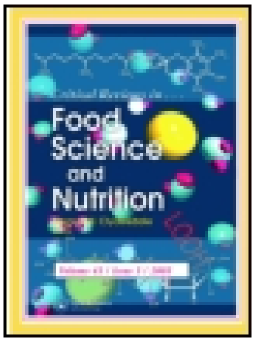

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Fried-food consumption and risk of overweight/obesity, type 2 diabetes mellitus, and hypertension in adults: a meta-analysis of observational studies

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CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
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REVIEW

Fried-food consumption and risk of overweight/obesity, type 2 diabetes mellitus, and hypertension in adults: a meta-analysis of observational studies

Pei Qin[a,b], Dechen Liu[c], Xiaoyan Wu[a], Yunhong Zeng[d], Xizhuo Sun[e], Yanyan Zhang[a], Yang Li[a], Yuying Wu[a], Minghui Han[d], Ranran Qie[d], Shengbing Huang[c], Yang Zhao[c], Yifei Feng[c], Xingjin Yang[c], Yu Liu[e], Honghui Li[e], Ming Zhang[a,b], Dongsheng Hu[a,b], and Fulan Hu[a,b]

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ABSTRACT

Recent studies have reported conflicting associations of fried-food consumption and risk of overweight/obesity, type 2 diabetes mellitus (T2DM) and hypertension, and a meta-analysis is not available. We aimed to explore the association between fried-food consumption and risk of overweight/obesity, T2DM and hypertension in adults through a meta-analysis. We searched PubMed, EMBASE, and Web of Science for studies published up to 17 June 2020. Pooled relative risks (RRs) and 95% confidence intervals (CIs) were calculated by random-effects models. In comparing the highest to lowest fried-food intake, the pooled RRs (95% CIs) were 1.16 (1.07-1.25; $I^2 = 71.0\%$, $P_{\text{heterogeneity}} < 0.001$) for overweight/obesity (cohort: 1.19 [0.97-1.47], n = 2; cross-sectional: 1.14 [1.03-1.27], n = 9), 1.07 (0.90-1.27; 84.7%) for T2DM (cohort: 1.01 [0.89-1.15], n = 9; case-control: 2.33 [1.80-3.01], n = 1), and 1.20 (1.05-1.38; I^2=91.8%) for hypertension (cohort: 1.06 [0.98-1.15], n = 8; cross-sectional: 2.16 [0.59-7.87], n = 3). Our meta-analysis indicates fried-food consumption is associated with increased risk of overweight/obesity and hypertension but not T2DM in adults, but the findings should be interpreted with caution due to high heterogeneity and unstable subgroup analyses of this meta-analysis. More studies are warranted to investigate the total fried-food consumption and these health outcomes.

KEYWORDS
Fried food; overweight/obesity; type 2 diabetes mellitus; hypertension; observational studies; meta-analysis

Introduction

Dietary factors play a substantial role for obesity, type 2 diabetes mellitus (T2DM) and hypertension (Pitsavos et al. 2006) and they are frequently observed to lead to high cardiovascular risk, morbidity, and mortality (Zanella, Kohlmann, and Ribeiro 2001). Previous studies have explored the protective or adverse effect of food group on overweight/obesity (Schlesinger et al. 2019), T2DM (Schwingshackl, Hoffmann, et al. 2017), hypertension (Schwingshackl, Schwedhelm, et al. 2017) and other chronic diseases (Schwingshackl et al. 2016). Cooking method may affect the chemical composition, nutrients and bioavailability in foods (Miglio et al. 2008; Xu et al. 2014). Frying is one popular cooking method in different culture and is widely used in the fast-food restaurants and domestic cooking. Nevertheless, the process of frying can change the nutrient composition such as generating more trans-fatty acids (Fillion and Henry 1998; Song et al. 2015), which have been shown to be a risk factor for obesity (Thompson, Minihane, and Williams 2011), T2DM (de Souza et al. 2015) and hypertension (Wang et al. 2010). Frying can also lead to the increased calories of foods and change the flavor and taste (İnanç and Maskan 2014), thereby inducing the excess intake of high energy foods and weight gain and associated disease. With the popularity of fried food worldwide, it is necessary to investigate the adverse effect of fried foods on overweight/obesity, T2DM, and hypertension.

Recently, increasing number of observational studies evaluated the association between fried-food consumption and risk of overweight/obesity (Al-Tawarah et al. 2010; Crovetto et al. 2018; Sayon-Orea et al. 2013; Sayon-Orea, Bes-Rastrollo, et al. 2014; Vaccaro, Zarini, and Huffman 2018; Kang and Kim 2016; Pengpid and Peltzer 2019; Guallar-Castillón et al. 2007), T2DM (Cahill et al. 2014; Farhadnejad et al. 2018; Konishi et al. 2019; Krishnan et al. 2010; Patel et al. 2009; Wallin et al. 2017; Xibiao, Cuiping, and Siding 2011) and hypertension (Borgi et al. 2016; Huang et al. 2019; Provido et al. 2020; Sayon-Orea, Bes-Rastrollo, et al. 2014; Kang and Kim 2016). However, these findings are inconsistent, with some studies showing the positive

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association of fried-food consumption and overweight/obesity (Guallar-Castillón et al. 2007; Al-Tawarah et al. 2010; Sayon-Orea et al. 2013), T2DM (Krishnan et al. 2010; Xibiao, Cuiping, and Siding 2011; Cahill et al. 2014; Wallin et al. 2017) and hypertension (Sayon-Orea, Bes-Rastrollo, et al. 2014; Kang and Kim 2016) while others showing no association for overweight/obesity (Pengpid and Peltzer 2019; Vaccaro, Zarini, and Huffman 2018; Sayon-Orea, Bes-Rastrollo, et al. 2014), T2DM (Patel et al. 2009; Farhadnejad et al. 2018) or hypertension (Vaccaro, Zarini, and Huffman 2018; Provido et al. 2020; Huang et al. 2019). To our knowledge, no meta-analysis of current evidence of the associations between fried-food consumption and overweight/obesity, T2DM and hypertension has been conducted.

Therefore, the objective of this study was to conduct a meta-analysis of observational studies to explore the association between fried-food consumption and risk of overweight/obesity, T2DM and hypertension in general adult population ($\geq$18 years). The findings from this meta-analysis is helpful to provide further information on the dietary advices on weight control and prevention of metabolic disease and associated morbidity and mortality and imply the directions for future research in fried-food consumption and the risk of overweight/obesity, T2DM and hypertension.

Materials and methods

This meta-analysis was conducted according to the guidelines of Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 (Shamseer et al. 2015).

Search strategy

PubMed, EMBASE, and Web of Science were searched until 17 June 2020 for relevant publications using a comprehensive list of search terms (Table S1), with restriction to English language. The reference lists of eligible articles and previous systematic reviews and meta-analysis were manually searched to identify further relevant studies. Two investigators (PQ and XW) independently systematic search, screen the articles, and reviewed the full text of articles, with any disagreements discussed with a third investigator (FH).

