

### **Supplementary Material Table Legends**

**Supplementary Material Table 1**, Systematic literature review search terms and strategy.

**Supplementary Material Table 2**, Characteristics of studies included in the meta-analysis of UPF consumption with CVEs and all-cause mortality.

**Supplementary Material Table 3**, Assessment of quality of included studies (Newcastle-Ottawa Quality Assessment Scale).

### **Supplementary Material Figure Legends**

**Supplementary Material Figure 1**, Sensitivity analysis for CVEs and all-cause mortality risk with highest versus lowest category (A&B) and each additional serving (C&D) of UPF.

**Supplementary Material Figure 2**, Funnel plot for CVEs and all-cause mortality risk with highest versus lowest category (A&B) and each additional serving (C&D) of UPF.

**Supplementary Material Figure 3**, Forest plot of study-specific relative risk statistics for CVD morbidity and mortality comparing the highest and lowest category group.

**Supplementary Material Figure 4**, Forest plot of study-specific relative risk statistics for CVD morbidity and mortality with each additional daily serving of UPF.

**Supplementary Material Table 1**, Systematic literature review search terms and strategy.

<b>Search terms for PubMed</b>
#1 ("ultra-processed food" [Title/Abstract] OR "ultraprocessed food*" [Title/Abstract] OR "ultra processed food*" [Title/Abstract] OR "minimally OR unprocessed food*" [Title/Abstract] OR "minimally processed food*" [Title/Abstract] OR "unprocessed food*" [Title/Abstract] OR "processed food*" [Title/Abstract] OR "NOVA food classif*" [Title/Abstract] OR "NOVA food*" [Title/Abstract] OR "NOVA food classif*" [Title/Abstract] OR "NOVA food classification system" [Title/Abstract])
#2 (“cerebrovascular disorders” OR "Cardiovascular Diseases" OR “cerebrovascular disorders” [Title/Abstract] OR “cardiovascular disease” [Title/Abstract] OR “cardiovascular diseases” [Title/Abstract] OR “CVD” [Title/Abstract] OR “coronary disease” [Title/Abstract] OR “coronary artery disease” [Title/Abstract] OR “coronary heart disease” [Title/Abstract] OR “CHD” [Title/Abstract] OR “ischemic heart disease” [Title/Abstract] OR “ischaemic heart disease” [Title/Abstract] OR “stroke” [Title/Abstract] OR “cerebrovascular disease” [Title/Abstract] OR “cerebrovascular disorders” [Title/Abstract] OR “heart disease” [Title/Abstract] OR “myocardial infarction” [Title/Abstract] OR “MI” [Title/Abstract] OR “heart failure” [Title/Abstract] OR “cerebral vascular accident” [Title/Abstract] OR “CVA” [Title/Abstract] OR “cardiovascular” [Title/Abstract] OR “coronary” [Title/Abstract] OR “myocardial” [Title/Abstract]) OR ("mortality" OR "death" OR "mortality"[Title/Abstract] OR "death"[Title/Abstract] OR "deaths"[Title/Abstract] OR "fatal"[Title/Abstract])
#1 AND #2
<b>Search terms for Embase</b>
#1 "ultra-processed food"/ OR "ultraprocessed food*".mp. OR "ultra processed food*".mp. OR "minimally OR unprocessed food*".mp. OR "minimally processed food*".mp. OR "unprocessed food*".mp. OR "processed food*".mp. OR "NOVA food classif*".mp. OR "NOVA food*".mp. OR "NOVA food classif*".mp. OR "NOVA food classification system".mp.
#2 "cerebrovascular disease"/ OR "Cardiovascular Diseases".mp. OR "cerebrovascular

disorders".mp. OR "cardiovascular disease".mp. OR CVD.mp. OR "coronary disease".mp. OR "coronary artery disease"/ OR "coronary artery disease".mp. OR "coronary heart disease".mp. OR "ischemic heart disease"/ OR CHD.mp. OR "ischemic heart disease".mp. OR stroke.mp. OR "cerebrovascular accident"/ OR "cerebrovascular disease".mp. OR "cerebrovascular disease"/ OR "cerebrovascular disorders".mp. OR "cerebrovascular disease"/ OR "heart disease".mp. OR "heart disease"/ OR "myocardial infarction".mp. OR "heart infarction"/ OR MI.mp. OR "heart failure".mp. OR "heart failure"/ OR "cerebral vascular accident".mp. OR "cerebrovascular accident"/ OR CVA. mp. OR "cardiovascular".mp. OR coronary.mp. OR myocardial.mp. OR mortality/ OR death/ OR mortality.mp. OR death.mp. OR deaths.mp. OR fatal.mp.

