

Supplementary Material

Association of ultra-processed food consumption with all cause and cause specific mortality: population-based cohort study

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Supplementary Table A. The percentage of missness in exposure and covariates in our cohorts

Variables	Health Professional Follow-up Study (No. of person-years = 542 076)	Nurses' Health Study (No. of person-years = 1 134 626)
Ultra-processed foods	0	0
Ultra-processed subgroups ^a	<0.1%	0.2%
Age	0	0
Sex	0	0
Race/ethnicity	0	0
Marrital status	0	0
Body mass index	0.3%	<0.1%
Total physical activity	<0.1%	3.2%
Alcohol drinking	0	0
AHEI score	0	0
Total energy intake	0	0
Smoking status and packyears	4.9%	2.1%
Physical examination for screening	0	0
Family history of cancer	0	0
Family history of myocardial infarction	0	0
Family history of diabetes	0	0

^a a) ultra-processed breads and breakfast foods, b) fat, condiments, and sauces, c) packaged sweet snacks and desserts, d) sugar and artificially sweetened beverages, e) ready-to-eat/heat mixed dishes, f) meat/poultry/seafood based ready-to-eat products, g) packaged savory snacks, h) dairy-based desserts, i) other.

Supplementary Table B. List of food items comprising the nine ultra-processed food subgroups

Ultra-processed food subgroups	List of food items ^a
1. Ultra-processed breads and breakfast foods	Whole grain (cold breakfast cereal; rye, pumpernickel bread; whole grain bread) ^b ; English muffins, bagels, rolls; White bread
2. Sauces, spreads, and condiments	Cream cheese, Ketchup, Margarine, Mayonnaise (regular and low fat), Non-dairy coffee whitener, Red chili sauce, Salad dressings, Salsa, Soy sauce, Spread butter
3. Packaged sweet snacks and desserts	Apple sauce; Candy bar with chocolate; Candy bar without chocolate; Chocolate bars; Dark chocolate bars; Breakfast bar; Energy bar; High protein, low carb candy bar; Brownies; Cookies; Fat-free/reduced fat doughnuts; Muffins or biscuits; Ready-made cake; Ready-made sweet rolls and coffee cakes; Ready-made pie; Jams, jellies, preserves, honey
4. Packaged savory snacks	Fat-free popcorn; Fat-free, light crackers; Regular crackers
5. Sugar and artificially sweetened beverages	Regular carbonated beverage with caffeine & sugar; Carbonated, low-cal 'diet' beverage with caffeine; Carbonated beverage without caffeine but with sugar; Fruit drinks/pouch, lemonade, Sunny D, Koolaid, sugared ice tea or other non-carbonated fruit drink – NOT juice
6. Meat/poultry/seafood-based ready-to-eat products	Bacon; Beef hotdogs or pork hotdogs; Breaded fish cakes, pieces, sticks; Chicken hotdogs or turkey hotdogs; Processed meats, sausages; Salami, bologna, processed meat sandwiches
7. Ready-to-eat/heat mixed dishes	Chowder or cream soup, French fries potatoes, Pizza, Ready-made soup from cans, Soup made with bouillon
8. Dairy based desserts	Artificially sweetened yogurt; Flavored yogurt without Nutrasweet; Frozen yogurt, ice cream, sherbet
9. Other ultra-processed foods	Nutrasweet or equal, Other artificial sweeteners, Splenda, Distilled alcohol ^c

^a This list is derived from the nutrient lines of food items included in the food frequency questionnaires. The food frequency questionnaires can be accessed via the public links: <https://nurseshealthstudy.org/participants/questionnaires>; <https://www.hsph.harvard.edu/hpfs/hpfs-questionnaires/>.

^b Whole grain (Cold breakfast cereal; Rye, pumpernickel bread; Whole grain bread) was excluded from total ultra-processed foods and the subgroup 'ultra-processed breads and breakfast foods' in the primary analysis.

^c Distilled alcohol was excluded from total ultra-processed foods and the subgroup 'Other ultra-processed foods' in the primary analysis.

Supplementary Table C. Pearson correlation coefficients among the nine ultra-processed food (UPF) subgroups (serving/day)

	Total UPF	Ultra-processed breads and breakfast foods	Sauces, spreads, and condiments	Packaged sweet snacks and desserts	Packaged savory snacks	Sugar and artificially sweetened beverages	Meat/poultry/seafood-based ready-to-eat products	Ready-to-eat/heat mixed dishes	Dairy based desserts	Other
Total UPF	1									
Ultra-processed breads and breakfast foods	0.416	1								
Sauces, spreads, and condiments	0.608	0.121	1							
Packaged sweet snacks and desserts	0.418	0.088	0.029	1						
Packaged savory snacks	0.265	0.005	0.029	0.065	1					
Sugar and artificially sweetened beverages	0.543	0.053	0.036	0.035	0.018	1				
Meat/poultry/seafood-based ready-to-eat products	0.257	0.145	0.073	0.038	-0.016	0.1	1			
Ready-to-eat/heat mixed dishes	0.191	0.055	0.005	0.052	-0.019	0.159	0.214	1		
Dairy based desserts	0.129	-0.054	-0.027	0.111	0.0009	0.033	-0.048	-0.028	1	
Other	0.297	0.004	0.119	0.012	0.005	0.117	0.004	-0.039	0.039	1

Supplementary Table D. Multivariable hazard ratios and 95% confidence intervals for mortality according to quarters of consumption of selected individual ultra-processed food categories (serving/day)