Study selection

Studies were included in this meta-analysis if they met the following inclusion criteria: 1) were population-based studies (cross-sectional studies, case-control studies, cohort studies, or nested case-control study); 2) included general adult population aged $\geq$18 years; 3) the exposure of interest was the fried-food consumption; 4) the outcome of interest was the overweight/obesity (defined by body mass index (BMI), waist circumference (WC) or waist-to-height ratio (WHtR)), T2DM, or hypertension; 4) risk estimates including odds ratios (ORs), relative risks (RRs) or hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were reported. We excluded reviews, comments, letters and editorials. If more than one article was based on the same data, the study with the larger number of cases and the total fried food as exposure was chosen.

Data extraction and quality assessment

With a standard data-extraction form, two investigators (PQ and XW) independently extracted the following information of the included studies: first author's last name, publication year, study location, study design, study name, mean/median age or age range, sex, number of participants, number of cases, follow-up duration if cohort studies, outcome assessment, fried food type, fried food measurement, number of cases and person-years/number of participants per fried food category, most adjusted risk estimates (OR, RRs or HRs) with their corresponding 95% CIs for each category, and adjustment factors. The Newcastle-Ottawa quality assessment scale (NOS) (Stang 2010) was used to assess the study quality of the included cohort studies and case-control studies in 8 aspects. The total score of NOS was up to 9 points. Scores of 0-3, 4-6 and 7-9 represented the poor, fair, and good quality, respectively. The Agency for Healthcare Research and Quality (AHRQ) scale was used to evaluate the study quality of cross-sectional studies (Rostom et al. 2004). The total score was up to 11 points in 11 items. Scores of 0-3, 4-7 and 8-11 represented the low, moderate and high quality, respectively.

Data synthesis and analysis

Articles reporting data separately for men and women, or different types of fried foods, or from different cohorts, or reporting more than one health outcome within an article were treated as separate studies. Random-effects model was used to calculate pooled RRs and 95% CIs for the highest versus lowest fried-food consumption (DerSimonian and Laird 2015). The heterogeneity between studies was evaluated by Cochran's Q and I^2 statistic (Julian P T Higgins et al. 2003). $P < 0.10$ was considered significant for the Cochran's Q statistic. I^2 values of 25%, 50%, and 75% represented the low, moderate, and high degrees of heterogeneity, respectively.

Publication bias (small-study effect) was evaluated by the Egger's linear-regression test (Begg and Mazumdar 1994) and visual inspection of funnel plots. The trim-and-fill method was used to correct publication bias if detected. Subgroup analysis were conducted by gender, age, country, type of study design, type of fried food, number of cases ($\geq$1000 and <1000), assessment of outcome (self-reported and objective-measured), and adjustments including body mass index [BMI; kg/m^2], energy intake, and physical activity) to investigate the potential sources of heterogeneity and robustness of the findings. Meta-regression analysis was conducted to calculate the P values for heterogeneity between subgroups. The sensitivity analysis by excluding one study at a time was conducted to assess the stability of findings. We also performed sensitivity analysis by removing studies with relatively low quality of $\leq$5 for NOS or $\leq$6 for AHRQ). All statistical analyses were performed using Stata version 12.1 (Stata Corp., College Station, TX, USA).

Strength of the evidence

The GRADE system (GRADEpro GDT 2020) was used to assess the strength of the evidence. The quality of evidence for each outcome was categorized as high, moderate, low, or very low. The strength of observational studies was first rated as low-quality evidence and then upgraded or downgraded according to the risk of bias, inconsistency, indirectness, imprecision, publication bias, large effect, plausible confounding, and dose-response gradient (Schünemann et al. 2013). Any disagreements were resolved by consensus between P. Q. and F. H.

Results

Literature search

The literature search and study selection process are summarized in Figure 1. We identified 5,176 potential eligible articles. After removing duplicate articles (n = 1,630) and those that did not fit the inclusion criteria (n = 3,407), 139 articles were retrieved for full-text review, from which 19 articles were finally included in the meta-analysis (Cahill et al. 2014; Al-Tawarah et al. 2010; Borgi et al. 2016; Konishi et al. 2019; Krishnan et al. 2010; Patel et al. 2009; Pengpid and Peltzer 2019; Sayon-Orea et al. 2013; Sayon-Orea, Bes-Rastrollo, et al. 2014; Sayon-Orea, Bes-Rastrollo, et al. 2014; Crovetto et al. 2018; Farhadnejad et al. 2018; Guallar-Castillón et al. 2007; Huang et al. 2019; Kang and Kim 2016; Provido et al. 2020; Vaccaro, Zarini, and

