Ultraprocessed food consumption and risk of overweight and obesity: the University of Navarra Follow-Up (SUN) cohort study[1,2]

*Raquel de Deus Mendonça,[3,4,6] Adriano Marçal Pimenta,[3,5] Alfredo Gea,[3,7,8] Carmen de la Fuente-Arrillaga,[3,7,8] Miguel Angel Martinez-Gonzalez,[3,7–9] Aline Cristine Souza Lopes,[4] and Maira Bes-Rastrollo[3,7,8]**

[3]University of Navarra, Department of Preventive Medicine and Public Health, Pamplona, Spain; Departments of [4]Nutrition and [5]Maternal-Child Nursing and Public Health, School of Nursing, Federal University of Minas Gerais, Belo Horizonte, Brazil; [6]CAPES Coordination for the Improvement of Higher Education Personnel Foundation, Ministry of Education of Brazil, Brasília, Brazil; [7]Navarra Health Research Institute, Pamplona, Spain; [8]Biomedical Research Center Network in Physiopathology of Obesity and Nutrition, Carlos III Health Institute, Madrid, Spain; and [9]Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA

ABSTRACT

Background: Ultraprocessed food consumption has increased in the past decade. Evidence suggests a positive association between ultraprocessed food consumption and the incidence of overweight and obesity. However, few prospective studies to our knowledge have investigated this potential relation in adults.

Objective: We evaluated the association between ultraprocessed food consumption and the risk of overweight and obesity in a prospective Spanish cohort, the SUN (University of Navarra Follow-Up) study.

Design: We included 8451 middle-aged Spanish university graduates who were initially not overweight or obese and followed up for a median of 8.9 y. The consumption of ultraprocessed foods (defined as food and drink products ready to eat, drink, or heat and made predominantly or entirely from processed items extracted or refined from whole foods or synthesized in the laboratory) was assessed with the use of a validated semiquantitative 136-item food-frequency questionnaire. Cox proportional hazards models were used to estimate adjusted HRs and 95% CIs for incident overweight and obesity.

Results: A total of 1939 incident cases of overweight and obesity were identified during follow-up. After adjustment for potential confounders, participants in the highest quartile of ultraprocessed food consumption were at a higher risk of developing overweight or obesity (adjusted HR: 1.26; 95% CI: 1.10, 1.45; *P*-trend = 0.001) than those in the lowest quartile of consumption.

Conclusions: Ultraprocessed food consumption was associated with a higher risk of overweight and obesity in a prospective cohort of Spanish middle-aged adult university graduates. Further longitudinal studies are needed to confirm our results. This trial was registered at clinicaltrials.gov as NCT02669602. *Am J Clin Nutr* 2016;104:1433–40.

Keywords: obesity, overweight, ultra-processed food, food-processing industry, SUN cohort, prospective studies

INTRODUCTION

Obesity is a worldwide problem with increasing prevalence. In 2014, more than half a billion adults were obese, and 39% were overweight. In the Americas, ∼30% of women and 25% of men were obese, and in the Eastern Mediterranean ∼25% of women and 15% of men were obese (1).

Changes in the food system continuously promote obesity. There is now a greater availability of ready-to-eat or -heat foods known as ultraprocessed foods, which are products that have little, if any, whole foods and are manufactured with substances extracted from foods or synthesized in laboratories (dyes, flavorings, and other additives) (2). They have high amounts of fat, sugar, and salt and a high energy density and low fiber content; they are extremely palatable foods that are aggressively advertised (3) and contain a large diversity of chemical additives. Examples of ultraprocessed foods include breakfast cereals, reconstituted meat products, soft drinks, and ready-to-eat foodstuffs (2).

Several prospective studies have been carried out to assess the relation between dietary components and obesity. An analysis of 3 American cohorts, the Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-Up Study, showed that the consumption of foodstuffs such as sweets, desserts, processed meats, fries, and sugar-sweetened beverages were strongly associated with weight gain in US adults (4). However, the relation between the consumption of foods aggregated according to their degree of processing (i.e., ultraprocessed foods) and excess weight has only recently been analyzed.

A cross-sectional times series study in 15 Latin American countries revealed an association between sales of ultraprocessed foods and changes in body weight in 12 countries from 2000 to 2009 (5). Cross-sectional studies have demonstrated an association between the consumption of these foods and the risk of metabolic syndrome in adolescents (6) and obesity in adolescents

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[2] Supplemental Table 1 is available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

*To whom correspondence should be addressed. E-mail: mbes@unav.es.

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and adults (7, 8). A study of children aged 3–8 y in a low-income community in Brazil showed that ultraprocessed food consumption was an important predictor of the increase in total cholesterol and LDL cholesterol (9). On the other hand, a study with data from the 2008–2012 United Kingdom National Diet and Nutrition Survey showed no association between ultraprocessed food consumption and body weight. However, diets with smaller quantities of ultraprocessed foods have better nutritional quality (10).

Studies have shown an association between specific types of ultraprocessed foods, such as soft drinks, and being overweight or obese. However, no prospective cohort study to our knowledge has been performed to evaluate the association between all ultraprocessed foods as a group and the incidence of overweight and obesity in adults. Therefore, in this study (NCT02669602), we evaluated the association of ultraprocessed food consumption with the incidence of overweight and obesity in a Mediterranean cohort with a prolonged follow-up.

