

# RESEARCH Review



# The association between ultra-processed food consumption and chronic insomnia in the NutriNet-Santé Study

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Table 2 is available at www.jandonline.org.

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#### ABSTRACT

**Background** The consumption of ultra-processed foods (UPF) is on the rise worldwide, and it has been linked to numerous health conditions, such as diabetes, obesity, and cancer. Few studies have focused on the effect of UPF consumption on sleep health and even fewer on chronic insomnia.

**Objective** This study investigated the association between UPF intake and chronic insomnia in a large population-based sample.

**Design** This was a cross-sectional analysis using the NutriNet-Santé study data, an ongoing Web cohort in France.

**Participants/setting** Thirty-eight thousand five hundred seventy adult males and females who had completed a sleep questionnaire (2014) and at least two 24-hour dietary records were included in the analysis.

**Main outcomes measures** Chronic insomnia was defined according to established criteria. Categorization of food and beverages as UPF was based on the NOVA–Group 4 classification.

**Statistical analyses performed** The cross-sectional association between UPF intake and chronic insomnia was assessed using multivariable logistic regression.

**Results** Among the 38,570 participants (mean age, 50.0  $\pm$ 14.8 years, 77.0% female) included in the analysis, 19.4% had symptoms of chronic insomnia. On average, UPF represented 16% of the total amount (g/day) of the overall dietary intake. In the fully adjusted model, UPF consumption was associated with higher odds of chronic insomnia (odds ratio [OR] for an absolute 10% greater UPF intake in the diet = 1.06; 95% confidence interval [CI]: 1.02–1.09). Sex-specific OR for chronic insomnia for an absolute 10% greater UPF intake in the diet were 1.09 (1.01–1.18) among males and 1.05 (1.01–1.09) among females.

**Conclusions** This large epidemiological study revealed a statistically significant association between UPF intake and chronic insomnia, independent of sociodemographic, lifestyle, diet quality, and mental health status covariates. The findings provide insights for future longitudinal research as well as nutrition- and sleep-focused intervention and prevention programs.

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IET IS A KEY DETERMINANT OF HEALTH AND chronic disease risk. The World Health Organization urges higher intakes of fruit, vegetables, legumes, and whole grains, all of which have proven health benefits, in parallel with lower intakes of sugar and animal fat.<sup>1,2</sup> A diet in which complex (rather than refined) carbohydrates and unsaturated (rather than saturated) fats predominate has been consistently associated with reduced incidence of obesity, type 2 diabetes (T2D), cardiovascular diseases (CVD), certain types of cancer, and premature mortality.<sup>3-7</sup> Beyond the nutritionally important components of the diet, the degree of food processing has been attracting

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research attention as an important independent contributor to chronic disease risk.<sup>8</sup>

Around the world, and across sex, age, socioeconomic status, and ethnic background, there is substantial and growing availability and consumption of industrially manufactured products,<sup>9,10</sup> some of them regarded as "ultra-processed" foods and beverages (UPF).<sup>11</sup> UPF include all foods that have undergone intense industrial processing.<sup>10</sup> Such products typically contain additives (eg, artificial flavorings, colorants), large amounts of sugar, fat, or salt, and a very low amount of dietary fiber.<sup>12</sup> UPF products are designed to be palatable and ready-to-eat; they are attractively packaged

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and ubiquitous in the marketplace.<sup>13</sup> The potential health risks associated with UPF consumption were first discussed over a decade ago.<sup>8</sup> Since then, epidemiological research has expanded and has fairly consistently associated UPF consumption with an increased risk of numerous chronic conditions such as obesity, metabolic syndrome, dyslipidemia, T2D, CVD, hypertension, eating disorders, irritable bowel syndrome, ulcerative colitis, non-alcoholic fatty liver disease, depressive symptoms, and several types of cancer.<sup>10,11,14-18</sup>

Diet quality also has been highlighted as a contributor to sleep quality<sup>19</sup>; however, reviews of the evidence for the role of UPF rarely include sleep health among the outcomes.<sup>20</sup> One recent meta-analysis of cross-sectional studies carried out among children, adolescents, and adults reported a statistically significant association between a high intake of any type of UPF and poor sleep quality.<sup>21</sup> Another systematic literature review focused on the association between UPF intake as defined by NOVA (described later), as an exposure or as an outcome, and various sleep parameters among adults (eg, average sleep duration, sleep quality, afternoon napping, and anxiety-induced sleep disturbance).<sup>20</sup> That review highlighted several methodological deficiencies of existing research (eg, sleep commonly assessed with a single question, reliance on food frequency questionnaires. lack of statistical control for pertinent confounders) as well as gaps in knowledge, including the absence of studies on chronic insomnia. Recent estimates suggest that approximately one third of adults in the general population experience occasional or chronic insomnia symptoms.<sup>22</sup> In addition, a review of the literature on the diet-sleep association concluded that the type and quality of intake might be more important than the quantity of intake regarding sleep health.<sup>23</sup> To our knowledge, there are no large-scale studies investigating the association between chronic insomnia, defined according to the Diagnostic and Statistical Manual of Mental Disorders-5<sup>th</sup> Edition (DSM-5)<sup>24</sup> and the International Classification of Sleep Disorders–3<sup>rd</sup> Edition (ICSD-3)<sup>25</sup> criteria, and intake of NOVA-defined UPF, derived from 24-hour records.

