair	4	1.32 (1.17, 1.49)	45.5%	0.138	<0.0001	
Energy adjust						
Yes	2	1.31 (1.14, 1.50)	0.0%	0.612	<0.0001	<0.0001
No	8	1.01 (1.00, 1.02)	85.0%	<0.0001	0.003	
BMI adjust						
Yes	2	1.25 (1.10, 1.43)	0.0%	0.754	0.001	0.002
No	8	1.01 (1.00, 1.02)	86.1%	<0.0001	0.003	
Exposure assessment tools						
Food record	5	1.01 (1.00, 1.02)	82.6%	<0.0001	0.007	<0.0001
FFQ	5	1.30 (1.18, 1.42)	60.9%	0.037	<0.0001	

BMI body mass index, *FFQ* food frequency questionnaire.

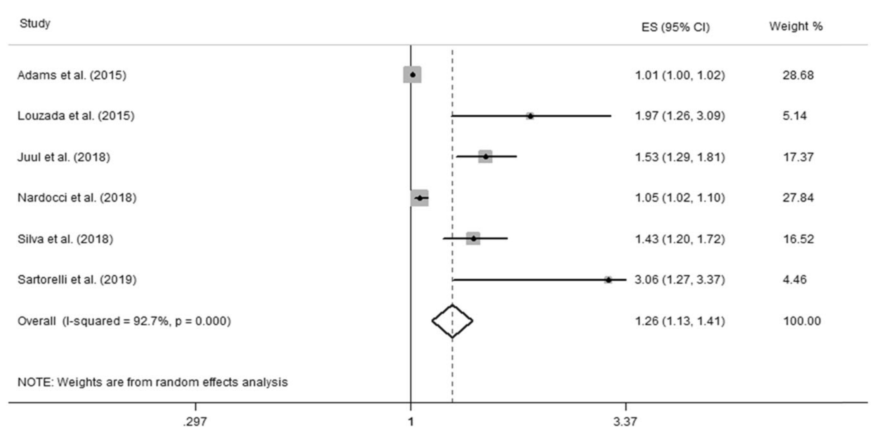

Fig. 3 Forest plot of the association between Ultra-processed food consumption and obesity using a random-effects model. Forest plot demonstrating meta-analysis of studies investigating the association between ultra-processed food consumption and obesity (ES and 95% CIs) using a random-effects model. ES, effect size; CI, confidence interval.

increased odds of obesity (pooled effect size: 1.26; 95% CI: 1.13, 1.41, $p < 0.001$), with significance heterogeneity ($I^2 = 92.7\%$, $p_{heterogeneity} < 0.001$) (Fig. 3). Furthermore, despite exclusion of study by Sartorelli et al. [23], performed exclusively in pregnant women, a significant association between consumption of ultra-processed foods and obesity persisted (pooled effect size: 1.19; 95% CI: 1.08, 1.32, $p < 0.001$) (I2 = 91.8%, $p_{heterogeneity} < 0.001$). Nonetheless, subgroup analysis did not reveal between-study heterogeneity (Table 3).

Sensitivity analysis determined that two studies, authored by Adams et al. [31] and Nardocci et al. [22], were outside the limit (Supplementary Fig. S2). When both studies were excluded in a repeat analysis, significant association was maintained (pooled effect size: 1.73; 95% CI: 1.36, 2.20, $p < 0.001$) ($I^2 = 67.7\%$, $p_{heterogeneity}$: 0.026).

Table 3 Subgroup analysis based on fixed effects models for the association between Ultra-processed food consumption and obesity (Odds ratios and 95% confidence intervals).

Subgroup	Effect sizes (*n*)	Effect sizes (95% CI)	I^2 (%)	*P* heterogeneity	*P* within	*P* between
Overall	6	1.26 (1.13, 1.41)	92.7%	<0.0001	<0.0001	–
Sample size						
<8000	2	1.01 (1.00, 1.02)	95.0%	<0.0001	0.039	<0.0001
>8000	4	1.09 (1.05, 1.13)	91.3%	<0.0001	<0.0001	
Continent						
Europa	1	1.00 (1.00, 1.02)	–	0.049	0.049	<0.0001
North America	2	1.07 (1.03, 1.11)	94.5%	<0.0001	<0.0001	
South America	3	1.61 (1.38, 1.89)	78.0%	0.011	<0.0001	
Score						
Good	1	1.25 (1.08, 1.44)	–	–	0.002	0.005
Fair	4	1.01 (0.99, 1.03)	67.3%	0.027	0.246	
Energy adjust						
Yes	2	1.57 (1.32, 1.85)	91.4%	<0.0001	<0.0001	<0.0001
No	4	1.01 (1.00, 1.02)	87.8%	0.004	0.004	
Exposure assessment tools						
Food record	5	1.01 (1.00, 1.02)	92.7%	<0.0001	0.003	<0.0001
FFQ	1	1.43 (1.19, 1.71)	–	–	<0.0001	

FFQ food frequency questionnaire.

Publication bias

We assessed the publication bias among the included articles with Begg's funnel plots. The funnel plots portrayed obvious asymmetry, indicating a potential risk of publication bias (Supplementary Figs. S3, S4). Therefore, we employed the trim and fill method to determine that four additional studies addressing excess body weight, and three evaluating obesity would be necessary to create symmetrical funnel plots. The pooled effect after the trim and fill analysis was insignificant (pooled effect size for excess weight: 1.04; 95% CI: 0.96, 1.13, *p*: 0.260) (pooled effect size for obesity: 1.06; 95% CI: 0.95, 1.20, *p*: 0.277).