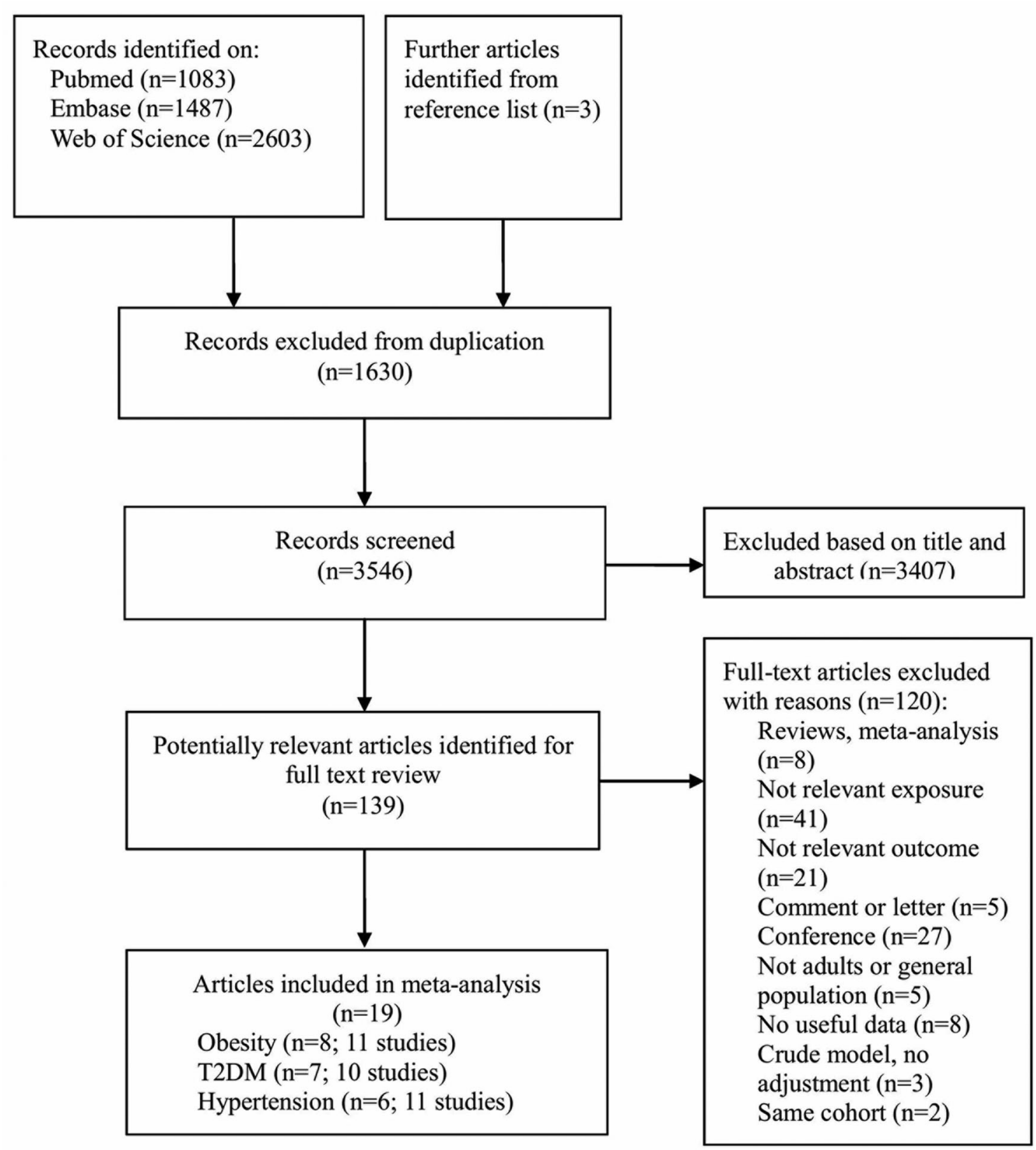

Figure 1. Flowchart of study selection for the meta-analysis.

Table 1. Characteristics of studies included in meta-analysis of associations of fried-food consumption with risk of overweight/obesity, type 2 diabetes mellitus and hypertension.

First author (year), Country	Date source	Study design	Mean age and age range	Sex	Total number	Total cases	Follow up Years	Exposure	Exposure measurement	Outcome definition	Outcome assessment	Adjustment
Overweight/Obesity												
Guallar-Castillón et al. (2007)*, Spain	EPIC	Cross-sectional	29–69	Men; women	10881 (men); 19167 (women)	general obesity: 3003 in men, 5309 in women; central obesity: 3754 in men, 8165 in women	NA	Fried food	Validated computerized diet history questionnaire	BMI $\geq$ 30 kg/m^2 (general obesity) WC $\geq$ 102 cm in men $\geq$88 cm in women (central obesity)	Measured	Age, sex, level of the metabolic syndrome component and physical activity index, smoking, dietary consumption of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index.
Al-Tawarah et al. (2010), Japan	National dietary survey by the Health and Labor Ministry of Japan	Cross-sectional	20.05 ± 1.06	Men & women	278	30	NA	Fried food	3 items on diet	BMI $\geq$ 25 kg/m^2 (overweight/obesity)	Self-reported	Age, sex, rugular meals, breakfast meals, daily meals except light meals, light meals, color vegetables, fruit, smoking, wether wamt to be slim, wether try to be on a diet, study year.
Sayon-Orea et al. (2013), Spain	SUN project	Cohort	38.1 ± 11.4	Men & women	6821	1068	6.1	Fried food	Validated 136 items FFQ	BMI $\geq$ 25 kg/m^2 (overweight/obesity)	Self-reported	Age, sex, h/week spent sitting down, baseline BMI, smoking status, physical activity, nuts intake, consumption of sugared-soft drinks, and dietary fiber intake, snacking between meals, total energy intake, family history of obesity, and fast food consumption.
Sayon-Orea, Bes-Rastrollo, et al. (2014), Spain	SUN project	Cohort	35.9 ± 10.4	Men & women	8289	NR	8.3	Fried food	Validated 136 items FFQ	WC $\geq$ 94 cm in males and 80 cm in females (central obesity)	Self-reported	Age, sex, baseline BMI, time spent sitting down, smoking status, physical activity, sugared soft drinks, fiber, fast food, snacking between meals, categories of Mediterranean diet, total energy intake, carbohydrates, fat and sodium intake.
Kang and Kim (2016), Korea	The fifth Korean National Health and Nutrition Examination Survey between 2010 and 2011.	Cross-sectional	52.74	Men & women	9221	NR	NA	Fried food	Validated 109-item FFQ	WC > 90 cm for men or >80 cm for women (central obesity)	Measured	Age, BMI, income level, education level, smoking status, alcohol consumption, physical activity, energy intake, dietary diversity score and disease
Crovetto et al. (2018), Chile	University students	Cross-sectional	NR	Men & women	1414	397	NA	Fried food	Validated self-assessment survey	BMI $\geq$ 25 kg/m^2 (overweight/obesity)	Measured	Smoking, salt consumption, dinner, physical activity, and university
Vaccaro, Zarini, and Huffman (2018), United States	NHANES 2009–2010	Cross-sectional	20–69	Men & women	2045	879	NA	Fried potatoes	The Dietary Screener Questionnaire	WHtR $\geq$ 0.59 (central obesity)	Measured	Age (years), sex, education, race/ethnicity, tobacco use (yes), soft drinks (yes), sports/energy drinks (yes), processed meats (yes)
Pengpid and Peltzer (2019), India	National Family Health Survey 2015–2016 in India	Cross-sectional	18–49	Women	582320	211382	NA	Fried food	Structured interview	BMI $\geq$ 23 kg/m^2 (overweight/obesity)	Self-reported	Age in years, education, wealth index, caste, fruits, dark vegetables, aerated drinks, tobacco use, drinks alcohol, hypertension, heart disease
T2DM												
Krishnan et al. (2010)*, United States	Black Women's Health Study.	Cohort	30–69	Women	9760 (Fried Chicken); 12303 (Fried fish)	2838 (Fried Chicken); 2777 (Fried fish)	10	Fried Chicken; Fried fish	Short-form National Cancer Institute (NCI)–Block FFQ	–	Self-reported	Age, time period, education, family history of diabetes, television watching, vigorous activity, smoking, coffee consumption, glycemic index of diet, and intake of cereal fiber, alcohol, sugar-sweetened soda, calcium, vitamin D, energy and BMI.
Patel et al. (2009) Europe	EPIC-Norfolk study	Cohort	40–79	Men & women	21984	725	10.2	Fried fish	Validated 130-item semiquantitative FFQ	1) confirmation of self-reported by another data source or 2) diagnosis captured by an external source alone, independently of participation in study follow-up questionnaires or visit.	Self-reported	Age and sex, family history of diabetes, smoking, education level, and physical activity, total energy intake, alcohol intake, and plasma vitamin C, BMI, and waist circumference.
Liu (2011) China	A hospital-based case-control study	Case-control	52.9 ± 13.8	Men & women	1002	501	NA	Fried food	Questionnaire	WHO diagnose criteria	Measured	Family history of diabetes, preference for sweets, eating fried foods, alcohol and beverage consumption, history of hypertension, history of high blood sugar, tending to stress or excitement, and giving a birth to macrosomia.