Therefore, the main objective of this cross-sectional study was to assess the association between UPF consumption and chronic insomnia in a large sample of males and females recruited from the general population. We hypothesized that greater UPF intake would be independently associated with increased insomnia symptoms across age and sex.

## METHODS

## The NutriNet-Santé Web Cohort

NutriNet-Santé (https://etude-nutrinet-sante.fr/) is an ongoing Web cohort launched in France in 2009. Detailed information about the design, protocol, objectives, and recruitment strategy has been published.<sup>26,27</sup> In brief, participants aged  $\geq$ 18 years with Internet access and ability to comprehend written French are recruited from the general population via online and offline media calls. NutriNet-Santé was approved by the Institutional Review Board of the French Institute for Health and Medical Research and by the National Commission on Informatics and Liberty. The cohort is registered (# NCT03335644) at https://www.ClinicalTrials.gov. Each eligible individual is required to provide informed consent before enrollment.

### **RESEARCH SNAPSHOT**

**Research Question:** Is the consumption of ultra-processed foods (UPF) associated with chronic insomnia?

**Key findings:** This cross-sectional study was conducted among French adults who had completed a sleep questionnaire and at least two 24-hour dietary records. It revealed a statistically significant association between UPF intake and chronic insomnia, independent of sociodemographic, lifestyle, diet quality, and mental health status characteristics.

At inclusion and yearly thereafter, participants complete a battery of instruments regarding their sociodemographic and lifestyle profiles, anthropometrics, physical activity and sedentary behavior, and health status. Additional questionnaires on specific health or nutrition topics are regularly administered as part of the follow-up.

#### Insomnia Assessment

A comprehensive and nonmandatory sleep questionnaire was developed for the cohort and administered between February and July 2014 to all NutriNet-Santé enrollees (n = 128,042) and was completed on a voluntary basis by 57,105 individuals.<sup>28</sup> Chronic insomnia was the main outcome in this analysis; it was defined according to the criteria set forth in the ICSD-3<sup>25</sup> and the DSM-5.<sup>24</sup> These criteria include experiencing sleep problems (difficulty falling asleep, frequent nighttime waking)  $\geq$ 3 nights/week over the past  $\geq$ 3 months, and experiencing negative repercussions of such problems in daily life.

# Dietary Data Collection and Estimation of UPF Consumption

In NutriNet-Santé, information on dietary intake is collected every 6 months. Each time, participants are asked to complete 3 nonconsecutive 24-hour dietary records over a 2week period. The diet tool has been validated against dietitian interviews and against nutritional status biomarkers.<sup>29-31</sup> For each diet assessment day, participants were asked to report any and all food, beverages, and composite dishes consumed, including the quantity or portion size, preparation method, and meal setting (eg, place, time). Portion sizes, for example, can be estimated using validated photographs<sup>32</sup> or standard serving containers, or can be reported directly in grams or milliliters of intake. NutriNet-Santé has its own food composition table with >3,500 items used to estimate mean daily energy and nutrient intake.<sup>33</sup> All reported dietary data were weighted to respect the 5:7 and 2:7 ratios of weekdays vs weekend days. Implausible/aberrant energy intake values were identified via Black's method.<sup>34</sup> For this analysis, each participant's dietary intake was averaged across a minimum of two 24-h dietary records and a maximum of 21 records completed between January 2013 and December 2015 (ie, 3-year window around the insomnia assessment date). Individuals with aberrant energy intake values or with fewer than two 24-h records were not eligible for this analysis.