#1 AND #2

#### **Search terms for Web of Science**

#1 TS= ("ultra-processed food" OR "ultraprocessed food\*" OR "ultra processed food\*" OR "minimally OR unprocessed food\*" OR "minimally processed food\*" OR "unprocessed food\*" OR "processed food\*" OR "NOVA food classif\*" OR "NOVA food\*" OR "NOVA food classif\*" OR "NOVA food classification system")

#2 TS= ("Cardiovascular Diseases" OR "cardiovascular disease" OR CVD OR "coronary disease" OR "coronary artery disease" OR "coronary heart disease" OR "ischemic heart disease" OR CHD OR stroke OR "cerebrovascular accident" OR "cerebrovascular disease" OR "cerebrovascular diseases" OR "cerebrovascular disorders" OR "heart disease" OR "myocardial infarction" OR "heart infarction" OR MI OR "heart failure" OR "cerebrovascular accident" OR CVA OR "cardiovascular" OR coronary OR myocardial OR mortality OR death OR deaths OR fatal)

#1 AND #2

**Supplementary Material Table 2, Characteristics of studies included in the meta-analysis of UPF consumption with CVEs and all-cause mortality.**

Author (year)	Country (Cohort name)	Follow-up years	Average Age (BMI)	Total participants	Outcome	Daily UPF intake	RRs (95%CI)	Exposure measurement	Definition and/or examples of UPF	Variable adjustment
Rico-Campà et al. (2019)	Spain (SUN)	10.4	37.6 (23.3)	19,899	CVD mortality (n=71)  All-cause mortality (n=335)	<2 (servings/d) 2-3 (servings/d) 3-4 (servings/d) >4 (servings/d)	1.00 0.77 (0.32-1.83) 1.14 (0.46-2.82) 2.16 (0.92-5.06)  1.00 1.06 (0.76-1.48) 1.38 (0.99-1.92) 1.62 (1.13-2.33)	136-item FFQ	<p><b>Definition:</b> UPF and drink products that are made predominantly or entirely from industrial substances and contain little or no whole foods. These products are ready to eat, drink, or heat—that is, carbonated drinks, sausages, biscuits (cookies), candy (confectionery), fruit yogurts, instant packaged soups and noodles, sweet or savoury packaged snacks, and sugared milk and fruit drinks.</p> <p><b>Examples:</b> Petit suisse; custard; flan; pudding; ice cream; ham; processed meat (chorizo, salami, mortadella, sausage, hamburger, morcilla); pate; foie-gras; spicy sausage/meatballs; potato chips; breakfast cereals; pizza, including pre-prepared pies; margarine; cookies; chocolate cookies; muffins; doughnuts; croissant or other on-handmade pastries; cakes; churros; chocolates and candies; nougat; marzipan; carbonated drinks; artificially sugared beverages; fruit drinks; milkshakes; instant soups and creams; croquettes; mayonnaise; and alcoholic drinks produced by fermentation followed by distillation such as whisky, gin, and rum</p>	Sex, age, marital status, physical activity, smoking status, snacking, special diet at baseline, BMI, total energy intake, alcohol consumption, family history of cardiovascular disease, diabetes at baseline, hypertension at baseline, self-reported hypercholesterolaemia at baseline, CVD at baseline, cancer at baseline, depression at baseline, education level and lifelong smoking stratified by recruitment period, deciles of age, sedentary index, and television viewing.

Kim et al. (2019)	USA (NHANES III)	19	41.0 (26.2)	18,779	CVD mortality (n=649)	0-2.6 (times/d) 2.6-3.8 (times/d) 3.8-5.2 (times/d) 5.2-29.8 (times/d)	1.00 1.10 (0.69-1.76) 0.94 (0.61-1.45) 1.13 (0.74-1.71)	24-h dietary recalls	<p><b>Definition:</b> UPF contains predominantly industrial substances and few whole foods, containing substances that are not typically used in culinary preparation such as hydrogenated oils, hydrolyzed protein, or emulsifiers, and have few whole foods. Ultra-processed foods contain industrial substances to mimic sensorial qualities of whole foods and create foods that are highly palatable.</p> <p><b>Examples:</b> Chocolate milk, ice cream, ice milk, milkshakes, bacon, sausage, processed meats, sweetened cereals, spaghetti/pasta with tomato sauce, cheese dishes, pizza, calzone, lasagna, salted snacks, cakes, cookies, brownies, fruit juices, sugar-sweetened and artificially sweetened beverages (Hi-C, Tang, Koolaid, diet colas, diet sodas, regular colas and sodas), hard liquor, margarine</p>	Sex, age, race/ethnicity, total energy intake, poverty level, education level, smoking status, physical activity, alcohol intake, body mass index, hypertension status, total cholesterol, and estimated glomerular filtration rate.
					All-cause mortality (n=2,451)		1.00 0.99 (0.83-1.18) 1.06 (0.87-1.30) 1.30 (1.08-1.57)			