METHODS

Study population

The SUN (University of Navarra Follow-Up) Project is a dynamic and multipurpose prospective cohort study with permanently open recruitment conducted in Spain among university graduates since December 1999. The participants are followed up biennially with the use of questionnaires distributed by post or electronic mail. Details of its design have been published elsewhere (11, 12).

Up to March 2012, the SUN data set included 21,291 participants who had answered the baseline questionnaire. In this study, we excluded those classified as overweight or obese [BMI (in kg/m^2) ≥25] at baseline (*n* = 6340), individuals who reported total energy intake values outside of predefined limits [low: <3347 kJ/d or <800 kcal/d in men and <2092 kJ/d or <500 kcal/d in women; high: >16,736 kJ/d or >4000 kcal/d in men and >14,644 kJ/d or >3500 kcal/d in women (*n* = 1713)] (13), women who were pregnant at baseline or became pregnant during the follow-up period (*n* = 2739), and individuals who reported a previously diagnosed chronic disease at baseline (e.g., diabetes, cancer, cardiovascular disease) (*n* = 618). In addition, we excluded participants with a weight change >10 kg in the 5 y preceding entry into the study to reduce potential sources of confounding by other causes of weight changes (*n* = 260). Among the remaining participants, 1106 subjects were lost to follow-up, and 64 participants had missing values in ≥1 variable of interest. After these exclusions, a total of 8451 participants were included in the final analyses (**Figure 1**). The retention rate of the study was ∼89%.

This study was conducted according to Declaration of Helsinki guidelines, and all procedures involving human subjects were approved by the University of Navarra institutional review board. Voluntary completion of the baseline self-administrated questionnaire was considered to imply informed consent.

Exposure assessment: ultraprocessed food consumption

Dietary exposures were assessed at baseline through a self-administered 136-item semiquantitative food-frequency questionnaire (FFQ) that was previously validated in Spain (14, 15). Frequencies of consumption were measured in 9 categories (ranging from never or almost never to >6 servings/d), and the FFQ included a typical portion size for each item. Daily food consumption was estimated by multiplying the portion size by the consumption frequency for each food item.

The foods were classified according to *NOVA* (2) based on the extent and purpose of applied food processing. There are 4 groups in this classification scheme. The first group includes foods that are fresh or processed in ways that did not add substances such as salt, sugar, oils, or fats and infrequently contain additives. Processes used are aimed to extend life, allow storage for long use, and facilitate or diversify preparation (freezing, drying, and pasteurization). Examples are fruits and vegetables, grains (cereals), flours, nuts and seeds, fresh and pasteurized milk, natural yogurt with no added sugar or artificial sweeteners, meat and fish, tea, coffee, drinking water, spices, and herbs. The second group contains processed culinary ingredients. These are substances obtained from the first group or from nature and may contain additives to preserve the original properties. Examples are salt, sugar, honey, vegetable oils, butter, lard, and vinegar. The third group is processed food made with the addition of substances such as salt, sugar, or oil and the use of processes such as smoking, curing, or fermentation. Examples are canned or bottled vegetables and legumes, fruits in syrup, canned fish, cheeses, freshly made bread, and salted or sugared nuts and seeds. The fourth group is ultraprocessed food 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. Examples include carbonated drinks, sausages, biscuits (cookies), candy (confectionery), fruit yogurts, instant packaged soups and noodles, sweet or savory packaged snacks, and sugared milk and fruit drinks (2). It is this fourth group that is the main subject of this study. **Supplemental Table 1** describes the classification of FFQ foods according to NOVA. The frequency of ultraprocessed food consumption was estimated with the use of the sum of the food items from the fourth group in the FFQ (total of 33 items). The sample was divided into quartiles according to total consumption (servings/d).

Outcome assessment

Self-reported weight and height were validated with a previous study (16). The outcome used the incidence of overweight and obesity (BMI ≥25) during follow-up and was defined as the first time participants reached a BMI of 25 during follow-up.

Assessment of other variables

The baseline questionnaire also included questions relating to the following variables: sex, age, marital status, educational status, smoking status, physical activity, television watching, siesta sleep, diet and dietary habits, and snacking between main meals. Physical activity was evaluated with the use of a validated 17-item questionnaire (17). Total energy, macronutrient, fiber, and alcohol intake and fruit, vegetable, fast-food, fried-food, processed meat, nonprocessed meat, and sugar-sweetened beverage consumption was assessed with the use of the FFQ (15). Nutrient intake scores were computed with the use of a computer program developed specifically by our dietitians for this purpose. Adherence to the Mediterranean dietary pattern was evaluated with the use of a well-known score (18).