 Table 1.
 Sociodemographic, health status, and lifestyle characteristics of the study sample according to insomnia status, NutriNet-Santé Study, France

		Participants with	Participants without	
	Full sample	chronic insomnia <sup>a</sup>	chronic insomnia	
	n = 38,570	<u>n = 7,467 (19.4%)</u>	<u>n = 31,103 (80.6%)</u>	P <sup>b</sup>
$\text{UPF}^{c}$ consumption, as percentage of total amount of food consumed, mean (% g/day) $\pm$ $\text{SD}^{d}$	16.2 ± 8.0	$16.6\pm8.5$	16.1 ± 7.9	<.001
Sex, n (%)				
Female	29,532 (76.6)	6,251 (83.7)	23,281 (74.9)	<.001
Male	9,038 (23.4)	1,216 (16.3)	7,822 (25.1)	
Age, years, mean $\pm$ SD	$50.0\pm14.8$	50.8 ± 13.4	49.8 ± 15.1	<.001
Age category, n (%)				
18—39 у	10,783 (27.0)	1,677 (22.5)	9,106 (29.3)	<.001
40—59 y	15,068 (39.1)	3,586 (48.0)	11,482 (36.9)	
$\geq$ 60 y	12,719 (33.0)	2,204 (29.5)	10,515 (33.8)	
Educational level, n (%)				
Less than high school	4,935 (12.8)	1,031 (13.8)	3,904 (12.6)	<.001
High school diploma or equivalent	6,347 (16.5)	1,272 (17.0)	5,075 (16.3)	
College, undergraduate degree	12,239 (31.7)	2,521 (33.8)	9,718 (31.2)	
Graduate degree	15,049 (39.0)	2,643 (35.4)	12,406 (39.9)	
Socio-professional category, n (%)				
Homemaker/disabled/unemployed/student	4,209 (10.9)	963 (12.9)	3,246 (10.4)	<.001
Manual/blue collar worker	960 (2.5)	177 (2.4)	783 (2.5)	
Office work/administrative staff	11,612 (30.1)	2,508 (33.6)	9,104 (29.3)	
Professional/executive staff	8,982 (23.3)	1,606 (21.5)	7,376 (23.7)	
Retired	12,807 (33.2)	2,213 (29.6)	10,594 (34.1)	
Marital status, n (%)				
Living alone (single, divorced, widowed)	9,850 (25.5)	2,048 (27.4)	7,802 (25.1)	<.001
Married/cohabiting	28,720 (74.5)	5,419 (72.6)	23,301 (74.9)	
Physical activity level, <sup>e</sup> n (%)				
Low	8,440 (21.9)	1,824 (24.4)	6,616 (21.3)	<.001
Moderate	16,765 (43.5)	3,247 (43.5)	13,518 (43.5)	
High	13,365 (34.7)	2,396 (32.1)	10,969 (35.3)	
Sedentariness $^{\rm e}$ (minutes spent sitting/day), mean $\pm$ SD	363.6 ± 185.5	368.8 ± 186.2	362.4 ± 185.3	.007
$BMI^{f}_{r}$ mean $\pm$ SD	$\textbf{23.6} \pm \textbf{4.2}$	$24.0\pm4.6$	$\textbf{23.6} \pm \textbf{4.1}$	<.001
BMI category, n (%)				
Underweight (<18.5)	2,026 (5.3)	413 (5.5)	1,613 (5.2)	<.001
Normal weight (18.5—24.9)	24,843 (64.4)	4,554 (61.0)	20,289 (65.2)	
Overweight (25.0–29.9)	8,436 (21.9)	1,653 (22.1)	6,783 (21.8)	
Obese (≥30)	3,265 (8.5)	847 (11.3)	2,418 (7.8)	
Smoking status, n (%)				
Never smoker	17,955 (46.6)	3,178 (42.6)	14,777 (47.5)	<.001
Former smoker	16,802 (43.6)	3,478 (46.6)	13,324 (42.8)	
Current smoker	3,813 (9.9)	811 (10.9)	3,002 (9.7)	
			(continued on nex	(t page)

Table 1. Sociodemographic, health status, and lifestyle characteristics of the study sample according to insomnia status, NutriNet-Santé Study, France (continued)

	Full sample n = 38,570	Participants with chronic insomnia <sup>a</sup> n = 7,467 (19.4%)	Participants without chronic insomnia n = 31,103 (80.6%)	Pb
Alcohol use, g ethanol/day, mean $\pm$ SD	7.3 ± 10.0	$7.1\pm9.9$	7.4 $\pm$ 10.0	.009
Total energy intake, kcal/day, mean $\pm$ SD	1,846 $\pm$ 421	1,808 $\pm$ 421	1,856 $\pm$ 421	<.001
Anxiety diagnosis and/or treatment, n (%)				
Yes	8,388 (21.7)	2,789 (37.4)	5,599 (18.0)	<.001
No	30,182 (78.3)	4,678 (62.6)	25,504 (82.0)	
Depression diagnosis and/or treatment, n (%)				
Yes	5,747 (14.9)	2,001 (26.8)	3,746 (12.0)	<.001
No	32,823 (85.1)	5,466 (73.2)	27,357 (88.0)	
Number of 24-hour dietary records, mean $\pm$ SD	$8.9\pm4.7$	$\textbf{8.7} \pm \textbf{4.7}$	$8.9\pm4.7$	<.001

<sup>a</sup>Chronic insomnia was defined according to the criteria of the International Classification of Sleep Disorders, 3<sup>rd</sup> edition,<sup>25</sup> and the *Diagnostic and Statistical Manual of Mental Disorders*, 5<sup>th</sup> edition<sup>24</sup>; this information was provided on a self-report sleep questionnaire developed for the NutriNet-Santé Study and administered in 2014.