Cahill et al. (2014)*, United States	NHS HPFS	Cohort	40–75	Women; Men	70842 NHS; 40789 HPFS	2687 NHS; 3091 HPFS	>10	Fried food	FFQ	–	Self-reported	Age (continuous), white (yes or no), family history of diabetes (yes or no), smoking status, alcohol intake, physical activity, total energy intake (quintiles), and diet quality as represented by the AHEI (quintiles), hypertension hypercholesterolemia, BMI.
Wallin et al. (2017), Sweden	Population-based Cohort of Swedish Men	Cohort	45–79	Men	35583	3624	15	Fried fish	Validated FFQ	–	Record linkage	Attained age, BMI, physical activity (metabolic equivalent hours per day; quartiles), education, cigarette smoking, total energy intake (kcal/day; quintiles), intake of alcohol (g/day; quartiles) and DASH diet component score (based on intake of fruits, vegetables, nuts and legumes, low-fat dairy, whole grains, sodium, sweetened beverages, and red and processed meats; quartiles), dietary exposure to polychlorinated biphenyls (ng/day, quintiles) and methyl mercury (μg/day, quintiles).
Farhadnejad et al. (2018), Iran	**Tehran Lipid and Glucose Study**	Cohort	38.9 ± 13.4	Men & women	1981	133	6	Fried potato	Validated and reliable FFQ	FPG $\geq$ 7.0 mmol/L or 2-h post-75 g glucose loads $\geq$ 11.1 mmol/L and on current therapy	Measured	Age, sex, BMI, physical activity, smoking, family history of diabetes, hypertension, serum triglycerides, high-density lipoprotein cholesterol, daily intakes of energy, saturated fat (g/d) and food groups intake (g/d), including fruit, whole grains, vegetables, nuts and legumes.
Konishi et al. (2019), Japan*	Takayama study	Cohort	51.5	Men; women	5,883 men 7,638 women	266 men; 172 women	10	Fried soy foods	Validated 169-item semiquantitative FFQ		Self-reported	Age, years of education, BMI, physical activity, smoking status, history of hypertension, glycemic load, and intake of total energy, total fat, alcohol, coffee, meat, vegetables, fruit, and multivitamins.
Hypertension												
Sayon-Orea, Bes-Rastrollo, et al. (2014) Spain	SUN project	Cohort	36.5 ± 10.8	Men & Women	13679	1232	6.3	Fried food	Validated 136-item FFQ	SBP $\geq$ 130 and/or DBP $\geq$ 85 mm Hg, antihypertensive drug treatment	Self-reported	Age, sex, family history of hypertension, self-reported hypercholesterolemia, physical activity, smoking status, total energy intake, alcohol intake, energy-adjusted Na, K, caffeine, fiber, olive oil, fruit, vegetable, low-fat and high-fat dairy product, sugar-sweetened beverage, fast food, and sweet consumption, and time spent watching television, baseline BMI
Borgi et al. (2016)* United States	NHS II HPFS NHS	Cohort	30-55	Women Men	88475 (NHS II) 36803 (HPFS) 62175 (NHS)	25246 (NHS II) 16752 (HPFS) 5728 (NHS)	>10	French fries; Potato chips	FFQ	A diagnosis of hypertension by a health professional was self-reported on the baseline and biennial questionnaires	Self-reported	Age, sex, baseline BMI, time spent sitting down, smoking status, physical activity, sugared soft drinks, fiber, fast food, snacking between meals, categories of Mediterranean diet, total energy intake, carbohydrates, fat and sodium intake.
Kang (2016) Korea	the fifth Korean National Health and Nutrition Examination Survey between 2010 and 2011.	Cross-sectional	44.90589958	Men & Women	9221	NR	NA	Fried food	Validated 109-item FFQ	SBP $\geq$ 140, DBP $\geq$ 90mmHg or current use of antihypertensive medication	Measured with a Baumanometer mercury sphygmomanometer	Age, BMI, income level, education level, smoking status, alcohol consumption, physical activity, energy intake, dietary diversity score and disease.
Huang et al. (2019) China	CHNS Cohort study	Cohort	39	Men & Women	11763	4033	11.3	Stir-fried potatoes	Three-day dietary recalls with a weighing and measuring technique	SBP $\geq$ 140, DBP $\geq$ 90mmHg, previously diagnosed by a physician, or current use of antihypertensive medication	Measured with a standard mercury sphygmomanometer	Age, sex, marital status, education levels, household income, and residency (urban, rural); BMI, physical activity, medical insurance, smoking status, and alcohol drinking status, total energy intake, total meat intake (red meat, poultry meat, and fish meat), total vegetables intake, total fruit intake, total sodium intake and total potassium intake.

(*continued*)

Table 1. Continued.

First author (year), Country	Date source	Study design	Mean age and age range	Sex	Total number	Total cases	Follow up Years	Exposure	Exposure measurement	Outcome definition	Outcome assessment	Adjustment
Vaccaro, Zarini, and Huffman (2018) United States	NHANES 2009–2010	Cross-sectional	20–69	Men & Women	2045	879	NA	Fried potatoes	Dietary Screener Questionnaire	SBP ≥ 130, DBP ≥ 80mmHg or current use of antihypertensive medication	Measured	Age (years), sex, education, race/ethnicity, tobacco use (yes), soft drinks (yes), sports/energy drinks (yes), processed meats (yes)
Provido et al. (2020) Filipino	Filipino women's diet and health study	Cross-sectional	20-57	Women	428	57	NA	Fried food	One-day 24-hour recall	SBP ≥ 140, DBP ≥ 90mmHg or current use of antihypertensive medication	Measured with a mercury sphygmomanometer	Age (years, continuous), education (high school or below, college or above), length of stay in Korea (years, continuous), smoking status (ever, never), alcohol intake (ever, never), and BMI (< 23, ≥ 23 kg/m2)

Abbreviation: BMI, body mass index; CHNS, China Health and Nutrition Survey; EPIC, the European Prospective Investigation into Cancer and Nutrition; FFQ, food frequency questionnaire; HPFS, the Health Professionals Follow-Up Study; NHANES, National Health and Nutrition Survey; NHS, Nurses' Health Study; PHS: Physicians' Health Study; SBP, systolic blood pressure; SUN, Seguimiento Universidad de Navarra Project; NA, not applicable; NR, not reported.

*Articles reported data separately for men and women, or different types of fried foods, more than one health outcome, or from different cohorts, which were treated as independent studies in this meta-analysis.