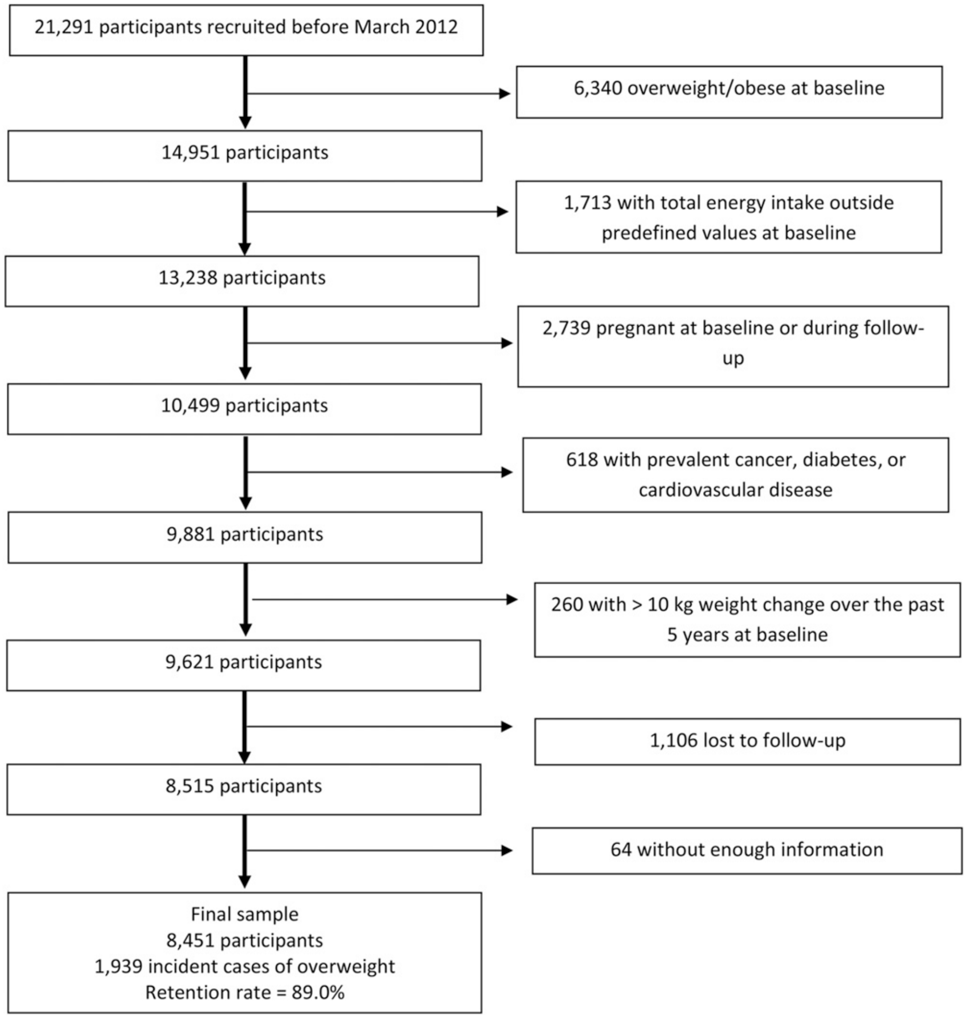

FIGURE 1 Flowchart of participants.

Statistical analyses

Differences in baseline characteristics of participants according to ultraprocessed food consumption quartiles were evaluated with ANOVA and adjusted for sex and age. To evaluate the relation between ultraprocessed food consumption at baseline and the subsequent risk of the development of overweight and obesity during follow-up, we used Cox proportional hazards models, and to estimate HRs and 95% CIs we used the lowest quartile as the reference category.

The follow-up period was defined as the interval between the date of recruitment and date of the return of the follow-up questionnaire in which the participant was classified as overweight or obese for the first time (for incident cases). The date of death or of the last questionnaire was used for noncases.

Tests for linear trends were conducted by assigning medians of ultraprocessed food consumption to each category and treating this variable as a continuous variable in the respective Cox regression model. We fitted a first model without any adjustment (crude), a second model adjusted for age and sex, and a third multivariable-adjusted model adjusted for age, sex, marital status, educational status, baseline BMI, physical activity, television watching, siesta sleep, smoking status, snacking between meals, and following a special diet. Total energy intake was not included as a covariate because it may plausibly mediate the association of ultraprocessed foods and overweight and obesity. We evaluated the interaction between exposure, sex, and BMI with the use of a likelihood ratio test that compared the fully adjusted Cox regression model and the same model with interaction product terms (3 df). Nelson-Aalen cumulative hazards estimates were plotted for overweight and obesity incidence according to ultraprocessed food consumption quartiles at baseline. We used inverse probability weighting to adjust the Nelson-Aalen curves for baseline potential confounders.

To test the proportional hazard assumption, we calculated a Cox regression with the exposure as a continuous time-varying covariate to check that the HR did not vary over time, obtaining a nonsignificant result, suggesting that the proportionality assumption was met. We also checked the proportionality of hazards model with the use of a Grambsch-Therneau test of the scaled Schoenfeld residuals from a Cox model on the 3 dummy variables of the upper ultraprocessed quartiles (19). The *P* value of the global test was 0.72.

To determine the contribution of each food item to the between-person variance in ultraprocessed food consumption (13), we constructed a series of nested least-squares linear regression models after stepwise-selection regression analyses. The additional contribution of a given food item was reflected in the change in the cumulative R^2.

Sensitivity analyses were conducted by repeating the multivariable-adjusted Cox regression models with the following changes: *1*) additional adjustment excluding fruit and vegetable consumption, *2*) exclusion of those participants under the 5th percentile and over the 95th percentile of total energy intake, *3*) additional adjustment for total energy intake, *4*) additional adjustment for family history of obesity, *5*) additional adjustment for weight gain >3 kg in the 5 y before entering the cohort, *6*) exclusion of participants who were early incident cases of overweight (those who became overweight after only 2 y of follow-up), and *7*) inclusion of subjects with prevalent chronic diseases.

All analyses were performed with Stata version 12.1 (StataCorp LP). $P < 0.05$ was considered significant.