Discussion

Our meta-analysis denotes that ultra-processed food intake is directly associated with excess weight gain. Moreover, the outcome revealed that intake of excess ultra-processed foods carries higher odds of obesity. To the best of our knowledge, this is the first comprehensive systematic review and meta-analysis to investigate the relation between intake of ultra-processed foods, and obesity and excess body weight among participants from both developed and developing countries. However, these outcomes must be interpreted with caution due to the immense heterogeneity among the included studies. Nonetheless, to address this heterogeneity, subgroup analysis was performed based on study design (cohort vs. cross-sectional), sample size, country of origin, quality of studies, energy and BMI adjustment, and dietary intake measurement tools. The results of this study correlate with those of previous studies such that they suggest limiting consumption of processed and ultra-processed foods may be a useful method for treatment and prevention of overweight and obesity [36, 37]. Moreover, the results of the present systematic review confirm those of previous studies that consumption of ultra-processed food has a positive association with the amount of body fat during childhood and adolescence [38, 39]. However, this study was conducted in a broader age group. Nevertheless, other studies have shown that the association of ultra-processed food intake with overweight and obesity is independent of age and other demographic factors [40].

Recently, investigators have suggested several potential mechanisms to describe the association between ultra-processed food intake and the risk of excessive body weight and obesity. Ultra-processed foods, generally, are denser in energy, comprise higher levels of saturated and trans fatty acids, and contain added sugar and sodium [5]. In addition, many ultra-processed foods contain high amount of refined carbohydrates, which may alter insulin levels, increase its effect on nutrients, and elevate storage in adipose tissue [28, 41]. Some investigators propose that ultra-processed foods with high fat or refined carbohydrate content may lead to alterations in reward neurocircuitry mechanism, which, in turn, may increase food craving and excessive intake [42, 43]. Furthermore, structural and physical properties of ultra-processed products may blunt satiety signaling [44]. Besides, multiple unique non-nutritional properties of ultra-processed products have been proposed as the risk factors for increasing odds of obesity [12]. Considered convenient, these products are generally prepared in large portion sizes, and endorsed through media advertising, leading to overconsumption [45–47]. Due to minimal required preparation, they may alter eating patterns of individuals in various age groups; these factors may lead to rapid food consumption while involved in alternate routine activities (e.g., eating while watching TV) [18, 37]. Thus, rapid and unconscious consumption associated with these intake behaviors can disturb digestive and neural functions that signal satiety and satiation, perhaps, causing overconsumption [48, 49]. Notably, home food preparation skills were cross-sectionally related to lower ultra-processed foods consumption [37]. Furthermore, diets high in ultra-processed foods may decrease total energy expenditure due to the reduced thermic effect of foods. Experimental studies have identified that mean after-meal energy expenditure was 50% lower after consuming highly processed products, compared to iso-energetic unprocessed foods. Such discrepancy results primarily from reduced health-protective nutrient and fiber content yet excessive amount of simple carbohydrates [50]. In addition, elevation in consumption of artificial ingredients and additives such as noncaloric sweeteners, colorants, preservatives, and chemical flavorings is another concern [51]. Furthermore, observational studies have indicated that daily consumption of artificial sweeteners is related to the occurrence of metabolic syndromes such as type 2 diabetes and obesity [52]. A recent systematic review article in this regard also proposed that artificial sweeteners, sugar alcohols, and fructose may cause obesity and metabolic dysfunctions by altering the gut microbiota, resulting in increased intestinal inflammation, enhanced energy extraction, and endotoxemia [53].

Strengths and limitations

Several strengths of this study can be highlighted. This systematic review with meta-analysis represents the most comprehensive search and analysis of the available evidence regarding the relationship between ultra-processed food intake and excess body weight. We employed a thorough search strategy with improbable likelihood of missing any large reported articles. Nonetheless, several limitations of this systematic review and meta-analysis can be identified. Significant variability in measurement methods, utilized to assess food consumption, was encountered among studies; however these differences were somewhat controlled through subgroup analyses. Comparable to all meta-analyses, our systematic review and findings relied heavily on the quality and content of articles that are available in the literature. For instance, solely one cohort study directly investigated the relationship between ultra-processed foods intake and obesity and excess body weight. Also, insufficient data rendered our analysis unable to investigate the effects of ultra-processed on other anthropometric parameters such as BMI and waist circumference. Overall, our outcomes summarize the most relevant and comprehensive data addressing the risk of excess body weight and obesity resulting from ultra-processed food intake; they also highlight potential gaps in our knowledge that demands further investigation. Studies with longitudinal designs and adequate control for confounding factors may allow these results to be applicable among patients of variable demographics; moreover, they may uncover any causality relationship of ultra-processed food intake with obesity and anthropometric parameters, independent of nutrient content.

Conclusion

Recent investigations provide fairly consistent support for the association of ultra-processed food intake with obesity and excessive body weight. Consequently, this meta-analysis of observational studies suggests that ultra-processed food intake is associated with overweight and obesity.

Author contributions MA, ED designed the study. MA and ED independently carried out the literature search and screening of articles; ED analyzed the data; MA, HSH, and JH wrote the manuscript. NT and ED edited the writing. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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