<sup>b</sup>P-values obtained from Student *t*-tests or  $\chi^2$  tests, as appropriate.

 $^{c}$ UPF = ultra-processed food and beverages. UPF consumption was assessed using  $\geq$ 2 24-hour dietary records, completed during 2013–2015, and the NOVA-4 classification.  $^{d}$ SD = standard deviation.

<sup>e</sup>Assessed with the International Physical Activity Questionnaire-Short Form according to established scoring criteria.<sup>38</sup>

<sup>f</sup>BMI = body mass index.

Ultra-processed food consumption was the main exposure in this analysis. It was defined using the 4-level NOVA classification.<sup>35</sup> Accounting for the extent and purpose of processing, NOVA assigns unprocessed and minimally processed food that does not contain added substances to group 1 (eg, nuts, plain yogurt, eggs); processed culinary ingredients to group 2 (eg, olive oil, honey); processed food to group 3 (eg, fresh bread, fresh cheese, dried fruits); and UPF containing multiple ingredients including substances not commonly used in culinary preparations (and typically absent from home kitchens) to group 4 (eg, instant noodles, sodas, fish and chicken nuggets, energy bars).<sup>13</sup> As previously described, a team of researchers and dietitians assigned each item in the NutriNet-Santé food composition table to 1 of the 4 NOVA groups.<sup>36</sup> In this study, the analysis pertained to NOVA group 4.

### **Covariate Data Collection**

Self-reported information about sex, age, education, socioprofessional category, marital status, alcohol consumption, and smoking status was collected with a validated online questionnaire.<sup>37</sup> Physical activity and sedentariness were assessed with the International Physical Activity Questionnaire-Short Form and scoring followed an established protocol.<sup>38</sup> Height and weight were self-reported using a validated anthropometric questionnaire.39 Next, selfreported information about diagnosis or prescription medication use for anxiety or depression was collected using the health status questionnaire. Energy intake and dietary patterns, derived from principal component analysis, were also included as covariates, as measures of diet quality.<sup>40</sup> Using 20 predefined food groups, two dietary patterns were extracted: (1) "healthy," characterized by intakes of fruit, vegetables, soups and broths, and whole grains and a low intake of processed meat; (2) "Western," characterized by relatively high intakes of alcoholic beverages, fats and sauces, offal, pasta and rice, potatoes and other tubers, and processed meat. As the questionnaire battery is administered at baseline and annually thereafter, the study relied on covariate data provided over a 3-year window around the completion of the sleep questionnaire (date closest to the sleep questionnaire administration).

### **Statistical Analysis**

Descriptive characteristics of the full sample and according to presence or absence of chronic insomnia are presented as number (%) obtained from  $\chi^2$  tests for categorical variables and as mean  $\pm$  SD obtained from Student *t* tests for continuous variables (Table 1). Next, a continuous measure of UPF consumption was calculated, representing the average proportion of the weight (expressed as %) of UPF in the diet. For covariates with missing data, mean or mode imputation was used, as appropriate. The associations between the main exposure, per 10-percentage points increment in %UPF intake in the diet, and insomnia were assessed using multivariable logistic regression models (no chronic insomnia as reference), providing odds ratios (OR) and 95% confidence intervals (CI). Model 1 was adjusted for age (years, continuous scale), sex, and socioprofessional category (homemaker/disabled/unemployed/student, manual/blue collar worker, office work/administrative staff, professional/executive staff, retired); model 2 was additionally adjusted for mean total energy intake without alcohol (kcal/d, continuous scale), alcohol consumption (g ethanol/d, continuous scale), smoking status (never, former, current smoker), physical activity level (low, moderate, high), sedentariness (minutes spent sitting/d, continuous scale), body mass index (BMI), marital status

(living alone or married/cohabiting), and diet quality (healthy and Western dietary patterns, continuous scale). Finally, model 3 was additionally adjusted for anxiety (yes/ no) and depression (yes/no). Given evidence for sex differences in the prevalence of insomnia,<sup>22</sup> interaction tests were carried out with that variable (significance level for the interaction tests < 0.15).