RESULTS

A total of 2967 (35.1%) men and 5484 (64.9%) women were included in this analysis, and the mean ± SD age of the participants was 37.6 ± 11.0 y. The main baseline characteristics of participants according to quartiles of total ultraprocessed food consumption are presented in **Table 1**. Participants in the fourth quartile of ultraprocessed food consumption had the highest BMI, were more likely to be current smokers, watched more television, and had the highest total energy and fat intake and the

TABLE 1
Baseline characteristics of participants according to their consumption of ultraprocessed foods[1]

	Quartile				
Characteristics	1	2	3	4	*P*
n	2118	2108	2116	2109	
Total ultraprocessed consumption, servings/d	1.5 ± 0.9	2.7 ± 0.9	3.8 ± 0.9	6.1 ± 0.9	<0.001
Marital status, %					
Single	47.8	44.8	45.8	48.6	0.29
Married	45.8	49.7	49.1	46.6	0.74
Educational status, %					
Graduated	79.3	77.4	76.9	76.7	0.09
Master or doctoral	16.4	19.2	19.4	18.4	0.19
Baseline weight, kg	61.9 ± 6.4	62.1 ± 6.3	62.6 ± 6.3	62.6 ± 6.4	<0.001
Baseline BMI, kg/m^2	21.9 ± 1.7	21.9 ± 1.6	22.0 ± 1.6	22.0 ± 1.7	0.004
Family history of obesity, %	20.4	20.7	20.2	21.5	0.55
Smoking status, %					
Current	19.9	19.8	22.8	24.1	<0.001
Former	26.4	25.8	25.9	24.5	0.25
Physical activity, MET-h/wk	23.3 ± 24.1	22.8 ± 23.5	22.4 ± 23.6	22.7 ± 23.9	0.41
Television watching, h/d	1.5 ± 1.2	1.5 ± 1.2	1.5 ± 1.2	1.6 ± 1.2	<0.001
Sleeping siesta, h/d	0.3 ± 0.8	0.3 ± 0.7	0.3 ± 0.7	0.3 ± 0.7	0.12
Total energy intake, kcal/d	1967 ± 542	2264 ± 527	2464 ± 529	2796 ± 535	<0.001
Macronutrients, % energy					
Carbohydrate intake	43.8 ± 7.4	43.8 ± 7.2	43.7 ± 7.2	43.8 ± 7.3	0.77
Protein intake	18.9 ± 3.2	18.2 ± 3.1	17.5 ± 3.1	17.0 ± 3.1	<0.001
Fat intake	35.2 ± 6.5	36.2 ± 6.3	36.9 ± 6.4	37.5 ± 6.4	<0.001
SFAs	11.6 ± 3.2	12.4 ± 3.1	12.8 ± 3.1	13.0 ± 3.1	<0.001
MUFAs	15.6 ± 3.8	15.6 ± 3.7	15.8 ± 3.7	15.9 ± 3.7	0.004
PUFAs	4.9 ± 1.6	5.0 ± 1.5	5.3 ± 1.5	5.4 ± 1.5	<0.001
Total dietary fiber intake, g/kcal	31.2 ± 10.4	28.5 ± 10.1	27.2 ± 10.1	25.5 ± 10.3	<0.001
Fruit consumption, g/d	358 ± 284	347 ± 277	338 ± 278	336 ± 281	0.01
Vegetable consumption, g/d	543 ± 341	507 ± 331	516 ± 333	517 ± 337	0.06
Fast-food consumption,[2] g/d	14.1 ± 18.8	19.8 ± 18.3	23.7 ± 18.4	29.2 ± 18.6	<0.001
Processed meat consumption,[3] servings/d	0.4 ± 0.5	0.6 ± 0.4	0.8 ± 0.4	1.0 ± 0.4	<0.001
Nonprocessed meat consumption, servings/d	0.7 ± 0.4	0.8 ± 0.4	0.8 ± 0.4	0.9 ± 0.4	<0.001
Fried food consumption, servings/wk	2.8 ± 4.4	3.5 ± 4.3	3.9 ± 4.3	4.6 ± 4.3	<0.001
Sugar-sweetened beverage consumption, mL/d	20.6 ± 108.9	35.9 ± 106.0	58.4 ± 106.4	119.2 ± 107.7	<0.001
Alcohol intake, g/d	5.0 ± 8.4	5.8 ± 8.1	6.1 ± 8.2	6.5 ± 8.3	<0.001
Between-meal snacking, %	22.5	28.0	31.5	39.0	<0.001
Mediterranean diet adherence score, %					
0–2	16.2	18.9	20.5	21.1	<0.001
3–6	70.0	69.5	70.5	70.0	0.95
7–9	13.8	11.6	9.0	8.9	<0.001
Special diet at baseline, %	8.0	5.0	5.0	5.8	0.01

[1] All values are means ± SDs unless otherwise indicated. *P* values were adjusted for sex and age with the use of ANOVA. MET, metabolic equivalent; SUN, University of Navarra Follow-Up.
[2] Sum of hamburgers, sausages, and pizza.
[3] Sum of sausages, hamburgers, and ham.