	Energy-adjusted ultra-processed food consumption (serving/day) ^a				P for trend	Per difference in medians between quarters 4 and 1
	Quarter 1	Quarter 2	Quarter 3	Quarter 4		
Total mortality						
Ultra-processed whole grains	1	1.02 (0.99, 1.05)	1.01 (0.98, 1.04)	0.96 (0.93, 0.98)	<0.0001	0.95 (0.92, 0.97)
Sugar sweetened beverages	1	1.03 (1.00, 1.05)	1.07 (1.04, 1.09)	1.11 (1.08, 1.14)	<0.0001	1.11 (1.08, 1.03)
Artificially sweetened beverages	1	1.01 (0.98, 1.03)	1.03 (1.00, 1.06)	1.04 (1.01, 1.06)	0.01	1.03 (1.01, 1.06)
Ultra-processed yogurt	1	1.10 (1.07, 1.13)	1.09 (1.06, 1.12)	1.09 (1.06, 1.12)	<0.001	1.03 (1.02, 1.05)
Ice cream/sherbet	1	1.02 (0.99, 1.05)	1.04 (1.02, 1.07)	1.05 (1.02, 1.08)	0.0003	1.05 (1.02, 1.07)
Dark chocolate bars	1	1.00 (0.97, 1.03)	0.95 (0.92, 0.97)	0.96 (0.94, 0.99)	0.002	0.96 (0.94, 0.99)
Cancer mortality						
Ultra-processed whole grains	1	1.03 (0.98, 1.08)	1.04 (0.99, 1.09)	0.97 (0.92, 1.02)	0.14	0.96 (0.92, 1.01)
Sugar sweetened beverages	1	1.07 (1.02, 1.12)	1.08 (1.03, 1.13)	1.12 (1.07, 1.18)	0.0001	1.09 (1.04, 1.14)
Artificially sweetened beverages	1	1.01 (0.96, 1.05)	1.00 (0.95, 1.04)	0.97 (0.92, 1.02)	0.10	0.96 (0.92, 1.01)
Ultra-processed yogurt	1	1.13 (1.08, 1.19)	1.14 (1.08, 1.21)	1.14 (1.08, 1.20)	<0.0001	1.06 (1.03, 1.10)
Ice cream/sherbet	1	1.03 (0.98, 1.08)	1.01 (0.97, 1.07)	1.02 (0.97, 1.07)	0.53	1.01 (0.97, 1.06)
Dark chocolate bars	1	0.98 (0.94, 1.03)	0.96 (0.92, 1.01)	0.98 (0.94, 1.03)	0.42	0.98 (0.94, 1.03)
Cardiovascular mortality						
Ultra-processed whole grains	1	1.03 (0.97, 1.09)	1.02 (0.96, 1.07)	0.96 (0.91, 1.01)	0.02	0.94 (0.89, 0.99)
Sugar sweetened beverages	1	0.99 (0.94, 1.04)	1.02 (0.97, 1.08)	1.06 (1.01, 1.12)	0.005	1.08 (1.02, 1.13)
Artificially sweetened beverages	1	0.99 (0.94, 1.04)	1.04 (0.99, 1.10)	1.08 (1.02, 1.14)	0.002	1.09 (1.03, 1.15)
Ultra-processed yogurt	1	1.10 (1.04, 1.16)	1.13 (1.06, 1.19)	1.07 (1.01, 1.13)	0.14	1.02 (0.99, 1.05)
Ice cream/sherbet	1	0.99 (0.93, 1.04)	1.02 (0.97, 1.08)	0.95 (0.90, 1.00)	0.03	0.94 (0.90, 0.99)
Dark chocolate bars	1	1.02 (0.97, 1.08)	0.96 (0.91, 1.02)	0.94 (0.89, 0.99)	0.009	0.93 (0.89, 0.98)
Other mortality						
Ultra-processed whole grains	1	1.01 (0.97, 1.05)	1.00 (0.96, 1.04)	0.96 (0.92, 0.99)	0.004	0.94 (0.91, 0.98)
Sugar sweetened beverages	1	1.02 (0.98, 1.06)	1.08 (1.04, 1.12)	1.13 (1.09, 1.17)	<0.0001	1.13 (1.09, 1.17)
Artificially sweetened beverages	1	1.02 (0.98, 1.05)	1.04 (1.00, 1.08)	1.06 (1.02, 1.10)	0.006	1.06 (1.02, 1.10)
Ultra-processed yogurt	1	1.11 (1.07, 1.15)	1.06 (1.02, 1.10)	1.09 (1.05, 1.14)	0.004	1.03 (1.01, 1.05)
Ice cream/sherbet	1	1.03 (0.99, 1.07)	1.07 (1.03, 1.12)	1.12 (1.08, 1.16)	<0.0001	1.12 (1.08, 1.17)

Dark chocolate bars	1	1.00 (0.96, 1.03)	0.93 (0.90, 0.97)	0.96 (0.92, 0.99)	0.03	0.96 (0.93, 1.00)
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^a The quarter-specific medians (serving/day) for each category: ultra-processed whole grains, 0.3, 0.7, 1.0, 1.8; sugar sweetened beverages, 0.01, 0.06, 0.2, 0.6; artificially sweetened beverages, 0.01, 0.08, 0.4, 1.3; ultra-processed yogurt, 0.009, 0.01, 0.01, 0.08; ice cream/sherbet, 0.05, 0.1, 0.2, 0.4; dark chocolate bars, 0, 0.04, 0.07, 0.22.

Supplementary Table E. Hazard ratios and 95% confidence intervals for mortality according to quarters of ultra-processed food consumption (serving/day) in each cohort