<p>Srouf et al (2019)</p>	<p>France (The NutriNet-Santé cohort)</p>	<p>5.2</p>	<p>42.7 (23.6)</p>	<p>103,750</p>	<p>CVD morbidity (n=1,409)</p>	<p>Women &lt;10.6 (%weight) 10.6-15.4 (%weight) 15.4-21.8 (%weight) &gt;21.8 (%weight)</p> <p>Men 10.80 (%weight) 10.8-15.6 (%weight) 15.6-22 (%weight) &gt;22 (%weight)</p>	<p>1.00 1.04 (0.91-1.19) 1.06 (0.92-1.23) 1.23 (1.04-1.45)</p>	<p>24-h dietary recalls</p>	<p><b>Definition:</b> UPF includes mass produced packaged breads and buns, sweet or savoury packaged snacks, industrialised confectionery and desserts, sodas and sweetened beverages, meatballs, poultry and fish nuggets, and other reconstituted meat products transformed with the addition of preservatives other than salt (eg, nitrites), instant noodles and soups, frozen or shelf stable ready meals, and other food products made mostly or entirely from sugar, oils, and fats, and other substances not commonly used in culinary preparations, such as hydrogenated oils, modified starches, and protein isolates. Industrial processes notably include hydrogenation, hydrolysis, extrusion, moulding, reshaping, and pre-processing by frying. Flavouring agents, colours, emulsifiers, humectants, non-sugar sweeteners, and other cosmetic additives are often added to these products to imitate sensorial properties of unprocessed or minimally processed foods and their culinary preparations, or to disguise undesirable qualities of the final product.</p> <p><b>Examples:</b> Carbonated drinks; sweet or savoury packaged snacks; ice-cream, chocolate, candies (confectionery); mass-produced packaged breads and buns; margarines and spreads; industrial</p>	<p>Sex, age, energy intake, number of 24-hour dietary records, smoking status, educational level, physical activity, BMI, alcohol intake, family history of cardiovascular disease, baseline prevalent type 2 diabetes, dyslipidemia, hypertension, and hypertriglyceridemia as well as treatments for these conditions.</p>
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									<p>cookies (biscuits), pastries, cakes, and cake mixes; breakfast 'cereals', 'cereal' and 'energy' bars; 'energy' drinks; flavoured milk drinks; cocoa drinks; sweet desserts made from fruit with added sugars, artificial flavours and texturizing agents; cooked seasoned vegetables with ready-made sauces; meat and chicken extracts and 'instant' sauces; 'health' and 'slimming' products such as powdered or 'fortified' meal and dish substitutes; ready to heat products including pre-prepared pies, pasta and pizza dishes; poultry and fish 'nuggets' and 'sticks', sausages, burgers, hot dogs, and other reconstituted meat products, and powdered and packaged 'instant' soups, noodles and desserts.</p>	
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Blanco-Rojo et al. (2019)	Spain (ENRICA)	7.7	46.9 (ND)	12,938	All-cause mortality (n=440)	155.50 (g/d) 304.70 (g/d) 436.90 (g/d) 641.20 (g/d)	1.00 1.08 (0.81-1.44) 1.21 (0.89-1.64) 1.46 (1.04-2.05)	Computer-based dietary history	<p><b>Definition:</b> UPF are those that were formulated mostly or entirely from substances derived from foods, with little or even no whole food content. These ingredients include modified starches, hydrogenated oils, protein isolates, and additives whose purpose is to imitate sensorial qualities of unprocessed or minimally processed foods and their culinary preparations, or to disguise undesirable qualities of the final product, such as colorants, flavorings, nonsugar sweeteners, emulsifiers, humectants, sequestrants, and firming, bulking, defoaming, anticaking, and glazing agents.</p>	Sex, age, educational level, whether they lived alone, smoking status, former drinker, physical activity index, time watching television, time devoted to other sedentary activities, the number of medications per day, and specific chronic conditions diagnosed by a physician (chronic respiratory disease, coronary heart disease, stroke, heart failure, osteoarthritis, cancer, and depression).
Schnabel et al. (2019)	France (The NutriNet-Santé Study)	7.1	56.7 (24.6)	44,551	All-cause mortality (n=602)	<9.3 (%weight) 9.3- 13.2 (%weight) 13.2- 18.0 (%weight) >18.0 (%weight)	1.00 1.06 (0.84-1.34) 1.18 (0.93-1.48) 1.25 (0.99-1.57)	24-h dietary records	<p><b>Definition:</b> UPF are manufactured industrially from multiple ingredients that usually include additives used for technological and/or cosmetic purposes. UPF are mostly consumed in the form of snacks, desserts, or ready-to-eat or -heat meals.</p> <p><b>Examples:</b> Carbonated drinks; sweet or savory packaged snacks; ice cream, chocolate, candies (confectionery); mass-produced packaged breads and buns; margarines and spreads; 'energy' bars; 'energy' drinks; flavored milk drinks; cocoa drinks; sweet desserts made from fruit with added sugars, artificial flavors and texturizing agents; cooked</p>	Sex, age, income level, education level, marital status, residence, BMI, physical activity level, smoking status, energy intake, alcohol intake, season of food records, first-degree family history of cancer or cardiovascular diseases, number of food records and modified Programme National Nutrition Santé Guideline Score