TABLE 2
Main sources of ultraprocessed foods[1]

Foods	Change in R^2	Cumulative R^2
Processed meat[2]	—	0.1901
Cookies[3]	0.1224	0.3125
Sugar-sweetened beverages	0.0974	0.4098
Pastries[4]	0.0716	0.4814
Breakfast cereals	0.0619	0.5433
Chocolate	0.0451	0.5884
Fruit drinks in bottles	0.0346	0.6229
Margarine	0.0262	0.6491

[1] Cumulative R^2 values were determined with the use of nested regression analyses after a stepwise selection.
[2] Includes ham, sausages, chorizo, salami, mortadella, and hamburgers.
[3] Includes biscuits and chocolate cookies.
[4] Includes muffins, doughnuts, croissants or other pastries, and confectionery.

lowest protein and total fiber than those in the first quartile. Moreover, on average, they consumed more fast food, fried foods, processed and other meats, and sugar-sweetened beverages. In contrast, they had the lowest intakes of vegetables and were less likely to follow special diets. In addition, they had the highest prevalence of snacking between main meals. In addition, the adherence to the Mediterranean diet score varied according to quartiles of ultraprocessed food (i.e., the higher the consumption of ultraprocessed foods, the less adherence to the Mediterranean diet).

The contributions of different food groups to ultraprocessed food intake are shown in **Table 2**. Processed meat, biscuits and cookies, sugar-sweetened beverages, and candies were among the major contributors to ultraprocessed food consumption variability.

During the follow-up period (median: 8.9 y; person-years: 66,625), we observed 1939 incident cases of overweight and obesity. In the multivariate models, when we assessed the risk of overweight and obesity according to quartiles of ultraprocessed foods consumption (**Table 3**), participants with higher ultraprocessed food intake (highest quartile) presented a 26% relatively higher risk of developing overweight or obesity than those in the lowest quartile (HR: 1.26; 95% CI: 1.10, 1.45). The estimates showed a statistically significant linear trend (P = 0.001). The Nelson-Aalen curves exhibited a higher incidence of overweight and obesity with increasing baseline quartiles of ultraprocessed food intake (**Figure 2**). No significant interaction between sex or BMI and ultraprocessed food consumption was observed. Results in the sensitivity analyses described previously were not substantially changed in any of the scenarios (**Table 4**).

DISCUSSION

In this prospective cohort study with initially healthy, middle-aged, Spanish adults, higher ultraprocessed food consumption was associated with an increased risk of overweight and obesity incidence for a mean of ∼9 y of follow-up, even after adjusting for potential confounding factors.

Recent ecological and cross-sectional studies on ultraprocessed food consumption and the risk of overweight and obesity have shown an association between increased ultraprocessed food consumption and obesity among adolescents and adults (5, 7, 8, 20). To our knowledge, this is the first prospective epidemiologic study to assess this association among adults.

The food and drinks classified as ultraprocessed foods are mostly manufactured by large and powerful transnational companies. These companies focus their marketing on the individual's lack of time compared with the expediency, convenience, and accessibility of these products (21, 22). However, ultraprocessed foods tend to be nutritionally unbalanced and have a high energy content and amounts of fat, added or free sugar, sodium, and chemical additives in addition to being poor in micronutrients and fiber (3, 21, 23, 24). This nutritional composition is caused by several industrial processes, such as the removal of water, which increases the shelf life and reduces transportation costs but increases the energy density per portion. In addition, to confer greater stability, ultraprocessed foods have a greater amount of *trans* and saturated fats and synthetic additives (24). Ultraprocessed foods are also designed to be irresistible and to favor consumption (because of the use of salt, sugar, and fat but also because of marketing and other characteristics such as portion size and convenience), and the processing also affects food behavior and the capacity for self-control (2, 3). This new classification proposal of foods according to the degree of processing (2) therefore seems to be a good way of assessing their intake and relation to health outcomes because it can identify the consumption of a group of foods and drinks with low nutritional quality rather than just a certain food or nutrient.

TABLE 3
Cox proportional HRs and 95% CIs for incident overweight and obesity according to baseline consumption of ultraprocessed foods[1]

	Quartile				
	1	2	3	4	P-trend
Incident cases	440	466	512	521	
Person-years	16,889	16,790	16,522	16,423	
Crude	1.00 (reference)	1.17 (1.03, 1.34)	1.40 (1.23, 1.59)	1.49 (1.31, 1.70)	<0.001
Age- and sex-adjusted	1.00 (reference)	1.12 (0.98, 1.28)	1.27 (1.11, 1.45)	1.29 (1.13, 1.47)	<0.001
Multivariable-adjusted[2]	1.00 (reference)	1.15 (1.01, 1.32)	1.24 (1.09, 1.43)	1.26 (1.10, 1.45)	0.001

[1] All values are HRs; 95% CIs in parentheses unless otherwise indicated.
[2] Adjusted for sex, age, marital status, educational status, physical activity, television watching, siesta sleep, smoking status, snacking between meals, following a special diet at baseline, baseline BMI, and consumption of fruit and vegetables.