	Energy-adjusted ultra-processed food consumption (serving/day)				<i>P</i> for trend	Per difference in medians between quarters 4 and 1
	Quarter 1	Quarter 2	Quarter 3	Quarter 4		
HPFS						
Median intake (IQR)	3.2 (1.1)	4.6 (0.7)	5.9 (0.7)	8.0 (2.0)		
Total mortality						
Number of cases	4491	4423	4572	4519		
Model 1 ^a	1	1.04 (0.99, 1.08)	1.07 (1.02, 1.11)	1.18 (1.13, 1.23)	<0.0001	1.18 (1.13, 1.23)
Model 2 ^b	1	1.07 (1.02, 1.11)	1.07 (1.03, 1.12)	1.07 (1.02, 1.12)	0.007	1.06 (1.02, 1.11)
Cancer mortality						
Number of cases	1317	1265	1 375	1347		
Model 1 ^a	1	1.01 (0.94, 1.10)	1.10 (1.02, 1.19)	1.15 (1.06, 1.24)	<0.0001	1.17 (1.08, 1.26)
Model 2 ^b	1	1.03 (0.95, 1.12)	1.09 (1.01, 1.17)	1.04 (0.96, 1.13)	0.26	1.05 (0.97, 1.13)
Cardiovascular mortality						
Number of cases	1284	1328	1289	1315		
Model 1 ^a	1	1.09 (1.00, 1.18)	1.05 (0.97, 1.14)	1.22 (1.13, 1.32)	<0.0001	1.21 (1.12, 1.31)
Model 2 ^b	1	1.09 (1.01, 1.18)	1.02 (0.94, 1.11)	1.06 (0.98, 1.15)	0.37	1.04 (0.96, 1.13)
Other mortality						
Number of cases	1890	1830	1908	1857		
Model 1 ^a	1	1.02 (0.95, 1.09)	1.05 (0.99, 1.13)	1.16 (1.09, 1.24)	<0.0001	1.17 (1.10, 1.25)
Model 2 ^b	1	1.07 (1.00, 1.15)	1.09 (1.02, 1.17)	1.09 (1.02, 1.17)	0.01	1.09 (1.02, 1.17)
Respiratory						
Number of cases	339	328	382	380		
Model 1 ^a	1	1.01 (0.86, 1.18)	1.15 (0.99, 1.33)	1.33 (1.15, 1.55)	<0.0001	1.38 (1.18, 1.60)
Model 2 ^b	1	1.00 (0.86, 1.18)	1.13 (0.97, 1.32)	1.07 (0.91, 1.25)	0.24	1.10 (0.94, 1.29)
Neurodegenerative						
Number of cases	392	401	381	344		
Model 1 ^a	1	1.08 (0.94, 1.25)	1.03 (0.89, 1.20)	1.11 (0.96, 1.29)	0.27	1.09 (0.94, 1.27)
Model 2 ^b	1	1.20 (1.03, 1.39)	1.11 (0.95, 1.29)	1.16 (0.99, 1.35)	0.14	1.12 (0.96, 1.31)
NHS						

Median intake (IQR)	3.0 (0.9)	4.2 (0.5)	5.3 (0.6)	7.1 (1.7)		
Total mortality						
Number of cases	7371	7259	7596	7962		
Model 1 ^a	1	1.07 (1.03, 1.10)	1.15 (1.11, 1.19)	1.24 (1.20, 1.28)	<0.0001	1.25 (1.21, 1.29)
Model 2 ^b	1	1.03 (1.00, 1.07)	1.07 (1.04, 1.11)	1.03 (1.00, 1.06)	0.08	1.03 (1.00, 1.06)
Cancer mortality						
Number of cases	2110	1995	2101	2047		
Model 1 ^a	1	1.00 (0.94, 1.07)	1.09 (1.02, 1.16)	1.07 (1.01, 1.14)	0.004	1.09 (1.03, 1.16)
Model 2 ^b	1	0.98 (0.92, 1.04)	1.02 (0.96, 1.08)	0.91 (0.85, 0.97)	0.08	0.96 (0.91, 1.00)
Cardiovascular mortality						
Number of cases	1533	1445	1510	1712		
Model 1 ^a	1	1.05 (0.97, 1.13)	1.13 (1.05, 1.22)	1.33 (1.24, 1.42)	<0.0001	1.35 (1.26, 1.45)
Model 2 ^b	1	0.99 (0.92, 1.06)	1.01 (0.94, 1.08)	1.04 (0.97, 1.12)	0.20	1.05 (0.98, 1.13)
Other mortality						
Number of cases	3728	3819	3985	4203		
Model 1 ^a	1	1.11 (1.06, 1.16)	1.19 (1.14, 1.24)	1.30 (1.24, 1.36)	<0.0001	1.31 (1.25, 1.37)
Model 2 ^b	1	1.08 (1.03, 1.13)	1.13 (1.08, 1.18)	1.10 (1.05, 1.15)	0.0002	1.09 (1.04, 1.14)
Respiratory						
Number of cases	541	594	629	733		
Model 1 ^a	1	1.21 (1.07, 1.36)	1.31 (1.16, 1.47)	1.58 (1.42, 1.77)	<0.0001	1.59 (1.42, 1.78)
Model 2 ^b	1	1.08 (0.96, 1.22)	1.09 (0.97, 1.23)	1.11 (0.99, 1.25)	0.11	1.10 (0.98, 1.23)
Neurodegenerative						
Number of cases	1241	1252	1194	1138		
Model 1 ^a	1	1.11 (1.02, 1.20)	1.09 (1.01, 1.18)	1.09 (1.01, 1.18)	0.07	1.08 (0.99, 1.17)
Model 2 ^b	1	1.16 (1.07, 1.26)	1.15 (1.06, 1.25)	1.07 (0.99, 1.17)	0.23	1.05 (0.97, 1.14)

Abbreviation: HPFS, Health Professionals Follow-up Study; IQR, interquartile range; NHS, Nurses' Health Study

^a Stratified by age (months) and questionnaire cycle (two-year interval) and adjusted for total energy intake.

^b Further adjusted for categorical covariates including race, marital status, physical activity, body mass index, smoking status and packyears, alcohol consumption, physical examination performed for screening purposes, family history of diabetes mellitus, myocardial infarction, or cancer; for women, also menopausal status and hormone use.

Supplementary Table F. Multivariable hazard ratios and 95% confidence intervals for mortality according to quarters of ultra-processed food consumption (serving/day) in the sensitivity analyses

