European Journal of Public Health, 2026, Vol. 36, No. 2, ckag049

https://doi.org/10.1093/eurpub/ckag049

Sex-specific associations of anxiety, insomnia, and their comorbidity with incident obesity in a general-population cohort

Pauline Duquenne[1], Cécilia Samieri[2], Stéphanie Chambaron[3], Gilles Feron[3], Marie-Claude Brindisi[3,4,5], Emmanuelle Kesse-Guyot[1], Florine Berthy[1], Damien Léger[6], Pilar Galan[1], Serge Hercberg[1], Mathilde Touvier[1], Valentina A. Andreeva[1,*,†], Léopold K. Fezeu[1,†]

[1]INSERM, INRAE, CNAM, Center for Research in Epidemiology and Statistics (CRESS), Nutritional Epidemiology Research Team (EREN), Sorbonne Paris Nord University and Paris Cité University, Bobigny, France
[2]Bordeaux Population Health, INSERM U1219, University of Bordeaux, Bordeaux, France
[3]Center for Taste and Feeding Behavior (CSGA), CNRS, INRAE, Agro Institute, University Burgundy Europe, Dijon, France
[4]Department of Endocrinology, Diabetology, Metabolic Diseases, and Nutrition, CHU, Dijon, France
[5]Specialized Obesity Center, CHU, Dijon, France
[6]VIFASOM, AP-HP Hôtel-Dieu, Center for Sleep and Vigilance, Paris-Cité University, Paris, France

*Corresponding author. Equipe de Recherche en Epidémiologie Nutritionnelle (EREN), Université Sorbonne Paris Nord, SMBH, 74 rue Marcel Cachin, 93017 Bobigny, France. E-mail: v.andreeva@eren.smbh.univ-paris13.fr.
†These authors contributed equally to this work. They are joint last authors.

Abstract

Sleep disorders and, to a lesser extent, anxiety disorders, have been studied independently for their association with weight status. However, these mental disorders are highly comorbid. We investigated the prospective associations of anxiety, insomnia, and anxiety-insomnia comorbidity with obesity risk in general-population adults. Enrollees in the ongoing NutriNet-Santé cohort were selected if they had anxiety (Spielberger's State-Trait Anxiety Inventory [STAI-T], 2013–16) and insomnia data (sleep questionnaire, 2014), were without obesity at baseline, and had body mass index (BMI) data during follow-up. Four baseline morbidity groups were modeled: neither insomnia nor anxiety (reference), high anxiety only (STAI-T $\geq$ 40), insomnia only, comorbid anxiety, and insomnia. The associations between each of these morbidity groups and incident obesity (BMI $\geq$30 kg/m^2) were assessed using adjusted Cox proportional hazards models. Among 23 797 participants, anxiety, insomnia, and comorbid anxiety and insomnia were present in 21%, 6%, and 7% of men, respectively, and in 29%, 8%, and 14% of women, respectively. Mean follow-up was 6.2 ± 2.0 years. An adjusted significant association between anxiety-insomnia comorbidity and incident obesity was found in men (HR = 1.71, 95% CI: 1.06–2.76) but not in women (HR = 1.00, 95% CI: 0.77–1.30) or in the full sample (HR = 1.12, 95% CI: 0.89–1.42). No associations were observed between anxiety alone or insomnia alone and incident obesity. This large prospective study advances public health knowledge about multimorbidity by suggesting a prospective, sex-specific association between anxiety-insomnia comorbidity and increased risk of new-onset obesity. Upon replication, the findings could help inform obesity prevention programs.

Introduction

Anxiety and sleep disorders have a relatively high prevalence in the general adult population [1]; they can influence weight gain via physiological, hormonal, and behavioral mechanisms [2, 3]. Because these mental disorders are potentially preventable and treatable, they could be addressed by public health actions targeting obesity. The most extensively studied sleep measures related to obesity are sleep duration and sleep quality. Quantitative and qualitative literature reviews [4, 5] have consistently shown that short sleep and poor sleep quality are associated with a greater obesity risk owing to altered hormone-driven appetite dysregulation and reduced energy expenditure [2]. Less research, primarily cross-sectional, has explored the insomnia-obesity link, producing inconclusive results [6]. Likewise, few general-population studies have investigated the independent association between anxiety and obesity. A study with >500 000 psychiatric patients reported a significant positive association between anxiety and 10-year obesity incidence, independent of antipsychotic or antidepressant use [7]. One limitation of existing research is the coupling of anxiety with depression, restricting the level of evidence for anxiety alone [8].