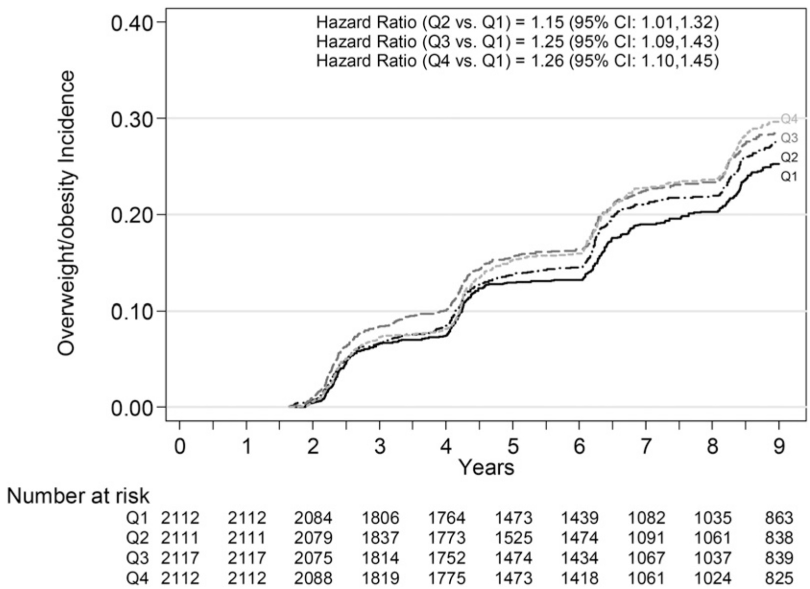

FIGURE 2 Nelson-Aalen curves showing the outcome of new-onset overweight depending on ultraprocessed food consumption at baseline. Adjusted for sex, age, marital status, educational status, physical activity, television watching, siesta sleep, smoking status, snacking between meals, following a special diet at baseline, baseline BMI, and consumption of fruit and vegetables with the use of inverse probability weighting. Q, quartile.

The sales of ultraprocessed foods increased between 2000 and 2013. Despite the United States being the largest buyer, sales of these products in Spain grew 18.5%, followed by Canada, Germany, and Mexico (5). In a longitudinal study of food and beverage consumer packaged goods purchased by US households, the 2000–2012 Nielsen Homescan Panel showed that 61% of the energy in purchases by US households in 2012 was derived from ultraprocessed foods (25). The 2008–2012 United Kingdom National Diet and Nutrition Survey, a large national cross-sectional study of diet, showed that diets with a higher intake of minimally processed foods and lower intake of ultraprocessed foods are associated with a more healthy food profile, but this was not associated with body weight (10). Studies from Canada and Brazil, conducted with data from national household food budget surveys, have also demonstrated a direct association between ultraprocessed food consumption and a diet with a high energy density and intake of sugars, sodium, and total and saturated fats and an inverse association with fiber intake (3, 21). Moreover, a study from Brazil that examined data from a national household food budget survey showed that higher ultraprocessed food consumption was associated with the lowest intakes of vitamin B-12, vitamin D, niacin, iron, selenium, and magnesium (26).

We believe that ultraprocessed food consumption may increase the risk of overweight and obesity by increasing the total intake of calories, added and free sugars, and fats and providing an inadequate relation of nutrients potentially involved in the genesis of the accumulation of body fat (1, 3, 21–24, 26). A cross-sectional study from the United States with data from NHANES 2009–2010 showed that ultraprocessed food represented 57.9% of energy intake and that ∼90% of this amount was derived

TABLE 4
Sensitivity analyses of HRs (95% CIs) for incident overweight and obesity according to quartiles of consumption of ultraprocessed foods[1]

		Quartile				
	Cases/person-years, *n*	1	2	3	4	*P*-trend
Overall	1939/66,625	1.00 (reference)	1.15 (1.01, 1.32)	1.24 (1.09, 1.43)	1.26 (1.10, 1.45)	0.001
Excluding adjustment for fruit and vegetable consumption	1939/66,625	1.00 (reference)	1.15 (1.01, 1.32)	1.25 (1.09, 1.43)	1.26 (1.10, 1.35)	0.001
Further adjusted for energy total intake	1939/66,625	1.00 (reference)	1.15 (1.01, 1.32)	1.25 (1.09, 1.44)	1.27 (1.09, 1.49)	0.003
Further adjusted for family history of obesity	1939/66,625	1.00 (reference)	1.16 (1.01, 1.33)	1.25 (1.10, 1.44)	1.27 (1.11, 1.45)	0.001
Further adjusted for weight gain >3 kg in the 5 y before entering the cohort	1939/66,625	1.00 (reference)	1.15 (1.00, 1.32)	1.24 (1.09, 1.42)	1.26 (1.10, 1.44)	0.001
Inclusion of prevalent cancer, diabetes, or cardiovascular disease	2073/70,617	1.00 (reference)	1.14 (1.00, 1.29)	1.20 (1.06, 1.37)	1.24 (1.09, 1.41)	0.002
Exclusion of early incident cases of overweight (until 2 y of follow-up)	1293/65,030	1.00 (reference)	1.17 (0.99, 1.38)	1.14 (0.97, 1.35)	1.32 (1.12, 1.56)	0.002
Energy limits between 5th and 95th percentiles	1828/63,401	1.00 (reference)	1.21 (1.06, 1.39)	1.21 (1.05, 1.39)	1.28 (1.12, 1.47)	0.002

[1] All values are HRs (95% CIs) unless otherwise indicated. Analyses were adjusted for sex, age, marital status, educational status, physical activity, television watching, siesta sleep, smoking status, snacking between meals, following a special diet at baseline, baseline BMI, and consumption of fruit and vegetables.

from added sugars (23). The participants in our cohort with a higher daily consumption of ultraprocessed foods had a higher consumption of total calories and fat, a lower consumption of proteins and fibers, and a lower adherence to the Mediterranean dietary pattern.

The Nurses' Health Study showed a strong association between the percentage of calories from saturated and *trans* fats and weight gain (27). Results from the Nurses' Health Study II also showed that an increase in dietary energy density was a risk factor for obesity (28). A meta-analysis of cohort studies and randomized clinical trials has provided evidence of the relation between the intake of sugar and the development of overweight and obesity (29). On the other hand, the consumption of natural foods such as fruits, vegetables, fish, and fiber—but not red meat—is inversely associated with the incidence of overweight and obesity (4, 30).