	Energy-adjusted ultra-processed food consumption (serving/day)				P for trend	Per difference in medians between quarter 4 and 1
	Quarter 1	Quarter 2	Quarter 3	Quarter 4		
Stop updating diet after diagnosis of cardiovascular diseases (myocardial infarction, stroke, angina, coronary artery bypass graft), cancer, and diabetes						
Total mortality	1	1.00 (0.97, 1.02)	1.01 (0.98, 1.03)	0.99 (0.96, 1.01)	0.37	0.99 (0.96, 1.01)
Cancer mortality	1	0.97 (0.92, 1.02)	0.96 (0.92, 1.01)	0.92 (0.88, 0.97)	0.001	0.92 (0.88, 0.97)
Cardiovascular mortality	1	0.97 (0.92, 1.03)	0.95 (0.90, 1.00)	0.96 (0.91, 1.02)	0.16	0.96 (0.91, 1.02)
Other mortality	1	1.03 (0.99, 1.07)	1.07 (1.03, 1.11)	1.04 (1.00, 1.08)	0.04	1.04 (1.00, 1.08)
Respiratory mortality	1	0.99 (0.90, 1.09)	1.04 (0.95, 1.15)	1.05 (0.96, 1.15)	0.19	1.06 (0.97, 1.16)
Neurodegenerative mortality	1	1.11 (1.03, 1.19)	1.09 (1.02, 1.17)	1.06 (0.99, 1.14)	0.20	1.05 (0.97, 1.13)
8-year lag between UPF measurement and outcome risk						
Total mortality	1	1.01 (0.98, 1.03)	1.04 (1.01, 1.07)	1.02 (0.99, 1.05)	0.10	1.02 (1.00, 1.05)
Cancer mortality	1	0.96 (0.91, 1.01)	1.01 (0.96, 1.06)	0.94 (0.89, 0.99)	0.05	0.95 (0.91, 1.00)
Cardiovascular mortality	1	1.02 (0.97, 1.08)	1.01 (0.96, 1.07)	1.04 (0.98, 1.10)	0.22	1.03 (0.98, 1.09)
Other mortality	1	1.03 (0.99, 1.07)	1.07 (1.03, 1.12)	1.06 (1.02, 1.10)	0.002	1.06 (1.02, 1.10)
Respiratory mortality	1	1.02 (0.93, 1.12)	1.08 (0.98, 1.18)	1.05 (0.95, 1.15)	0.28	1.05 (0.96, 1.15)
Neurodegenerative mortality	1	1.08 (1.01, 1.16)	1.09 (1.02, 1.17)	1.06 (0.99, 1.14)	0.14	1.06 (0.98, 1.14)
Adjust for smoking status (never, former, current) rather than smoking status and packyears						
Total mortality	1	1.06 (1.03, 1.09)	1.09 (1.07, 1.12)	1.09 (1.07, 1.12)	<0.0001	1.09 (1.06, 1.12)
Cancer mortality	1	1.02 (0.97, 1.07)	1.07 (1.02, 1.13)	1.01 (0.96, 1.06)	0.44	1.02 (0.97, 1.07)
Cardiovascular mortality	1	1.05 (0.99, 1.10)	1.03 (0.97, 1.08)	1.09 (1.03, 1.15)	0.004	1.08 (1.02, 1.14)
Other mortality	1	1.10 (1.05, 1.14)	1.14 (1.10, 1.18)	1.14 (1.10, 1.19)	<0.0001	1.14 (1.10, 1.18)
Respiratory mortality	1	1.12 (1.02, 1.23)	1.19 (1.08, 1.31)	1.27 (1.15, 1.39)	<0.0001	1.27 (1.16, 1.39)
Neurodegenerative mortality	1	1.17 (1.09, 1.25)	1.14 (1.06, 1.23)	1.10 (1.02, 1.18)	0.008	1.10 (1.03, 1.19)
Not adjust for BMI						

Total mortality	1	1.04 (1.01, 1.07)	1.07 (1.04, 1.10)	1.05 (1.02, 1.08)	0.0007	1.05 (1.02, 1.07)
Cancer mortality	1	1.00 (0.95, 1.04)	1.04 (0.99, 1.09)	0.96 (0.91, 1.00)	0.12	0.96 (0.92, 1.01)
Cardiovascular mortality	1	1.05 (0.99, 1.10)	1.04 (0.98, 1.10)	1.09 (1.04, 1.15)	0.002	1.09 (1.03, 1.15)
Other mortality	1	1.07 (1.03, 1.11)	1.10 (1.06, 1.14)	1.08 (1.04, 1.12)	<0.0001	1.08 (1.04, 1.12)
Respiratory mortality	1	1.02 (0.93, 1.12)	1.06 (0.96, 1.16)	1.04 (0.95, 1.14)	0.36	1.04 (0.95, 1.14)
Neurodegenerative mortality	1	1.14 (1.06, 1.22)	1.10 (1.03, 1.19)	1.04 (0.97, 1.12)	0.59	1.02 (0.95, 1.10)
Additionally adjust for AHEI						
Total mortality	1	1.03 (1.00, 1.05)	1.05 (1.02, 1.07)	1.01 (0.99, 1.04)	0.54	1.01 (0.98, 1.04)
Cancer mortality	1	1.00 (0.95, 1.05)	1.04 (0.99, 1.10)	0.95 (0.90, 1.00)	0.07	0.96 (0.91, 1.00)
Cardiovascular mortality	1	1.02 (0.97, 1.08)	1.00 (0.94, 1.05)	1.03 (0.97, 1.09)	0.44	1.02 (0.97, 1.08)
Other mortality	1	1.05 (1.01, 1.09)	1.07 (1.03, 1.12)	1.04 (1.00, 1.08)	0.08	1.04 (1.00, 1.08)
Respiratory mortality	1	1.00 (0.91, 1.10)	1.04 (0.94, 1.14)	1.00 (0.91, 1.10)	0.93	1.00 (0.91, 1.11)
Neurodegenerative mortality	1	1.15 (1.07, 1.23)	1.12 (1.04, 1.20)	1.07 (0.99, 1.15)	0.29	1.04 (0.96, 1.13)
Include whole grain in the total UPF definition						
Total mortality	1	1.03 (1.00, 1.06)	1.05 (1.02, 1.07)	1.01 (0.99, 1.04)	0.48	1.01 (0.98, 1.04)
Cancer mortality	1	0.98 (0.94, 1.03)	1.02 (0.97, 1.07)	0.94 (0.89, 0.99)	0.02	0.94 (0.90, 0.99)
Cardiovascular mortality	1	1.05 (0.99, 1.11)	1.02 (0.97, 1.08)	1.02 (0.97, 1.08)	0.67	1.01 (0.96, 1.07)
Other mortality	1	1.05 (1.01, 1.09)	1.08 (1.04, 1.12)	1.05 (1.01, 1.09)	0.01	1.05 (1.01, 1.09)
Respiratory mortality	1	1.10 (0.99, 1.21)	1.02 (0.93, 1.12)	1.03 (0.94, 1.13)	0.93	1.00 (0.92, 1.10)
Neurodegenerative mortality	1	1.15 (1.07, 1.24)	1.17 (1.09, 1.26)	1.12 (1.04, 1.20)	0.009	1.10 (1.03, 1.19)
Include distilled alcohol in the total UPF definition						
Total mortality	1	1.06 (1.03, 1.09)	1.09 (1.06, 1.12)	1.06 (1.03, 1.09)	<0.0001	1.06 (1.03, 1.08)
Cancer mortality	1	1.01 (0.96, 1.07)	1.05 (1.00, 1.10)	0.96 (0.91, 1.01)	0.09	0.96 (0.91, 1.01)
Cardiovascular mortality	1	1.09 (1.03, 1.15)	1.06 (1.00, 1.12)	1.08 (1.02, 1.14)	0.03	1.06 (1.01, 1.12)
Other mortality	1	1.07 (1.03, 1.11)	1.13 (1.09, 1.17)	1.12 (1.08, 1.16)	<0.0001	1.12 (1.08, 1.16)
Respiratory mortality	1	1.06 (0.96, 1.17)	1.09 (0.99, 1.20)	1.12 (1.02, 1.23)	0.02	1.11 (1.02, 1.22)
Neurodegenerative mortality	1	1.11 (1.03, 1.19)	1.11 (1.03, 1.19)	1.10 (1.03, 1.19)	0.02	1.09 (1.02, 1.17)
Include both whole grain and distilled alcohol (i.e., use the standard UPF definition)						
Total mortality	1	1.04 (1.01, 1.07)	1.06 (1.04, 1.09)	1.03 (1.00, 1.06)	0.06	1.03 (1.00, 1.05)
Cancer mortality	1	1.00 (0.95, 1.05)	1.02 (0.97, 1.07)	0.94 (0.90, 0.99)	0.09	0.94 (0.90, 0.99)
Cardiovascular mortality	1	1.06 (1.00, 1.12)	1.04 (0.98, 1.10)	1.04 (0.99, 1.10)	0.30	1.03 (0.98, 1.08)