To estimate the robustness of the associations, a sensitivity analysis was performed after excluding participants with fewer than six 24-hour dietary records.

The main tests were 2-sided, and P < .05 was considered as evidence for statistical significance. R version 4.1.2 was used for all statistical analyses.<sup>41</sup>

## RESULTS

### **Description of Sample**

A total of 57,105 participants completed the sleep questionnaire in 2014 and were thus eligible for this analysis. Of these, 387 had incomplete/invalid sleep data; an additional 18,148 participants had fewer than two 24-hour dietary records or aberrant dietary data (ie, over- or under-reported energy intake) and were excluded from the analysis sample. Thus, the final sample included 38,570 participants (77% females, mean age =  $50.0 \pm 14.8$ ) (Fig).

Descriptive characteristics across chronic insomnia status are presented in Table 1. The final sample was predominantly composed of females, nonsmokers, with a high level of education. Participants with chronic insomnia had a higher percentage of UPF in their diet than those without insomnia, and were also more likely to be female, have obesity, be current smokers, live alone, and have worse mental health profiles (all P < .001). In the full sample, the mean number of 24-h dietary records was  $8.9 \pm 4.7$  (range, 2-21). Supplementary Table 2 displays the participant characteristics expressed in row percentages.

# Association Between UPF Intake and Chronic Insomnia

Given the statistically significant quantitative interaction of % UPF by sex, the main analyses were carried out in the full sample and by sex. Table 3 presents logistic regression results of the association between UPF intake and chronic insomnia. In the full sample, in the fully adjusted model (model 3), a statistically significantly higher OR for an absolute 10-percentage point incrementally greater %UPF in the diet was observed for chronic insomnia (OR = 1.06; 1.02–1.09). Next, statistically significantly higher ORs for an absolute 10-percentage point incrementally greater %UPF in the diet were observed for chronic insomnia in each sex in the fully adjusted analysis, with the risk estimates being slightly higher among men than among women: OR = 1.09 (95% CI, 1.01–1.09) among females,  $p_{interaction} = 0.14$ .

#### Sensitivity Analysis

Table 4 presents the results of the sensitivity analysis in which 10,910 participants with fewer than six 24-hour dietary records were excluded, and the same models were then re-fitted. Even though no substantial change in the main results was observed, the effect sizes became stronger, especially among men.

### DISCUSSION

This large cross-sectional epidemiological study revealed a statistically significant association between greater UPF consumption and chronic insomnia among adult men and women, confirming the main hypothesis. These associations were independent of sociodemographic, lifestyle, diet quality, and mental health status covariates. Given sex differences in insomnia prevalence, and despite the smaller proportion of men vs women in the sample, the results also showed a quantitative interaction by sex, with the effect size being



**Figure.** Selection of NutriNet-Santé participants for the study of the cross-sectional association between ultra-processed food intake and chronic insomnia. <sup>a</sup>The comprehensive sleep/insomnia questionnaire was developed for the NutriNet-Santé cohort and includes items based on the chronic insomnia criteria as defined in the *Diagnostic and Statistical Manual of Mental Disorders*—5<sup>th</sup> Edition<sup>24</sup> and the International Classification of Sleep Disorders—3<sup>rd</sup> Edition.<sup>25</sup> <sup>b</sup>In NutriNet-Santé, information on dietary intake is collected every 6 months via 3 nonconsecutive and nonmandatory 24-hour dietary records. Aberrant dietary intake values were identified via Black's method.<sup>34</sup>

Table 3. Association between ultra-processed food intake (per 10-percentage-points greater UPF in the diet) and chronic insomnia in the full sample and by sex, NutriNet-Santé Study, France

		Model 1		Model 2			Model 3		
	OR <sup>a</sup> (9	95% CI <sup>b</sup> )	Р	OR (9	5% CI)	Р	OR (9	5% CI)	Р
Full sample (n=38,570)									
Chronic insomnia									
n = 7,467	1.12	(1.08—1.15)	<.001	1.09	(1.05-1.13)	<.001	1.06	(1.02-1.09)	.002
Women (n = 29,532)									
Chronic insomnia									
n = 6,251	1.12	(1.08—1.16)	<.001	1.08	(1.04-1.12)	<.001	1.05	(1.01-1.09)	.016
Men (n = 9,038)									
Chronic insomnia									
n = 1,216	1.13	(1.04-1.21)	.002	1.12	(1.03-1.21)	.007	1.09	(1.01-1.18)	.030

No chronic insomnia = reference.

Model 1 is a multivariable logistic regression adjusted for sex (analysis in full sample only), age (years, continuous scale), and socio-professional category.