Our findings stress the importance of promoting and enhancing healthy and sustainable food standards, which requires structural and behavioral changes. Food systems should improve the supply of healthy foods and foster healthier food choices (31). This may be accomplished by promoting and enhancing eating habits based on foods and cuisine, such as the Mediterranean dietary pattern. Several studies have demonstrated its association with the reduction of weight gain because it consists predominantly of fruits, vegetables, legumes, nuts, olive oil, and fish (17, 32). Therefore, the Mediterranean diet is based on the consumption of fresh foods; multiple studies have demonstrated its preventive effect against chronic diseases (32–35).

Some limitations may be observed in this study. The assessment of ultraprocessed food consumption was performed with the use of an FFQ that was not specifically designed to collect data regarding this new classification of foods. Therefore, there is the potential for some degree of misclassification of ultraprocessed food consumption inherent in our methodology. However, our FFQ was previously validated and represents the main foods ingested by the studied population (15), including ultraprocessed foods. Hamburgers are classified as an ultraprocessed food according to NOVA (2). Hamburgers are not ground beef but are a dish made of industrial breads, sauces, reconstituted meat, processed cheese, bacon, etc. Therefore, we included hamburgers in the ultraprocessed food group. Some hamburgers can be homemade, and doubts may arise about their inclusion in this group. Unfortunately, our study could not differentiate between fast-food and homemade hamburgers. Even when we removed hamburgers from the ultraprocessed foods, the results were only slightly attenuated (HR: 1.23; 95% CI: 1.07, 1.41; P-trend = 0.003).

Self-reported data were used to evaluate the BMI and to classify the overweight and obesity incident cases. This may not be precise enough, especially because we cannot accurately specify the date of onset of the overweight or obese status. Nevertheless, this method was previously validated (16). In addition, the participants were health professionals, and this fact is likely to have increased the validity of their self-reported anthropometric data.

Potential confounding may still be possible. Nevertheless, we adjusted for several potential confounding factors related to lifestyle. Caution is needed in extrapolating the results to the general population because the SUN participants are volunteer university graduates. This group could be more aware of health, thus causing a selection bias that implies that the magnitude of the risk between ultraprocessed food consumption and excess weight may be even greater in the general population. Conversely, the participants have a higher educational status and are capable of providing better quality self-reported data, thus reducing the potential for misclassification bias. Nevertheless, we must be cautious with regard to the generalization of the results because they do not depend on the statistical representativeness of the sample but on the biological mechanisms underlying the observed association.

The main strengths of this study are its prospective design, the use of validated methods (15, 16), the relatively large sample size, and the long follow-up period. In addition, this is one of the first longitudinal studies to our knowledge to evaluate the relation between ultraprocessed food intake and overweight and obesity. Further studies should be performed to investigate whether there is a relation between increased ultraprocessed food intake and major causes of death, such as cardiovascular diseases and cancer.

The results suggest that increased ultraprocessed food consumption is associated with a greater risk of overweight and obesity. Strategies for reducing the consumption of this group of foods, such as the maintenance of a traditional food culture and strengthening of the Mediterranean diet, should be encouraged as preventive approaches for obesity. However, further longitudinal studies in different contexts are necessary to confirm our findings.

The authors' responsibilities were as follows—RdDM, ACSL, and MB-R: analyzed the data and drafted the manuscript; MB-R: obtained the funding and designed the study; AMP, AG, and CdlF-A: helped to design the study and interpreted the data; MAM-G: helped to design the study and was the founder of the SUN project; and all authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

REFERENCES

1. WHO. Global status report on noncommunicable diseases 2014. Geneva (Switzerland): WHO; 2014.
2. Monteiro CA, Cannon G, Levy R, Moubarac JC, Jaime P, Martins AP, Canella D, Louzada M, Parra D, Ricardo C, et al. Food classification. Public health. J World Public Health Nutr 2016;7:28–38.
3. Moubarac JC, Martins AP, Claro RM, Levy RB, Cannon G, Monteiro C. Consumption of ultra-processed foods and likely impact on human health. Evidence from Canada. Public Health Nutr 2013;16:2240–8.
4. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. N Engl J Med 2011;364:2392–404.
5. Pan American Health Organization. Ultra-processed food and drink products in Latin America: trends, impact on obesity, policy implications. Washington (DC): Pan American Health Organization; 2013.
6. Tavares LF, Fonseca SC, Garcia Rosa ML, Yokoo EM. Relationship between ultra-processed foods and metabolic syndrome in adolescents from a Brazilian family doctor program. Public Health Nutr 2012;15: 82–7.
7. Louzada MLC, Baraldi LG, Steele EM, Martins AP, Canella DS, Moubarac JC, Levy RB, Cannon G, Afshin A, Imamura F, et al. Consumption of ultra-processed foods and obesity in Brazilian adolescents and adults. Prev Med 2015;81:9–15.
8. Canella DS, Levy RB, Martins APB, Claro RM, Moubarac JC, Baraldi LG, Cannon G, Monteiro CA. Ultra-processed food products and obesity in Brazilian households (2008–2009). PLoS One 2014;9: e92752.
9. Rauber F, Campagnolo PD, Hoffman DJ, Vitolo MR. Consumption of ultra-processed food products and its effects on children's lipid profiles: a longitudinal study. Nutr Metab Cardiovasc Dis 2015;25:116–22.