									seasoned vegetables with ready-made sauces; meat and chicken extracts and 'instant' sauces; 'health' and 'slimming' products such as powdered or 'fortified' meal and dish substitutes; ready to heat products including pre-prepared pies, pasta and pizza dishes; poultry and fish 'nuggets' and 'sticks', sausages, burgers, hot dogs, and other reconstituted meat products, and powdered and packaged 'instant' soups, noodles and desserts.	
Zhong et al. (2021)	USA (PLCO Cancer Screening Trial)	13.5	65.3 (ND)	91,891	CVD mortality (n=5,490)	0.1 (servings/d) 0.8 (servings/d) 1.6 (servings/d) 3.0 (servings/d) 8.2 (servings/d)	1.00 1.00 (0.91, 1.09) 1.01 (0.92, 1.11) 1.20 (1.09, 1.31) 1.50 (1.36, 1.64)	137-item FFQ	<p><b>Definition:</b> UPF are industrial formulations mostly or entirely made from substances derived from additives and foods, with little or even no whole foods. They are usually ready-to-eat, highly affordable, hyper-palatable, and energy-dense, and are marketed intensively and packaged attractively.</p> <p><b>Examples:</b> Sour cream, cream cheese, ice cream, frozen yogurt, fried foods, breads, cookies, cakes, pastries, salty snacks, breakfast cereals, instant noodles and soups, sauces, margarine, candy, soft drinks, fruit drinks, restaurant/industrial hamburgers, hot dogs, and pizza</p>	Sex, age, race, educational level, marital status, study center, aspirin use, history of hypertension, history of diabetes, smoking status, alcohol consumption, BMI, physical activity, and energy intake from diet.

Bonaccio et al. (2021)	Italy (The Moli-sani Study)	8.2	55.5 (28.0)	22,475	CVD mortality (n=439)	4.8 (%weight)	8.2 (%weight)	12.1 (%weight)	18.5 (%weight)	188-item FFQ	<p><b>Definition:</b> UPF comprises products "created mostly or entirely from substances extracted from foods or derived from food constituents with little if any intact food, which often contain flavours, colours and other additives that imitate or intensify the sensory qualities of foods or culinary preparations made from foods", and are highly convenient (ready-to-consume), attractive (hyper-palatable), inexpensive, have a long shelf-life, and are highly competitive with foods that are naturally ready to consume and freshly prepared dishes and meals</p> <p><b>Examples:</b> Processed meat, pizza, cakes, pies, pastries, puddings (non-milk based), ice-cream, crispbread/rusks, fruit yoghurts, dry cakes, biscuits, snacks, chocolate, breakfast cereals, candy bars, confectionery non chocolate, margarine, salty biscuits, aperitif biscuits, crackers, mayonnaise and similar, fruit drinks, carbonated/soft/isotonic drinks, diluted syrups, spirits, and brandy</p>	Sex, age, energy intake, educational level, housing tenure, smoking, BMI, leisure-time physical activity, history of cancer, CVD, diabetes, hypertension, hyperlipidemia, residence, and Mediterranean Diet Score
					All-cause mortality (n=1,216)	1.00	1.07 (0.92-1.23)	1.17 (1.02-1.36)	1.26 (1.09-1.46)			