Huffman 2018; Wallin et al. 2017; Xibiao, Cuiping, and Siding 2011) (Figure 1). Among these 19 articles (32 studies), 11 studies specifically reported results on overweight/obesity (Al-Tawarah et al. 2010; Crovetto et al. 2018; Guallar-Castillón et al. 2007; Sayon-Orea et al. 2013; Sayon-Orea, Bes-Rastrollo, et al. 2014; Vaccaro, Zarini, and Huffman 2018; Kang and Kim 2016; Pengpid and Peltzer 2019), 10 studies on T2DM (Cahill et al. 2014; Farhadnejad et al. 2018; Konishi et al. 2019; Krishnan et al. 2010; Patel et al. 2009; Wallin et al. 2017; Xibiao, Cuiping, and Siding 2011), and 11 studies on hypertension (Borgi et al. 2016; Huang et al. 2019; Sayon-Orea, Bes-Rastrollo, et al. 2014; Pengpid and Peltzer 2019; Provido et al. 2020; Vaccaro, Zarini, and Huffman 2018; Kang and Kim 2016).

Study characteristics

Table 1 shows the main characteristics of the included studies. Two articles reporting data separately for men and women (Guallar-Castillón et al. 2007; Konishi et al. 2019), 2 reporting different types of fried foods (Krishnan et al. 2010; Borgi et al. 2016), 2 including different cohorts (Cahill et al. 2014; Borgi et al. 2016), and 2 reporting more than one health outcome (Kang and Kim 2016; Vaccaro, Zarini, and Huffman 2018) were treated as separate studies. Of 32 studies, 19 studies were cohort studies (2 on overweight/obesity, 9 T2DM, and 8 hypertension) and 12 cross-sectional (9 overweight/obesity and 3 hypertension), and 1 case-control study (1 T2DM). Geographically, 12 studies were conducted in the North America, 9 in Europe, 10 in Asia, and 1 in South America. A total of 13 studies included both men and women, 12 studies included women, and 7 study included men. For the types of fried food, 16 reported the total fried food, 10 reported the fried potatoes, 3 reported the fried fish, 2 reported the fried soy foods, and 1 reported the fried chicken. Sample sizes varied greatly from 428 (Provido et al. 2020) to 88475 (Borgi et al. 2016). More than half studies measured fried-food consumption by FFQ, 4 by dietary history, and 2 by dietary recall. The definition of outcomes in 9 articles (18 studies) were self-reported, while others were based on measurement or record linkage. Table S2-4 shows the results of quality assessment. The mean quality score was 5.48 $(5-8)$ by the NOS for cohort studies and 5.00 by the NOS for case–control study and 6.58 $(4-9)$ by the AHRQ for cross-sectional studies.

Fried-food consumption and risk of overweight/obesity

Eleven studies (2 cohort (Sayon-Orea et al. 2013; Sayon-Orea, Bes-Rastrollo, et al. 2014) and 9 cross-sectional studies (Al-Tawarah et al. 2010; Crovetto et al. 2018; Guallar-Castillón et al. 2007; Vaccaro, Zarini, and Huffman 2018; Kang and Kim 2016; Pengpid and Peltzer 2019)) were pooled to estimate the risk of overweight/obesity in individuals with fried food, with a total of 638,388 participants and more than 18,326 cases. Of these studies, 2 studies reported the risk of general obesity and both were defined as BMI $\geq 30\,kg/m^2$ (Guallar-Castillón et al. 2007; Sayon-Orea et al.

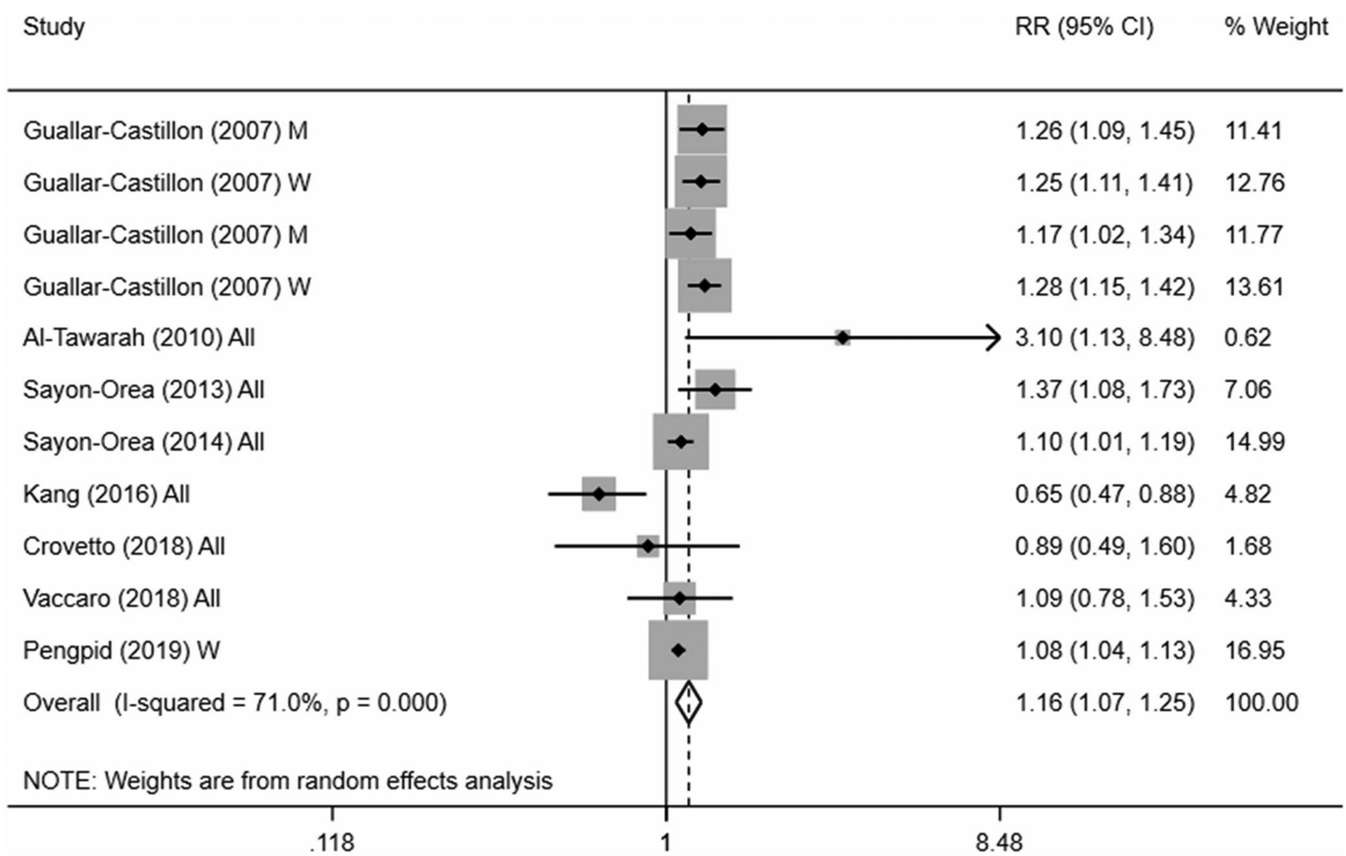

Figure 2. Forest plot of relative risk of overweight/obesity for the highest versus lowest fried-food consumption.
RR, relative risk; 95% CI, 95% confidence interval. *Squares* represent study-specific RR. *Square areas* represent the weight of the study. *Horizontal lines* represent 95% CIs. *Diamonds* represent the pooled RR and 95% CIs.