10. Adams J, White M. Characterisation of UK diets according to degree of food processing and associations with socio-demographics and obesity: cross-sectional analysis of UK National Diet and Nutrition Survey (2008–12). Int J Behav Nutr Phys Act 2015;12:160.
11. Seguí-Gómez M, de la Fuente C, Vázquez Z, de Irala J, Martínez-González MA. Cohort profile: the 'Seguimiento Universidad de Navarra' (SUN) study. Int J Epidemiol 2006;35:1417–22.
12. Martínez-González MA, Sanchez-Villegas A, de Irala J, Marti A, Martínez JA. Mediterranean diet and stroke: objectives and design of the SUN project. Seguimiento Universidad de Navarra. Nutr Neurosci 2002;5:65–73.
13. Willett W. Nutritional epidemiology. 3rd ed. New York: Oxford University Press; 2013.
14. de la Fuente-Arrillaga C, Ruiz ZV, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. Public Health Nutr 2010;13:1364–72.
15. Martín-Moreno JM, Boyle P, Gorgojo L, Maisonneuve P, Fernandez-Rodriguez JC, Salvini S, Willett WC. Development and validation of a food frequency questionnaire in Spain. Int J Epidemiol 1993;22:512–9.
16. Bes-Rastrollo M, Pérez VR, Sánchez-Villegas A, Alonso A, Martinez-Gonzalez MA. Validation of the weight and body mass index self-declared by participants in a cohort of university graduates. Rev Esp Obes 2005;3:352–8.
17. Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martinez JA. Validation of the Spanish version of the physical activity questionnaire used in the Nurses' Health Study and Health Professionals' Follow-up Study. Public Health Nutr 2005;8:920–7.
18. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 2003;348:2599–608.
19. Royston P, Lambert PC. Flexible parametric survival analysis using Stata: beyond the Cox model. College Station (TX): Stata Press; 2011.
20. Juul F, Hemmingsson E. Trends in consumption of ultra-processed foods and obesity in Sweden between 1960 and 2010. Public Health Nutr 2015;18:3096–107.
21. Monteiro CA, Levy RB, Claro RM, de Castro IR, Cannon G. Increasing consumption of ultra-processed foods and likely impact on human health: evidence from Brazil. Public Health Nutr 2011;14:5–13.
22. Moodie R, Stuckler D, Monteiro C, Sheron N, Neal B, Thamarangsi T, Lincoln P, Casswell S. Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. Lancet 2013;381:670–9.
23. Martínez Steele E, Baraldi LG, Louzada MLC, Moubarac JC, Mozaffarian D, Monteiro CA. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. BMJ Open 2016;6:e009892.
24. Ludwig DS. Technology, diet, and the burden of chronic disease. JAMA 2011;305:1352–3.
25. Poti JM, Mendez MA, Ng SW, Popkin BM. Is the degree of food processing and convenience linked with the nutritional quality of foods purchased by US households? Am J Clin Nutr 2015;101:1251–62.
26. Louzada MLC, Martins APB, Canella DS, Baraldi LG, Levy RB, Claro RM, Moubarac JC, Cannon G, Monteiro CAImpact of ultra-processed foods on micronutrient content in the Brazilian diet. Rev Saúde Pública 2015;49:45.
27. Field A, Willett W, Lissner L, Colditz GADietary fat and weight gain among women in the Nurses' Health Study. Obesity 2007;15:967e76.
28. Bes-Rastrollo M, van Dam RM, Martínez-Gonzalez MA, Li TY, Sampson LL, Hu FB. A prospective study of dietary energy density and weight gain in women. Am J Clin Nutr 2008;88:769–77.
29. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomized controlled trials and cohort studies. BMJ 2012;346:e7492.
30. Zazpe I, Bes-Rastrollo M, Canela MR, Sánchez-Villegas A, Serrano-Martínez M, Martínez-González MA. A brief assessment of eating habits and weight gain in a Mediterranean cohort. Br J Nutr 2011;105:765–75.
31. Anand SS, Hawkes C, Souza RJ, Mente A, Dehghan M, Nugent R, Zulyniak MA, Weis T, Bernstein AM, Krauss RM, et al. Food consumption and its impact on cardiovascular disease: importance of solutions focused on the globalized food system. J Am Coll Cardiol 2015;66:1590–614.
32. Beunza JJ, Toledo A, Hu FB, Bes-Rastrollo M, Serrano-Martínez M, Sánchez-Villegas A, Martínez JA, Martínez-González MA. Adherence to the Mediterranean diet, long-term weight change, and incident overweight or obesity: the Seguimiento Universidad de Navarra (SUN) cohort. Am J Clin Nutr 2010;92:1484–93.
33. Martínez-González MA, Salas-Salvado J, Estruch R, Corella D, Fitó M, Ros E. Benefits of the Mediterranean diet: insights form the PREDIMED Study. Prog Cardiovasc Dis 2015;58:50–60.
34. Martínez-González MA, Estruch R, Corella D, Ros E, Salas-Salvadó J. Prevention of diabetes with Mediterranean diets. Ann Intern Med 2014;161:157–8.
35. Toledo E, Salas-Salvadó J, Donat-Vargas C, Buil-Cosiales P, Estruch R, Ros E, Corella D, Fitó M, Hu FB, Arós F, et al. Mediterranean diet and invasive breast cancer risk among women at high cardiovascular risk in the PREDIMED Trial: a randomized clinical trial. JAMA Intern Med 2015;175:1752–60.