Model 2: Model 1 + BMI (continuous scale), marital status, physical activity level, sedentariness, smoking status, alcohol consumption, energy intake, healthy and Western dietary patterns. Model 3: Model 2 + diagnosis or treatment for anxiety or depression.

Values are rounded off to two decimal places.

 $^{a}OR = odds ratio.$ 

 ${}^{\rm b}{\rm CI} = {\rm confidence}$  interval.

somewhat larger in men than in women. The observed association of UPF consumption with risk of insomnia is consistent with the large body of scientific evidence

**Table 4.** Sensitivity analyses of the association between ultra-processed food intake (per 10-percentage points greater UPF in the diet) and chronic insomnia among participants with  $\geq$ 6 24-hour dietary records (NutriNet-Santé Study, France)

	Model 3					
	OR <sup>a</sup> (9	Р				
Full sample (n $=$ 27,660) Chronic insomnia						
n = 5,226	1.07	(1.03-1.12)	.002			
Women (n = 20,622)						
Chronic insomnia						
n = 4,329	1.06	(1.01-1.09)	.016			
Men (n = 7,038)						
Chronic insomnia						
n = 897	1.12	(1.01-1.24)	.030			

No chronic insomnia = reference. Results from a multivariable logistic regression adjusted for sex (analysis in full sample only), age (years, continuous scale), socioprofessional category, BMI (continuous scale), marital status, physical activity level, sedentariness, smoking status, alcohol consumption, energy intake, healthy and Western dietary patterns, + diagnosis or treatment for anxiety and depression. Values are rounded off to two decimal places.

 $^{a}OR = odds ratio.$ 

<sup>b</sup>Cl = confidence interval.

regarding the deleterious impact of UPF on a wide range of physical and mental health outcomes.<sup>10,11,14-18,21</sup>

Sleep disorders and insomnia represent major public health challenges, given the health status complications they entail. They have been associated with anxiety and depression, but also with physical disorders, such as CVD and T2D.<sup>42</sup> The American Heart Association recently added sleep duration to *Life's Simple 7*, renaming this cardiovascular health tool as *Life's Essential 8.*<sup>43</sup> Moreover, in Healthy People 2030, which is a set of goals and objectives designed to guide US health promotion and disease prevention programs, sleep health is a behavioral goal in its own right.<sup>44</sup> A better understanding of sleep disorders and their determinants therefore seems essential to develop well-targeted prevention strategies.

Mechanistically, UPF exposure has been positively associated with appetitive drive and hedonic valence.<sup>45</sup> The impact of diet on sleep also has been explained by neuroendocrine regulation (eg, serotonin, orexin, histamine, norepinephrine) and neuro-inflammatory processes that alter brain functionality via the gut-brain axis.<sup>23</sup> The proper functioning of the sleep-wake cycle is promoted by melatonin, which is synthesized exclusively from dietary tryptophan, via serotonin.<sup>19</sup> Various dietary sources of tryptophan, serotonin, and melatonin, such as dairy, fish, fruit, and vegetables, have been shown to have sleep-promoting effects.<sup>19,46</sup> These fresh foods typically fall outside of the UPF category, NOVA group 4. Next, reviews of the epidemiological and mechanistic evidence have highlighted the central role of the intestinal microbiota in connecting UPF and health status via alterations in the composition and function of the microbiota that are involved in food digestion, metabolism, and maturation of host immunity.<sup>10,11</sup>

A large share of UPF in one's diet has been associated in a direct, dose-response fashion with the dietary content of

saturated fat, trans fat, sodium, free or added sugars, and energy density, whereas an inverse dose—response association has been found with protein, fiber, vitamins A, C, D, and E, calcium, zinc, magnesium, phosphorus, potassium<sup>47</sup> and water intake.<sup>48</sup> Higher UPF intakes have been inversely associated with intake of fruit, vegetables, legumes, and seafood,<sup>49</sup> which are all sources of sleep-promoting compounds. Indeed, prospective research has shown that individuals adhering to nutrient-dense and fiber-rich diets, such as the Mediterranean diet, have better sleep health<sup>50</sup> and lower risk of insomnia.<sup>51</sup> In contrast, higher dietary glycemic index and glycemic load, underscored by an increased intake of added sugars, starch, and refined grains (all present in UPF), have been suggested as independent risk factors for insomnia incidence.<sup>52</sup>

This study contributes to the body of evidence for the deleterious impact of UPF intake on health-related outcomes. Data were collected by validated instruments and chronic insomnia was measured according to established criteria in a sociodemographically diverse sample of adults. The study relied on an average of close to nine 24-hour dietary records, which is a major strength of the study given that the use of multiple 24-hour dietary records is preferable over food frequency questionnaires for UPF estimation.<sup>10</sup> Another important strength was the use of group 4 of the NOVA classification system to identify UPF, which can facilitate comparison of findings across studies and across countries. The NOVA classification system has been recognized by the Food and Agriculture Organization of the United Nations and by the Pan American Health Organization as a valid tool for nutrition and public health research and policy development.<sup>13,47</sup>