Juul et al. (2021)	USA (FOS)	20.2	53.9 (27.3)	3,003	CVD morbidity (n=648)  CVD mortality (n=108)  All-cause mortality (n=713)	4 (servings/d) 5.9 (servings/d) 7.0 (servings/d) 8.5 (servings/d) 11.9 (servings/d)	each additional daily serving of UPF  1.05 (1.02-1.08)  1.09 (1.02-1.16)  1.01 (0.99-1.04)	131-item FFQ	<b>Definition:</b> Industrial formulations made with no or minimal whole foods and produced with additives such as dye, flavorings and preservatives.  <b>Examples:</b> Bread, sweets and desserts, ultra-processed meats, salty snack foods, sugar-sweetened beverages, low-calorie soft drinks, fast foods, breakfast cereals, yoghurt, and others.	Sex, age, education, smoking status, alcohol intake, and physical activity as time-varying covariates.
Du et al. (2021)	USA (ARIC)	27	54.0 (ND)	13,548	Coronary artery disease (n=1899)	3.9 (servings/d) 5.4 (servings/d) 6.4 (servings/d) 8.4 (servings/d)	1.00 1.05 (0.92-1.19) 1.08 (0.95-1.23) 1.19 (1.05-1.35)	66-item FFQ	<b>Definition:</b> UPF are defined as food and drink products formulated through industrial processes, and they generally contain nonculinary substances (e.g., hydrolyzed protein, modified starches, hydrogenated oils) and additives (e.g., colorants, nonsugar sweeteners, emulsifiers, humectants). UPF usually contain high amounts of refined carbohydrates, saturated fat, salt, and sugar, and are low in fiber and vitamins  <b>Examples:</b> Ice cream, margarine and spreads,	Sex, age, race-center, total energy intake, education level, smoking status, drinking status, and physical activity score

									<p>hamburgers, processed meats (sausage, salami, bologna), meats prepared with added sauce; catsup, hot sauce and soy or steak sauces; hot dogs, chocolate bars or pieces (Hershey's, Plain M&amp;M's, Snickers, Reese's), candy without chocolate, ready-made pie, donut, biscuits or cornbread; Danish pastry, sweet roll, coffee cake and croissant; cookies, cold breakfast cereal, potato chips or corn chips, French fried potatoes, food fried away from home, low calorie and regular soft drinks, orange and grapefruit juice, fruit-flavored punch or non-carbonated beverages (lemonade, Kool-Aid, Hawaiian Punch), hard liquor</p>	
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Romero Ferreiro et al. (2021)	Spain (DRECE)	27	30.5 (24.2)	4,679	CVD mortality (n=ND)  All-cause mortality (450)	ND	every 10% increase in total energy intake  1.14 (1.01-1.29)  1.15 (1.03-1.27)	FFQ	<p><b>Definition:</b> UPF are industrial formulations made from substances derived from food or synthesised in laboratories (dyes, flavourings and other additives) usually containing little or no whole food These are characterised by being food products with a low nutritional quality.</p> <p><b>Examples:</b> Ham, processed meat (cold cuts, sausage, hamburger), pate, foie-gras, ultra-processed cheese, salty snacks, sauces and dressings, liquors, sugar sweetened beverages, juice boxes, milkshakes, cookies, chocolate cookies, muffins, doughnuts or other non-handmade pastries, churros, chocolates and candies, breakfast cereals, sweetened yoghurt sugared 'fruit' yoghurts, Petit Suisse, ice cream and margarine</p>	Sex, age, BMI, physical activity, alcohol intake, smoking status, total energy intake, family history of CVD, history of diabetes, hypertension, angina, myocardial infarction and atherosclerosis
Orlich et al. (2022)	USA& Canada (AHS-2)	7.46	59.3 (27.2)	77,437	All-cause mortality (n=9,293)	0-17.0 (%kal) 17.1-24.5 (%kal) 24.6-31.5 (%kal) 31.6-40.5 (%kal) 40.6-95.8 (%kal)	1.00 1.03 (0.96-1.10) 1.08 (1.00-1.16) 1.09 (1.01-1.17) 1.14 (1.05-1.23)	>200 item FFQ	<p><b>Definition:</b> UPF are produced to "optimize" taste, texture, shelf-life, and production costs, not health. They tend to be higher in a variety of nutrients of potential concern (when consumed in excess), such as added sugars, trans fats and saturated fats, and sodium.</p> <p><b>Examples:</b> Fruit jams, preserves, fruit pie fillings, French fries, hash browns, fried potatoes catsup,</p>	Sex, age, race, geographic region, education, marital status, smoking, alcohol, exercise, sleep duration, menopause, hormone replacement, BMI, total dietary energy, prevalent cardiovascular disease, and diabetes mellitus active or treated in the last 12 months

									chili with beans, nut candies, white breads other breads (bagels, biscuits, corn bread) gluten steaks, special K (Kelloggs), frosted flakes (Kelloggs), frosted mini wheats (Kelloggs), honey bunches of oats (post), ccinnamon toast crunch (general mills) 100% natural oats, or oats & honey (quaker), salad dressings mayo or miracle whip gravies, etc., margarines, potato chips, doughnuts, cookies (store-bought) cake, ice cream, milk shakes, ice milk, frozen yogurt, other sweets, meal replacement drinks, cheese (American processed and cheddar), cream cheese/spreads, other (whipping cream/sour cream), evaporated/condensed milk, soy/imitation cheese, soy/rice drinks, processed red meat, processed white meat, soft drinks/soda, other (hot chocolate, etc), spirits/liqueurs, macaroni and cheese, pizza	
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ND: No data available; FFQ: Food Frequency Questionnaire; CVD: Cardiovascular Disease.