2013); 5 studies reported the risk of central obesity, with 2 studies defined obesity as WC ≥102 cm for men and ≥88 cm for women(Guallar-Castillón et al. 2007), 1 study defined as WC ≥94 cm for men or ≥80 cm for women (Sayon-Orea, Bes-Rastrollo, et al. 2014), 1 study defined as WC >90 cm for men or >80 cm for women (Kang and Kim 2016), and 1 study defined as WHtR ≥ 0.59 (Vaccaro, Zarini, and Huffman 2018); 4 studies investigated the risk of overweight/obesity, which defined as BMI ≥ 25 kg/m^2 in 3 studies (Al-Tawarah et al. 2010; Crovetto et al. 2018; Sayon-Orea et al. 2013) and BMI ≥ 23 kg/m^2 in 1 study (Pengpid and Peltzer 2019). The pooled RR (95% CI) was 1.16 (1.07-1.25) for the highest versus lowest category, with moderate heterogeneity (I^2 = 71.0%, $P_{heterogeneity}$ < 0.001; Figure 2). Visual inspection of the funnel plots (Figure S1) and non-significant Egger's test (P = 0.424) suggested no evidence of publication bias. Subgroup analyses showed a significant association in subgroups of cross-sectional studies, measurement of total fried food, studies conducted in Europe, cases ≥1000, both sexes, both age groups, those with high or low study quality, and those without adjustment for BMI and energy intake and with adjustment for physical activity (Table S5). On sensitivity analysis, excluding one study at a time, the pooled RRs persisted significant for overweight/obesity, ranging from 1.14 to 1.18 (data not shown). After excluding the studies with relatively low quality, the summary RR remained significant (RR = 1.17, 95% CI, 1.06-1.30; I^2 = 73.0%, $P_{heterogeneity}$ = 0.001).

Fried-food consumption and risk of T2DM

Ten studies (9 cohort (Cahill et al. 2014; Farhadnejad et al. 2018; Konishi et al. 2019; Krishnan et al. 2010; Patel et al. 2009; Wallin et al. 2017) and 1 case–control studies (Xibiao, Cuiping, and Siding 2011)) were pooled to estimate the risk of T2DM, with a total of 207,765 participants and 16,814 cases eligible to be included. The pooled RR was 1.07 (95% CI, 0.90-1.27), with a high heterogeneity (I^2 = 84.7%, $P_{heterogeneity}$ < 0.001) (Figure 3). No evidence of publication bias was observed by visual inspection of the funnel plots (Figure S2) and the nonsignificant Egger's test (P = 0.371). Subgroup analyses showed a significant association for subgroup of total fried food (RR = 1.46; 95% CI, 1.03-2.07), studies conducted in the United States (RR = 1.16; 95% CI, 1.02-1.32) and Asia (RR = 1.37; 95% CI, 1.08-1.73), and subgroup of cases ≥1000 (RR = 1.16; 95% CI, 1.05-1.27) (Table S6). Meta-regression analyses found a significant heterogeneity between subgroups stratified by study design (P = 0.014), follow-up years, adjustment of BMI (P = 0.014) and physical activity (P = 0.014) (Table S6). Sensitivity analysis via excluding one study at a time did not change the results (data not shown). After excluding the studies with

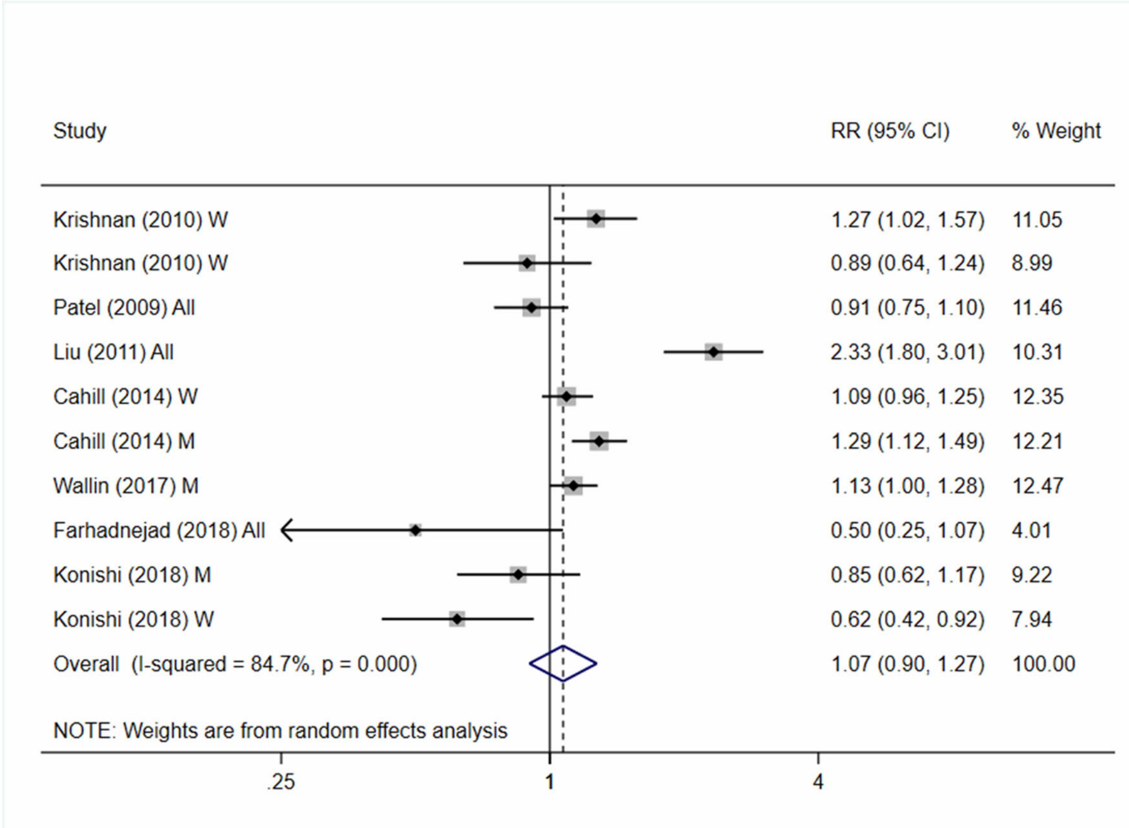

Figure 3. Forest plot of relative risk of type 2 diabetes mellitus for the highest versus lowest fried-food consumption.
RR, relative risk; 95% CI, 95% confidence interval. *Squares* represent study-specific RR. *Square areas* represent the weight of the study. *Horizontal lines* represent 95% CIs. *Diamonds* represent the pooled RR and 95% CIs.

relatively low quality, the summary RR was 1.09 (95% CI, 0.96-1.22; $I^2 = 63.3\%$, $P_{\text{heterogeneity}} = 0.012$).