Other mortality	1	1.05 (1.01, 1.09)	1.11 (1.07, 1.15)	1.08 (1.04, 1.12)	<0.0001	1.08 (1.04, 1.12)
Respiratory mortality	1	1.06 (0.96, 1.17)	1.09 (0.99, 1.20)	1.15 (0.96, 1.16)	0.35	1.05 (0.95, 1.14)
Neurodegenerative mortality	1	1.12 (1.04, 1.20)	1.14 (1.06, 1.23)	1.11 (1.03, 1.20)	0.008	1.10 (1.03, 1.19)

Abbreviation: AHEI, alternative Healthy Eating Index; BMI, body mass index; UPF, ultra-processed food

Supplementary Table G. Multivariable hazard ratios and 95% confidence intervals for total mortality associated with ultra-processed food consumption (serving/day) stratified by lifestyle factors

Risk factor	Number of cases	Energy-adjusted ultra-processed food consumption (serving/day)	
		Per difference in medians between quarter 4 and 1	<i>P</i> for interaction
Body mass index (kg/m²)			
<25	24 313	1.05 (1.01, 1.09)	0.06
25-29.9	17 329	1.02 (0.97, 1.06)	
≥30	6551	1.04 (0.96, 1.12)	
Physical activity (MET-hr/week)			
<7.5	14 885	0.98 (0.93, 1.03)	0.14
7.5-14.9	11 590	1.04 (0.98, 1.10)	
≥15	21 718	1.04 (1.00, 1.09)	
Alcohol (grams/day)			
Never	9981	1.06 (1.00, 1.12)	0.005
0.1-13.9	28 334	1.05 (1.02, 1.09)	
≥14	9878	0.96 (0.90, 1.02)	
Smoking status			
Never	17 867	1.05 (1.00, 1.10)	<0.0001
Former	24 353	1.03 (0.99, 1.07)	
Current	4240	0.91 (0.83, 1.01)	

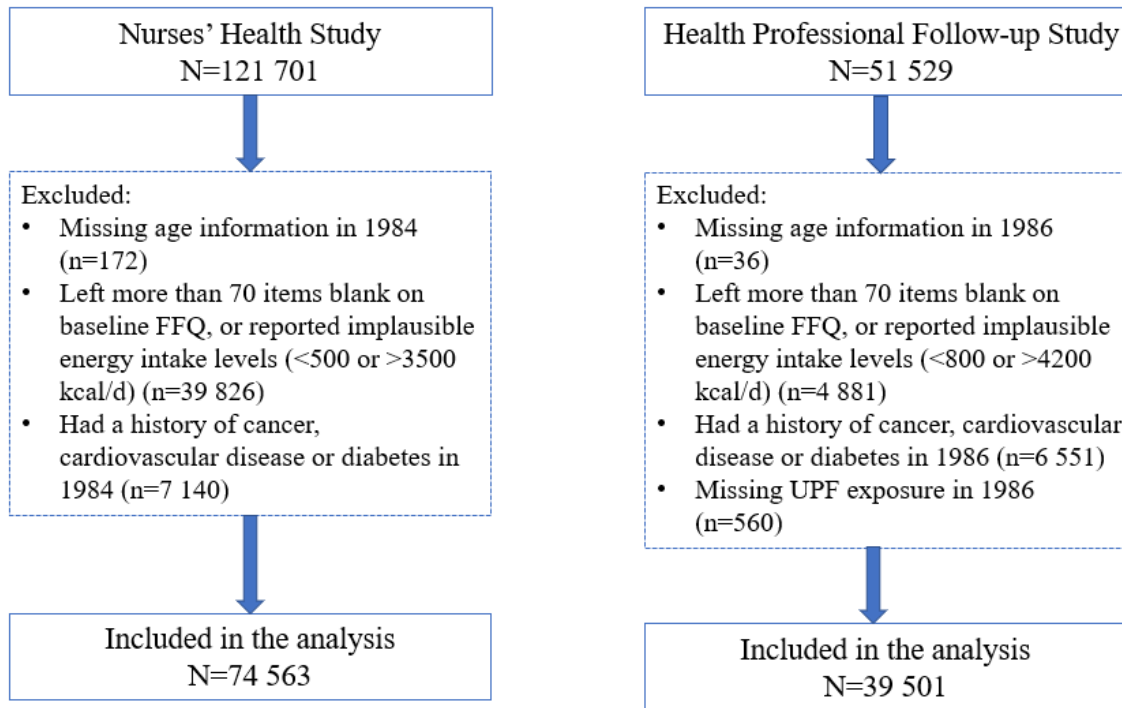
Supplementary Table H. Hazard ratios and 95% confidence intervals for mortality according to quarters of ultra-processed food consumption (% of energy)