SUN: The Seguimiento Universidad de Navarra project.

NHANES III: The Third National Health and Nutrition Examination Survey.

ENRICA: The Study on Nutrition and Cardiovascular Risk in Spain.

PLOC Cancer Screening Trial: The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

FOS: The Framingham Offspring Study.

DRECE: The multicentre study Diet and Risk of Cardiovascular Diseases (CVD) in Spain.

AHS-2: The Adventist Health Study-2.

USA: the United States of America; BMI: Body Mass Index; FFQ: Food Frequency Questionnaire.

**Supplementary Material Table 3**, Assessment of quality of included studies (Newcastle-Ottawa Quality Assessment Scale).

<b>Author (year)</b>	<b>a</b>	<b>b</b>	<b>c</b>	<b>d</b>	<b>e</b>	<b>f</b>	<b>g</b>	<b>h</b>	<b>Total score</b>
Rico-Campà et al. (2019)	0	0	1	1	2	1	1	1	7
Kim et al. (2019)	1	1	0	1	2	1	1	0	7
Srouf et al. (2019)	1	1	0	1	2	1	0	1	7
Blanco-Rojo et al. (2019)	1	1	1	1	2	1	0	1	8
Schnabel et al. (2019)	1	1	0	1	2	1	0	1	7
Zhong et al. (2021)	1	1	1	1	2	1	1	1	9
Bonaccio et al. (2021)	1	1	1	1	2	1	0	1	8
Juul et al. (2021)	1	1	1	1	2	1	0	1	8
Du et al. (2021)	1	1	1	1	1	1	1	0	7
Romero Ferreiro et al. (2021)	1	1	1	1	2	1	1	1	9
Orlich et al. (2022)	0	1	1	1	2	1	0	1	7

a. Representativeness of the exposed cohort.

b. Selection of the non-exposed cohort.

c. Ascertainment of exposure.

d. Demonstration that outcome of interest was not present at start of study.

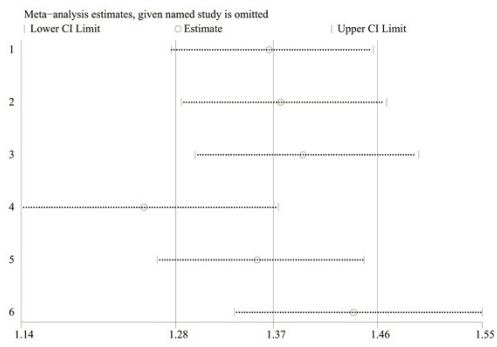
e. Comparability of cohorts on the basis of the design or analysis (adjusted for age and any other factors).

f. Assessment of outcome.

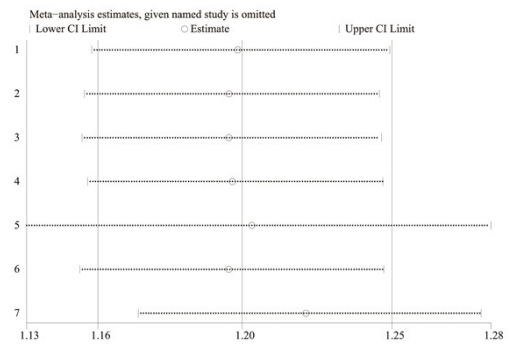
g. Was follow-up long enough for outcomes to occur?

h. Adequacy of follow-up of cohorts.