The current study is subject to some limitations. First, it cannot provide any evidence of causal effects because of its cross-sectional and observational design. This is pertinent, given evidence of a bidirectional association between UPF and sleep parameters.<sup>20</sup> Second, despite the inclusion of many pertinent covariables, residual confounding by unmeasured constructs (eg, ethnic background, family history of insomnia, geographical situation) might be present. Third, in spite of efforts to avoid systematic bias, potential NOVA misclassification of some food items cannot be entirely ruled out. Moreover, despite validation against interviews with a dietitian and against various biomarkers of nutritional status,<sup>29,30</sup> the self-reported 24-hour dietary record—as any dietary data collection method-has weaknesses stemming from respondent burden and social desirability.53 As for chronic insomnia assessment, although based on validated criteria, it also relies on self-reported data. Finally, caution is advised when generalizing the findings, because NutriNet-Santé includes a higher proportion of females and individuals of high socioeconomic status compared with the general French population.<sup>54</sup> However, UPF intake in NutriNet-Santé was shown to be similar to that found in a nationally representative sample.<sup>55</sup> The data were collected around 2014 and might not fully represent current food consumption and sleeping patterns.

## CONCLUSION

To our knowledge, this is the first large epidemiological study to report significant independent associations between UPF consumption and chronic insomnia among men and women recruited from the general population. In the future, prospective epidemiological as well as clinical and experimental research could advance knowledge about causality and mediation pathways.

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#### STATEMENT OF POTENTIAL CONFLICT OF INTEREST

Dr. St-Onge has provided consulting for Nestlé.

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#### AUTHOR CONTRIBUTIONS

M. T. and S. H. designed and implemented the NutriNet-Santé cohort study; V. A. A. implemented the sleep questionnaire and coordinated insomnia data collection; M.-P. S.-O. conceived the research question; B. S. and M. T. developed the ultraprocessed food intake assessment in the NutriNet-Santé cohort based on the NOVA classification; P. D., L. K. F., V. A. A., and M.-P. S.-O. provided theoretical and methodological guidance; J. C. performed the statistical analyses; V. A. A. performed the literature search; P. D. and V. A. A. jointly led the writing; all authors critically revised the work for important intellectual content. All authors approved the final version of the manuscript and its submission.

#### DATA AVAILABILITY

Researchers at public institutions can submit a project collaboration request that includes information about their institution and a brief description of the project to: collaboration@etude-nutrinet-sante.fr. All requests are reviewed by the steering committee of the NutriNet-Santé study. In case of approval, a signed data access agreement will be requested and additional authorizations from the competent administrative authorities may be needed regarding human participants' data protection. In accordance with existing regulations, no personally identifiable data will be made available.

# RESEARCH

**Supplementary Table 2.** Sociodemographic, health status, and lifestyle characteristics (row percentages) of the study sample according to insomnia status, NutriNet-Santé Study, France