	Ultra-processed food consumption (% of energy)				P for trend	Per 10% increment
	Quarter 1	Quarter 2	Quarter 3	Quarter 4		
Median intake (IQR)	16.11 (5.09)	23.01 (2.85)	28.73 (3.09)	36.89 (6.85)		
Total mortality						
Model 1 ^a	1	1.07 (1.04, 1.09)	1.18 (1.15, 1.21)	1.32 (1.28, 1.35)	<0.0001	1.13 (1.12, 1.15)
Model 2 ^b	1	1.02 (1.00, 1.05)	1.08 (1.05, 1.11)	1.06 (1.03, 1.09)	<0.0001	1.03 (1.02, 1.04)
Cancer mortality						
Model 1 ^a	1	1.04 (0.99, 1.09)	1.13 (1.08, 1.19)	1.22 (1.16, 1.28)	<0.0001	1.09 (1.07, 1.11)
Model 2 ^b	1	1.00 (0.95, 1.05)	1.03 (0.98, 1.08)	0.98 (0.94, 1.03)	0.67	1.00 (0.98, 1.02)
Cardiovascular mortality						
Model 1 ^a	1	1.05 (1.00, 1.11)	1.15 (1.10, 1.22)	1.23 (1.17, 1.29)	<0.0001	1.10 (1.08, 1.12)
Model 2 ^b	1	0.99 (0.94, 1.05)	1.03 (0.98, 1.09)	0.97 (0.92, 1.02)	0.56	0.99 (0.97, 1.02)
Other mortality						
Model 1 ^a	1	1.08 (1.05, 1.13)	1.23 (1.18, 1.27)	1.42 (1.37, 1.48)	<0.0001	1.18 (1.16, 1.20)
Model 2 ^b	1	1.05 (1.01, 1.09)	1.13 (1.09, 1.18)	1.15 (1.11, 1.19)	<0.0001	1.07 (1.05, 1.09)
Respiratory						
Model 1 ^a	1	1.12 (1.02, 1.23)	1.35 (1.23, 1.48)	1.90 (1.74, 2.08)	<0.0001	1.33 (1.29, 1.38)
Model 2 ^b	1	1.01 (0.92, 1.11)	1.12 (1.02, 1.23)	1.28 (1.17, 1.41)	<0.0001	1.12 (1.08, 1.16)
Neurodegenerative						
Model 1 ^a	1	1.09 (1.02, 1.17)	1.15 (1.07, 1.23)	1.28 (1.19, 1.37)	<0.0001	1.12 (1.09, 1.15)
Model 2 ^b	1	1.10 (1.02, 1.18)	1.13 (1.05, 1.21)	1.13 (1.05, 1.22)	<0.0001	1.07 (1.03, 1.10)

^a Stratified by age (months), questionnaire cycle (two-year interval), and cohort.

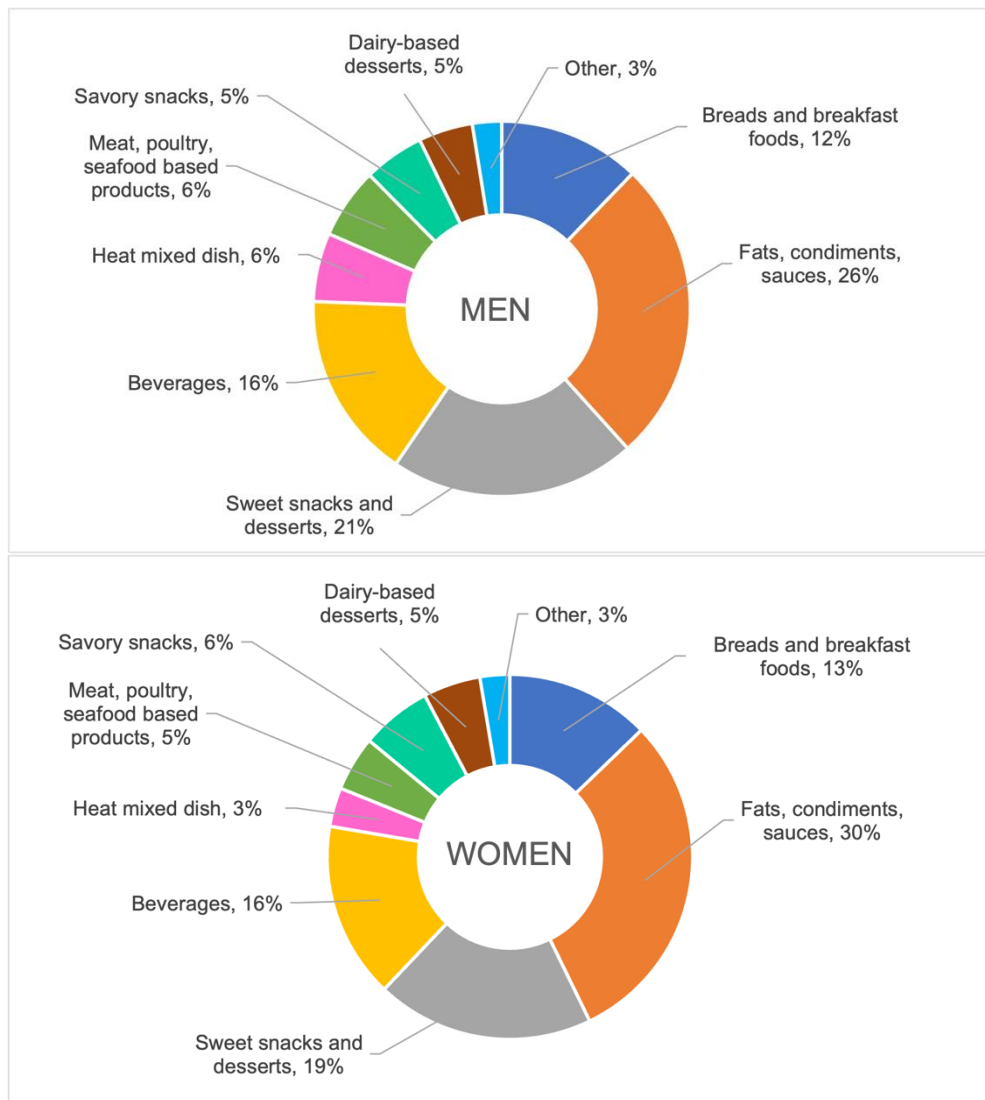
^b Further adjusted for categorical covariates including race, marital status, physical activity, body mass index, smoking status and packyears, alcohol consumption, physical examination performed for screening purposes, family history of diabetes mellitus, myocardial infarction, or cancer; for women, also menopausal status and hormone use.