Fried-food consumption and risk of hypertension

Eleven studies (8 cohort (Borgi et al. 2016; Huang et al. 2019; Sayon-Orea, Bes-Rastrollo, et al. 2014; Pengpid and Peltzer 2019) and 3 cross-sectional studies (Provido et al. 2020; Vaccaro, Zarini, and Huffman 2018; Kang and Kim 2016)) investigated the association between fried-food consumption and risk of hypertension, including 222,544 participants and more than 55,813 cases. The pooled RR was 1.20 (95% CI, 1.05-1.38; $I^2 = 91.8\%$, $P_{\text{heterogeneity}} < 0.001$) for the highest versus lowest category (Figure 4). No evidence of publication bias was observed by visual inspection of the funnel plots (Figure S3) and nonsignificant Egger's test ($P = 0.075$). Subgroup analyses showed a non-significant association when stratified by study design (cohort and cross-sectional), type of fried food (total fried food and fried potato), or assessment of hypertension (self-reported and objective-measured) or high study quality (yes or no) (Table S7). Meta-regression analyses found significant heterogeneity between subgroups stratified by study design ($P = 0.035$) and type of fried food ($P = 0.020$) (Table S7). Most sensitivity analyses via excluding one study at a time did not change the results, except for a non-significant association (RR = 1.06; 95% CI, 0.98-1.15) when excluding the study by Kang et al (Kang and Kim 2016) (data not shown). When excluding the studies with relatively low quality, the summary RR remained significant 1.21 (95% CI, 1.05-1.340; $I^2 = 93.4\%$, $P_{\text{heterogeneity}} < 0.001$).

Grading of the evidence

Table S8 shows the GRADE assessment for the certainty of the evidence for the association of fried-food consumption and the risk of overweight/obesity, T2DM, and hypertension. The evidence was rated as very low for all outcomes, which was mainly because of high risk of bias, low precision and high inconsistency.

Discussion

Dietary recommendations are of particular public health concern to target at controlling overweight/obesity, T2DM and hypertension and thereafter reducing the risk of the related morbidity and mortality. To our knowledge, this is the first meta-analysis to explore the relation between fried-food consumption and overweight/obesity, T2DM, and hypertension. This meta-analysis included more than 200,000 participants in each outcome and found significant associations between fried-food consumption and risk of overweight/obesity and hypertension by comparing the highest to lowest consumption categories. However, a non-significant association was found on fried-food consumption and the risk of T2DM, although the subgroup analysis

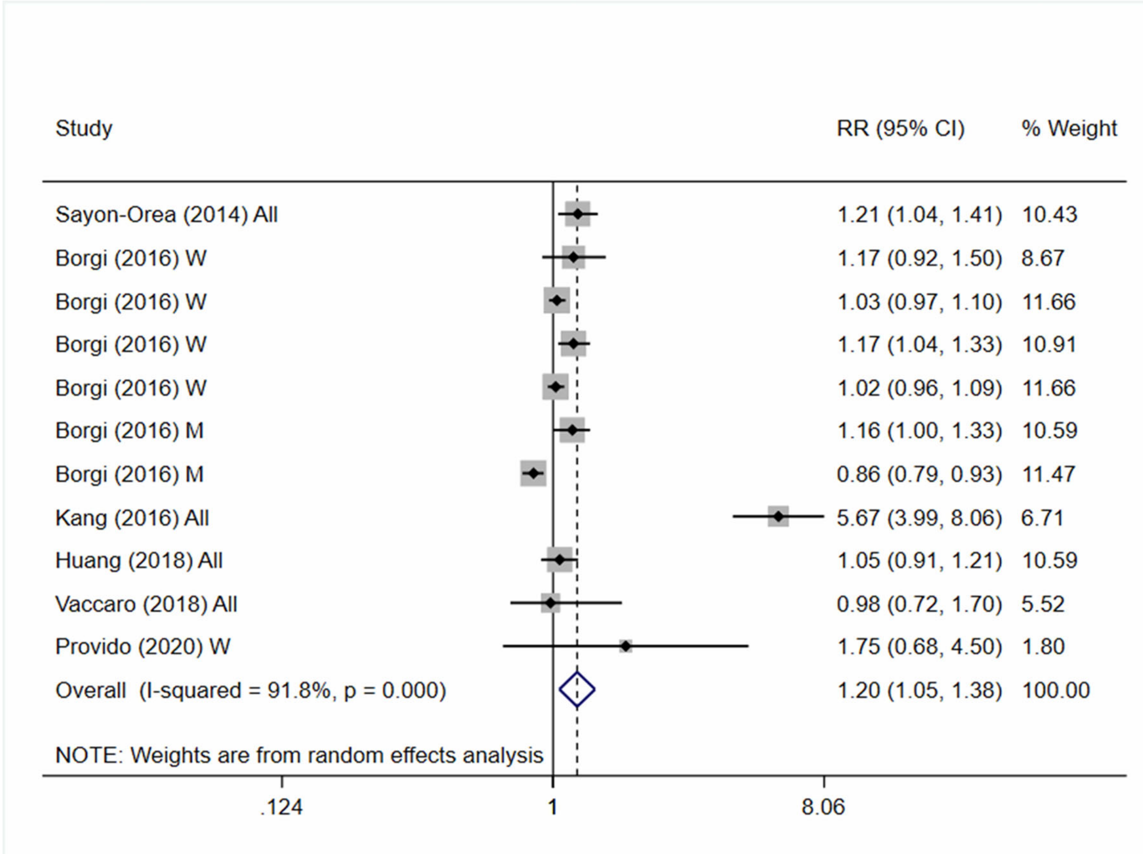

Figure 4. Forest plot of relative risk of hypertension for the highest versus lowest fried-food consumption.
RR, relative risk; 95% CI, 95% confidence interval. *Squares* represent study-specific RR. *Square areas* represent the weight of the study. *Horizontal lines* represent 95% CIs. *Diamonds* represent the pooled RR and 95% CIs.

showed a significantly positive association when pooling studies that investigated total fried food, studies conducted in the United States or Asia, and studies with cases more than 1000.