	Full sample n = 38,570	Participants with chronic insomnia <sup>a</sup> n = 7,467 (19.4%)	Participants without chronic insomnia n = 31,103 (80.6%)	P <sup>b</sup>
	16.2   8.0		161   70	< 001
of food consumed mean (% $q/d$ ) + SD <sup>d</sup>	$16.2 \pm 8.0$	$10.0 \pm 8.5$	10.1 ± 7.9	<.001
Sex n (%)				
Female	29 532 (76 6)	6 251 (21 2)	23 281 (78 8)	< 001
Male	9.038 (23.4)	1 216 (13 5)	7 822 (86 5)	2.001
Age, years, mean $+$ SD	$50.0 \pm 14.8$	$50.8 \pm 13.4$	$49.8 \pm 15.1$	< 001
Age category, n (%)		50.0 ± 15.1		2.001
18–39 v	10 783 (27 0)	1 677 (15 6)	9 106 (84 4)	< 001
40-59 v	15,068 (39.1)	3 586 (23.8)	11 482 (76 2)	2.001
>60 v	12,719 (33.0)	2 204 (17 3)	10 515 82 7)	
Educational level. n (%)	12,717 (33.0)	2,201 (17.3)	10,515 02.17	
Less than high school	4 935 (12 8)	1 031 (20 9)	3 904 (79 1)	< 001
High school diploma or equivalent	6.347 (16.5)	1,272 (20.0)	5.075 (80.0)	2.001
College undergraduate degree	12 239 (31 7)	2 521 (20.6)	9718 (794)	
Graduate degree	15,049 (39,0)	2,643 (17.6)	12 406 (82 4)	
Socio-professional category, n (%)	,	<u>_</u> ,e .e (e)	,	
Homemaker/disabled/unemployed/student	4,209 (10,9)	963 (22.9)	3.246 (77.1)	<.001
Manual/blue collar worker	960 (2.5)	177 (18.4)	783 (81.6)	
Office work/administrative staff	11.612 (30.1)	2,508 (21.6)	9,104 (78,4)	
Professional/executive staff	8,982 (23,3)	1,606 (17.9)	7,376 (82,1)	
Retired	12,807 (33.2)	2,213 (17.3)	10,594 (82.7)	
Marital status, n (%)	9,850 (25.5)	2,048 (20.8)	7,802 (79.2)	<.001
Living alone (single, divorced, widowed)	28,720 (74.5)	5,419 (18.9)	23,301 (81.1)	
Married/cohabiting				
Physical activity level, <sup>e</sup> n (%)				
Low	8,440 (21.9)	1,824 (21.6)	6,616 (78.4)	<.001
Moderate	16,765 (43.5)	3,247 (19.4)	13,518 (80.6)	
High	13,365 (34.7)	2,396 (17.9)	10,969 (82.1)	
Sedentariness <sup>e</sup> (minutes spent sitting/day), mean $\pm$ SD	363.6 ± 185.5	$\textbf{368.8} \pm \textbf{186.2}$	$\textbf{362.4} \pm \textbf{185.3}$	.007
BMI, <sup>f</sup> mean $\pm$ SD	$\textbf{23.6} \pm \textbf{4.2}$	$\textbf{24.0} \pm \textbf{4.6}$	$\textbf{23.6} \pm \textbf{4.1}$	<.001
BMI category, n (%)				
Underweight (<18.5)	2,026 (5.3)	413 (20.4)	1,613 (79.6)	<.001
Normal weight (18.5—24.9)	24,843 (64.4)	4,554 (18.3)	20,289 (81.7)	
Overweight (25.0–29.9)	8,436 (21.9)	1,653 (19.6)	6,783 (80.4)	
Obese (≥30)	3,265 (8.5)	847 (25.9)	2,418 (74.1)	
Smoking status, n (%)				
Never smoker	17,955 (46.6)	3,178 (17.7)	14,777 (82.3)	<.001
Former smoker	16,802 (43.6)	3,478 (20.7)	13,324 (79.3)	
Current smoker	3,813 (9.9)	811 (21.3)	3,002 (78.7)	
			(continued on nex	xt page)

**Supplementary Table 2.** Sociodemographic, health status, and lifestyle characteristics (row percentages) of the study sample according to insomnia status, NutriNet-Santé Study, France (*continued*)

	Full sample n = 38,570	Participants with chronic insomnia <sup>a</sup> n = 7,467 (19.4%)	Participants without chronic insomnia n = 31,103 (80.6%)	P <sup>b</sup>
Alcohol use, g ethanol/d, mean $\pm$ SD	$\textbf{7.3} \pm \textbf{10.0}$	7.1 ± 9.9	7.4 ± 10.0	.009
Total energy intake, kcal/d mean $\pm$ SD	1,846 $\pm$ 421	1,808 $\pm$ 421	1,855 $\pm$ 421	<.001
Anxiety diagnosis and/or treatment, n (%)				
Yes	8,388 (21.7)	2,789 (33.2)	5,599 (66.8)	<.001
No	30,182 (78.3)	4,678 (15.5)	25,504 (84.5)	
Depression diagnosis or treatment, n (%)				
Yes	5,747 (14.9)	2,001 (34.8)	3,746 (65.2)	<.001
No	32,823 (85.1)	5,466 (16.7)	27,357 (83.3)	
Number of 24-hour dietary records, mean $\pm$ SD	$8.9\pm4.7$	$8.7\pm4.7$	$8.9\pm4.7$	<.001

<sup>a</sup>Chronic insomnia was defined according to the criteria of the International Classification of Sleep Disorders, 3<sup>rd</sup> edition,<sup>25</sup> and the *Diagnostic and Statistical Manual of Mental Disorders*, 5<sup>th</sup> edition.<sup>24</sup>

<sup>b</sup>P-values obtained from Student *t*-tests or  $\chi^2$  tests, as appropriate.

 $^{c}$ UPF = ultra-processed food and beverage. UPF consumption was assessed using  $\geq$ 2 24-hour dietary records and NOVA-4 classification.

 $^{d}SD = standard deviation.$ 

<sup>e</sup>Assessed with the International Physical Activity Questionnaire-Short Form according to established scoring criteria.

<sup>f</sup>BMI = body mass index.