Supplementary Figure A. Flow chart of study participants

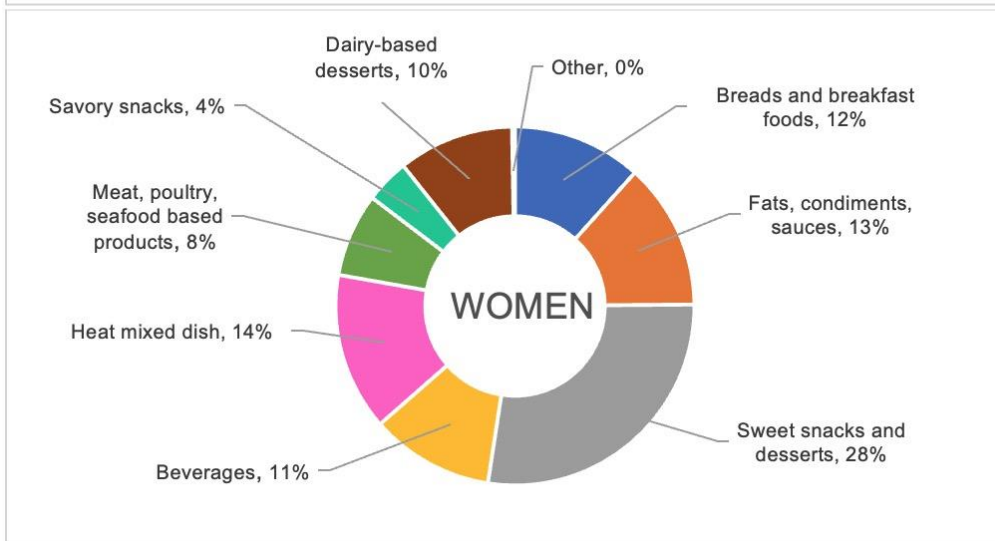
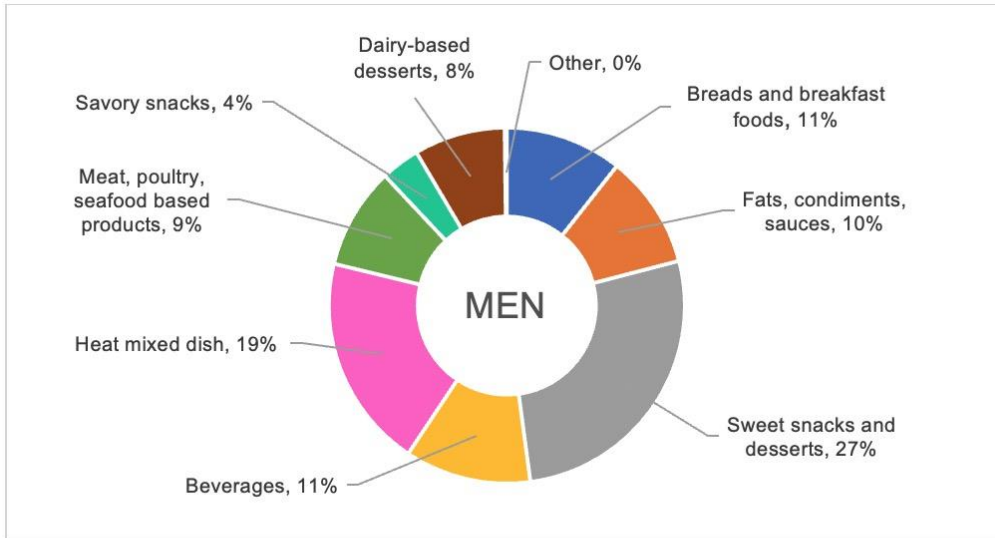


Supplementary Figure B. The relative contribution of each subgroup to total ultra-processed food consumption

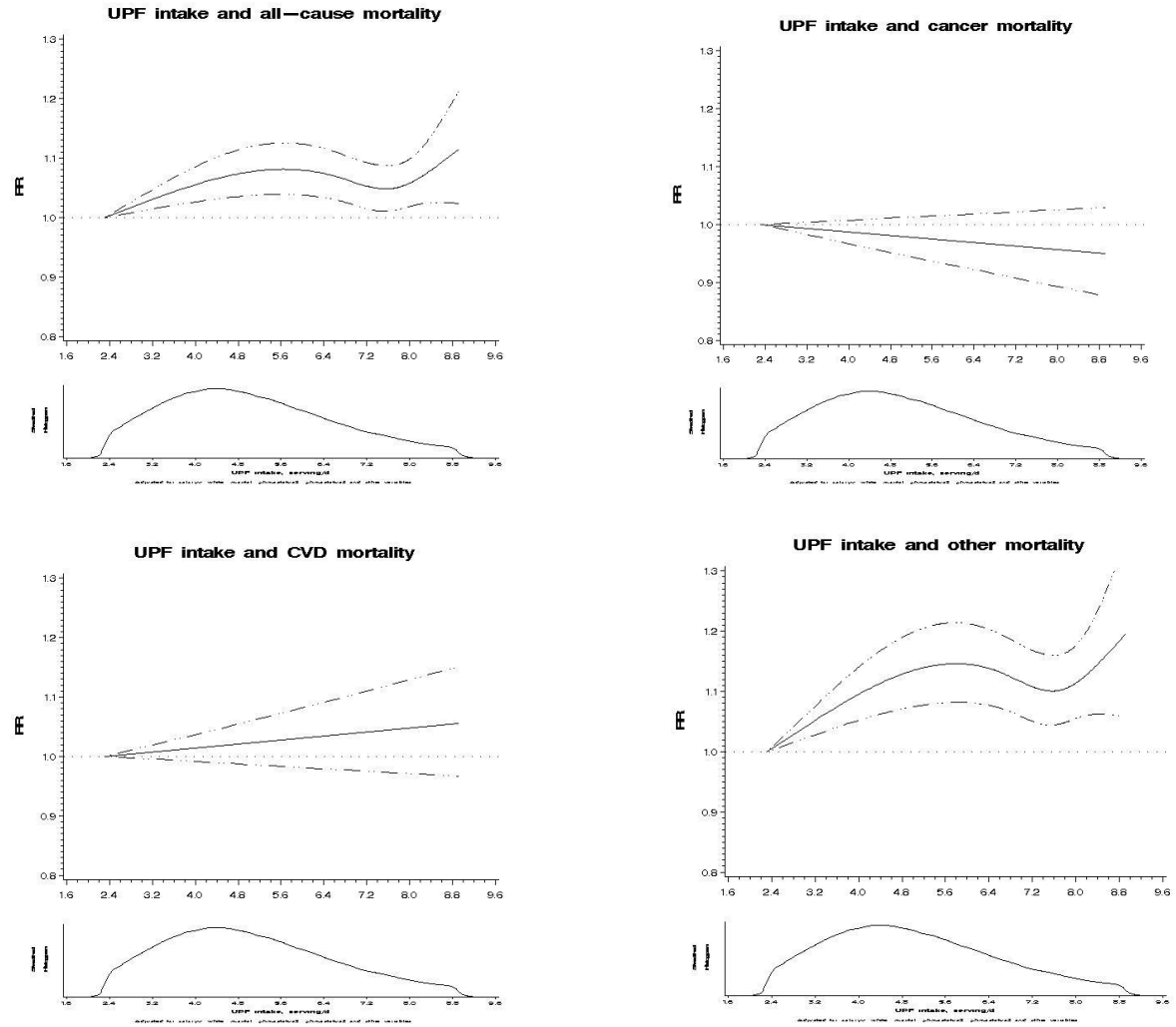
(A) Using servings per day as measurement unit