We conducted subgroup analyses and sensitivity analyses to test the robustness of the results. The sensitivity analyses showed a relatively consistent finding of significantly positive association of fried-food consumption and risk of overweight/obesity and hypertension and nonsignificant association with risk of T2DM. However, the results were unstable for the subgroup analyses of overweight/obesity, T2DM and hypertension. For overweight/obesity, it is noteworthy that we observed a significant association was observed in subgroups of cases ≥1000 and total fried food, which may suggest including large cases to have enough statistical power to detect the association and measuring total fried food instead of specific fried food may be more accurate to evaluate the association. Also, we observed significant association for cross-sectional studies but not for cohort studies, which may due to the very small number of studies included ($n = 2$). For T2DM, the association became significant when limiting studies to total fried food or fried chicken but nonsignificant for other types of fried foods including fried fish, fried potato, and fried soy foods. The inconsistent findings may result from the inaccurate ascertainment of T2DM from self-reported data and limited number of T2DM cases included, because only one study that defined T2DM based on objective measurement and included a relatively large number of T2DM cases ($n = 3624$) (Wallin et al. 2017), which showed a significantly increased T2DM risk. Nevertheless, the difference in the effect of different types of fried foods on metabolic health may also lead to the discrepancy. Future studies should explore and compare the effect of different types of fried foods on metabolic health. Additionally, a significant association of fried-food consumption and T2DM was found in the subgroup of cases ≥1000, indicating future studies should include a large sample size of T2DM cases. Therefore, the nonsignificant association in this meta-analysis of T2DM may be because of the underestimation of the association from only investigating one specific type of fried food instead of total fried-food consumption and a reduced statistical power to detect a significant association due to the small number of cases to be included. For hypertension, the results varied in some subgroups and showed a significant finding in subgroups of age <50, cases ≥1000, or adjustment of BMI, physical activity or total energy intake, which may indicate the importance of including a lager sample size and adjusting for BMI, physical activity or total energy intake. The nonsignificant association in the subgroup of age ≥50 might result from the underestimation of the risk estimate of the association because that the studies with a mean/median age ≥50 only investigated the fried potato instead of total fried food (Borgi et al. 2016). Additionally, the unstable risk estimates in the subgroup analyses may be due to the fewer number of studies in some subgroups. Furthermore, unstable results were also found when stratifying by study design. For overweight/obesity, significant association with overweight/obesity was observed for cross-section studies but not for cohort studies, however, only 2 cohort studies (Sayon-Orea et al. 2013; Sayon-Orea, Bes-Rastrollo, et al. 2014) were included, which may lead to the non-significant association for cohort studies. For T2DM and hypertension, non-significant association was observed when limiting studies to cohort studies, which may due to the limited number of cohort studies investigating the total fried food (only 2 for T2DM (Cahill et al. 2014) and 1 for hypertension (Sayon-Orea, Bes-Rastrollo, et al. 2014)). These results indicate that more cohort studies with measurement of total fried food are needed in the future to investigate the association of fried-food consumption with overweight/obesity, T2DM and hypertension.

To discover potential sources of heterogeneity, we performed various subgroup analyses and Meta-regression. We found the moderate heterogeneity for studies of overweight/obesity and meta-regression found that study quality may be the source of heterogeneity. The Meta-regression also indicated that the observed high heterogeneity for studies of T2DM may result from the differences in the study design, follow-up years and adjustment of BMI and physical activity. The heterogeneity for studies of hypertension may arise from differences in the study design, and type of fried food to be investigated in the studies. Furthermore, the heterogeneity for studies of fried food may result from the difference in the frying technique and the type of food and oil that might affect the energy and composition to some extent (Saguy and Pinthus 1995; Song et al. 2015).

The mechanism of the association of fried-food consumption with overweight/obesity and hypertension risk may involve the high energy intake and chemicals generated by frying such as trans-fatty acids as well as the high sodium intake and other fast food intake together with fried food. Frying can increase the fat content and an increased energy density (Fillion and Henry 1998) and lead to weight gain. The process of frying can induce the generation of trans-fatty acids (Fillion and Henry 1998; Song et al. 2015), which can in turn increase the risk of obesity (Thompson, Minihane, and Williams 2011) and hypertension (Wang et al. 2010). Additionally, fried foods such as fried chicken and French fries are processed restaurant foods that are usually high in added sodium, which can increase the risk of obesity (Yi and Kansagra 2014) and hypertension (Grillo et al. 2019). Moreover, people who consume fried food frequently might be more likely to have other unhealthy dietary behaviors such as increased sugar-sweetened beverages consumption (Larson et al. 2011; Buscemi 2014; Williams, Odum, and Housman 2017), thereby increasing the risk of obesity (Rosenheck 2008) and hypertension (Qin et al. 2020). Sayon-Orea et al (Sayon-Orea, Bes-Rastrollo, et al. 2014) found the association between fried-food consumption and hypertension attenuated after adjustment of incident obesity or yearly body weight change based on a prospective cohort from Spain. This finding underscored a potential mediating effect of obesity in the fried-food consumption and hypertension relation.

To our knowledge, this meta-analysis is the first to assess the associations between fried-food consumption and the risk of overweight/obesity, T2DM and hypertension risk. Additionally, this meta-analysis included a relatively large sample size and number of cases. The included studies were of moderate and high quality. We found no significant publication bias in our included studies.

However, this study has some limitations that merit discussion. First, there are few studies on the association of fried-food consumption and overweight/obesity, T2DM and hypertension risk, especially the relation of total fried-food consumption and T2DM and hypertension risk, which may underestimate the risk estimates, reduced the statistical power to detect an association, and destabilized the associations in the subgroup analyses. Second, more than half of the included studies measured the fried-food consumption and T2DM and hypertension based on self-reported data, which may imply recall bias. Third, although the results in most studies adjusted for socio-demographic and other lifestyle factors, residual confounding cannot be avoided due to some unmeasured confounders. For example, 3 studies (Al-Tawarah et al. 2010; Vaccaro, Zarini, and Huffman 2018; Pengpid and Peltzer 2019) did not adjust for physical activity when investigating the association between fried-food consumption and obesity, although physical activity plays a key role in the development of obesity. However, excluding the studies yielded similar results. Forth, the certainty of the evidence in the effect estimates was considered very low, mainly owing to downgrading for high risk of bias, indirectness and imprecision. These results suggest that further research is likely to change the confidence in the effect estimates of association. Moreover, the findings in this meta-analysis can not be generalized to children and adolescents.

Conclusions

Our meta-analysis found that fried-food consumption was associated with increased risk of overweight/obesity and hypertension but not T2DM in adults, despite of a significant association between fried-food consumption and T2DM is in the subgroups of total fried food and large number of cases. These findings may suggest the dietary advice to decrease fried-food consumption for preventing overweight/obesity, hypertension and T2DM. However, the findings should be interpreted with caution due to potential recall and misclassification biases for fried-food consumption from the original studies, and high heterogeneity and unstable results from subgroup analysis of this meta-analysis. More studies are warranted to investigate the association of total fried-food consumption and T2DM and hypertension as well as the effect of different types of fried foods.

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PQ, MZ, FH, and DH conceived, designed and performed the work. PQ, XW, DL, XS, YZ, YL, YW, XL, YZ, QC, TW, XC, YL, HL extracted, analyzed or interpreted the data. PQ drafted the manuscript. YZ, XW, DL, XS, YZ, YL, YW, MH, RQ, SH, YZ, YF, XY, XL, TW,

XC, YL, HL, MZ, DH, and FH revised the manuscript. All authors approved the final manuscript.

Disclosure statement

The authors declare that they have no competing interests.

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