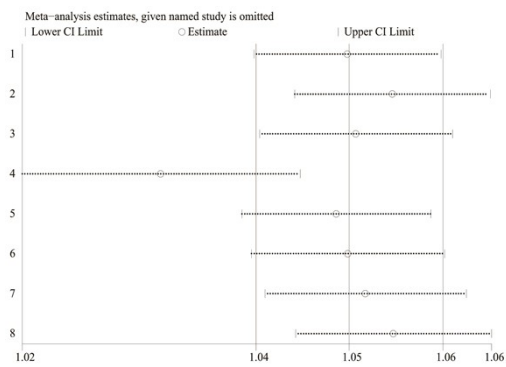




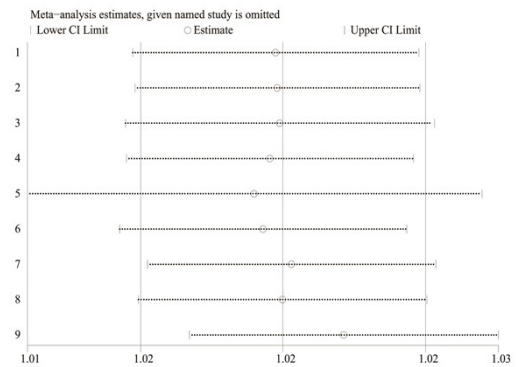
A. CVEs



B. All-cause mortality

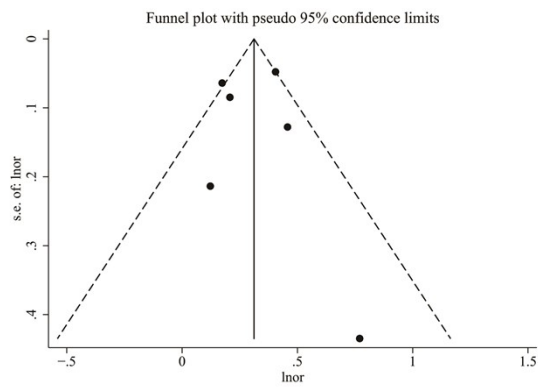


C. CVEs

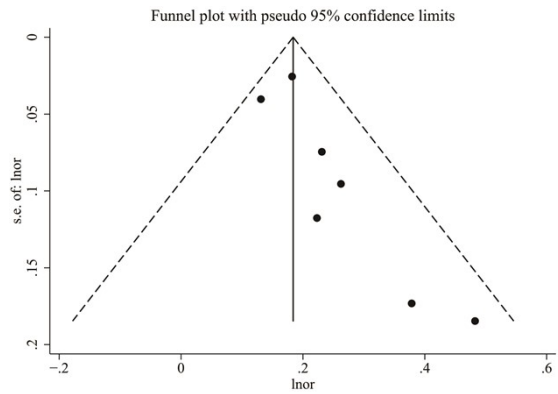


D. All-cause mortality

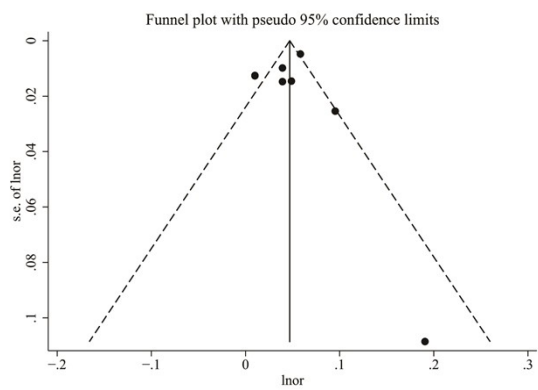
**Supplementary Material Figure 1**, Sensitivity analysis for CVEs and all-cause mortality risk with highest versus lowest category (A&B) and each additional serving (C&D) of UPF.