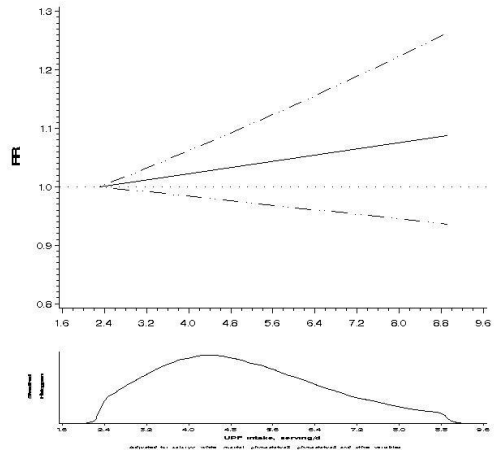
(B) Using % of energy as measurement unit



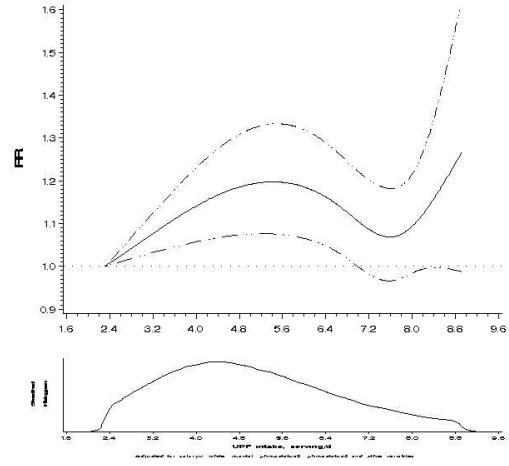
Supplementary Figure C. Restricted spline analysis of ultra-processed food consumption (serving/day) and mortality



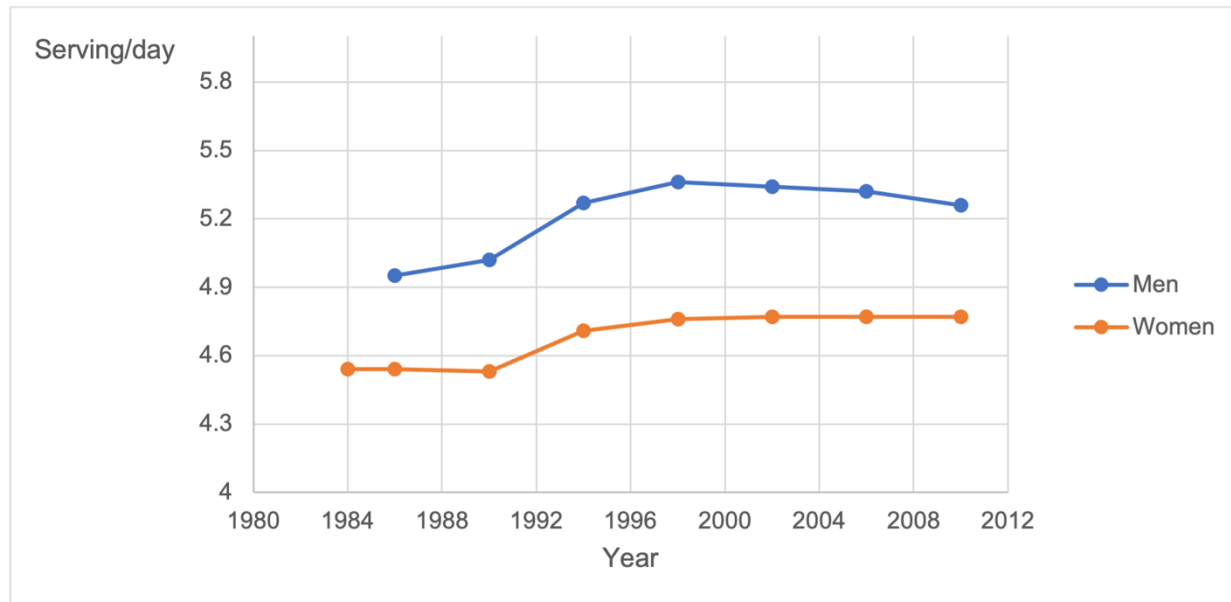
UPF intake and respiratory mortality



UPF intake and neurodegenerative mortality



Supplementary Figure D. The trend of energy-adjusted ultra-processed food consumption (serving/day) by year



Supplementary Figure E. The trend of energy-adjusted consumption of ultra-processed food subgroups (serving/day) by year