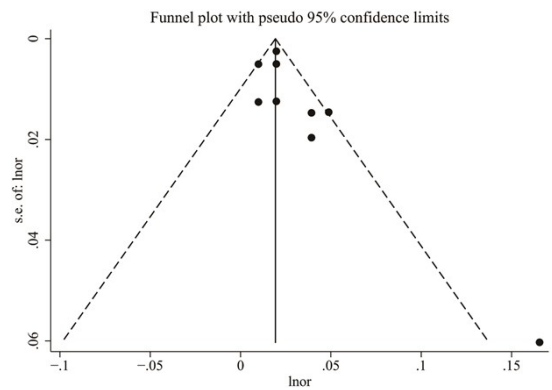
A. CVEs



B. All-cause mortality

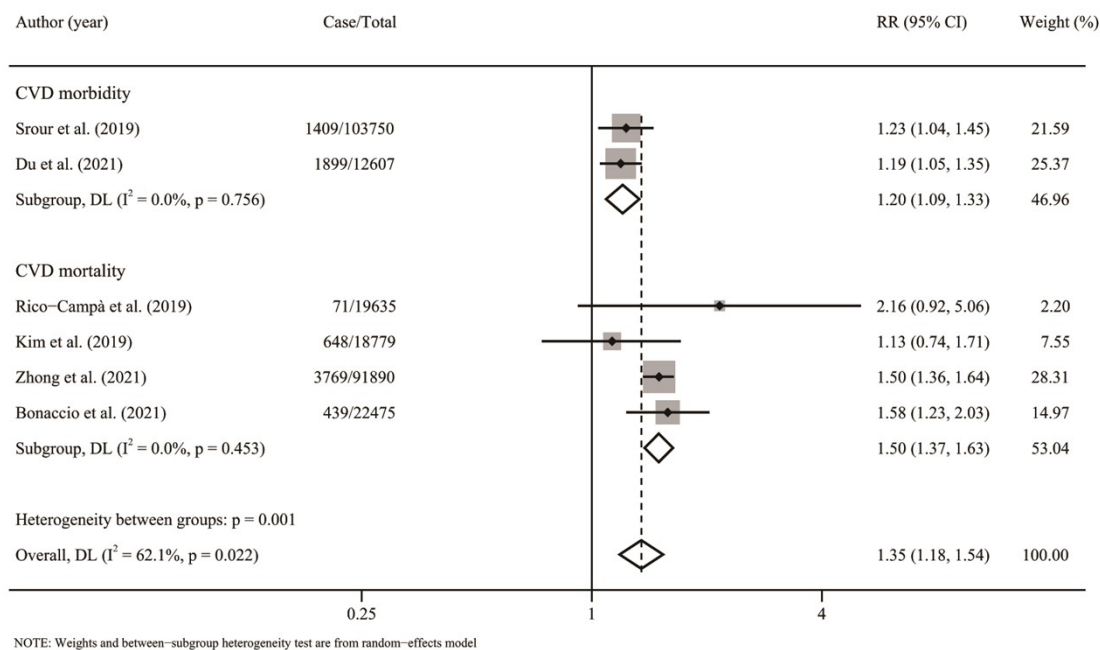


C. CVEs

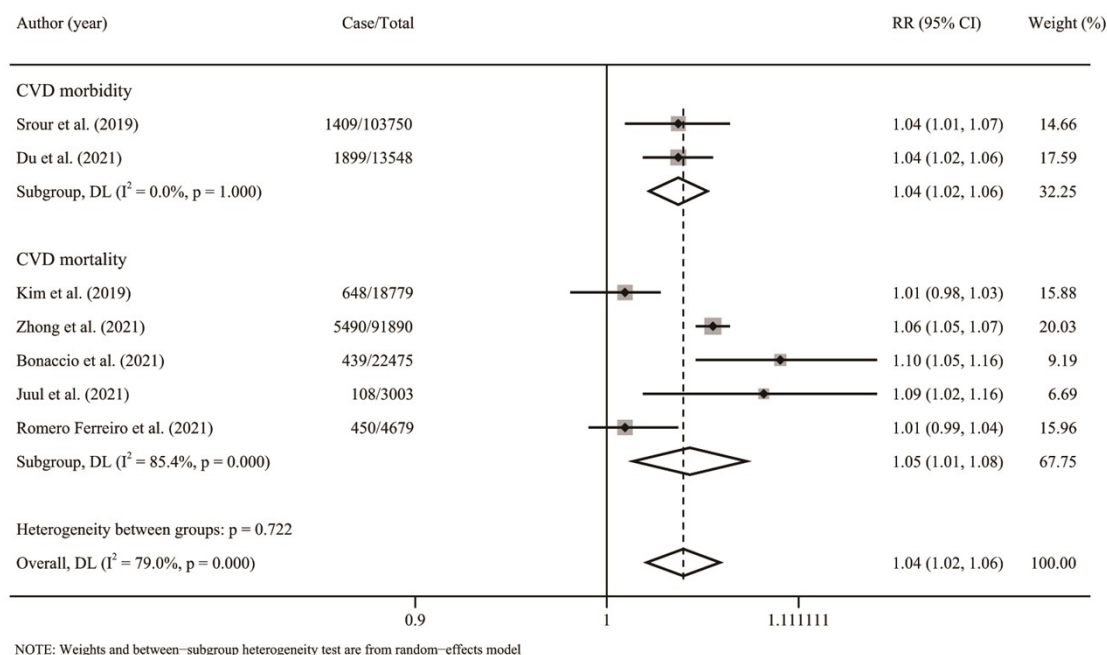


D. All-cause mortality

**Supplementary Material Figure 2**, Funnel plot for for CVEs and all-cause mortality risk with highest versus lowest category (A&B) and each additional serving (C&D) of UPF.



**Supplementary Material Figure 3**, Forest plot of study-specific relative risk statistics for CVD morbidity and mortality comparing the highest and lowest category group.



**Supplementary Material Figure 4**, Forest plot of study-specific relative risk statistics for CVD morbidity and mortality with each additional daily serving of UPF.