Anxiety and insomnia tend to be comorbid; it has been estimated that between a quarter and a half of individuals with anxiety also have severe insomnia symptoms [9]. The deleterious effect of comorbid mental disorders on somatic health appears to be greater than the sum of the individual effects of the conditions [10]. To our knowledge, only one epidemiological study has addressed the comorbidity of anxiety and insomnia in relation to metabolic disorders, showing that adults with anxiety-insomnia comorbidity were at 40% greater risk of incident type 2 diabetes than were their counterparts without either disorder [11]. Presently, the main hypothesis was that adults with anxiety-insomnia comorbidity would present a higher risk of incident obesity than their counterparts with neither condition or with either condition in its pure form. Our secondary hypothesis was that the strength of the associations would vary by sex [12].

Methods

This study is part of the MEMORIES project [13] focused on mental-physical multimorbidity among general-population adults. The epidemiological data for MEMORIES came from the ongoing NutriNet-Santé cohort (https://etude-nutrinet-sante.fr/) launched in

2009. Its design and methodology have been described [14]. Men and women from the general population, aged ≥18 years, with Internet access and ability to follow an online protocol in French are eligible for inclusion. 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. Each volunteer provides electronic informed consent prior to enrollment. Next, participants complete a baseline battery of questionnaires assessing sociodemographic and anthropometric characteristics, physical activity and sedentary behavior, physical and mental health status, and dietary intake.

In this study, the outcome was incident obesity assessed with the body mass index (BMI; kg/m^2). At enrollment and biannually thereafter, participants self-report their height and weight using a questionnaire that has been compared against clinical measures [15]. Obesity was defined as a BMI $\geq 30\,kg/m^2$. In turn, anxiety and insomnia were the main exposures. Anxiety was evaluated by self-reports on the 20-item trait anxiety subscale of Spielberger's State-Trait Anxiety Inventory Form Y (STAI-T), validated for use in the French general population [16]. The total score range is 20–80 points, with higher scores indicating greater anxiety proneness. As in previous research, STAI-T ≥ 40 defined high anxiety [17]. The scale was administered between November 2013 and December 2016 to 119 451 participants enrolled for ≥2.5 years; $n = 40\ 809$ completed it once, on a voluntary basis. The STAI-T completion date was considered as baseline for this analysis.

A sleep questionnaire was administered between February and July 2014 to all enrollees at that time ($n = 128\ 042$). In total, 56 718 individuals completed it on a voluntary basis. As previously reported [12], the definition of chronic insomnia (presence versus absence) followed the International Classification of Sleep Disorders—Third Edition (ICSD-3) [18] and the Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (DSM-5) [19]. The criteria included suffering from ≥1 sleep problem (difficulty falling asleep, frequent night waking, etc.) ≥3 nights per week in the past ≥3 months.

As covariates, we used self-reported information on sex, age, education, employment, marital status, smoking, and alcohol consumption. Weekly total physical activity and sedentary behavior (minutes spent sitting) were derived from the International Physical Activity Questionnaire—Short Form [20]. Depressive symptomatology was assessed with the 20-item Center for Epidemiologic Studies-Depression Scale (CES-D) [21]. It assesses symptoms associated with depression over the past week; higher scores indicate higher depressive symptomatology. CES-D cutoffs of ≥ 17 for men and ≥ 23 for women, validated for the French population, were used [21]. Eating disorder (ED) proneness was assessed with the five-item Sick-Control-One-Fat-Food (SCOFF) questionnaire where ≥2 positive responses indicates a strong likelihood of having an ED [22]. Medication use data (e.g. antidepressants, corticoids, oral contraceptives) that might promote weight gain were also collected using reimbursement information from the national health insurance database to which NutriNet-Santé is linked. Finally, mean daily energy intake without alcohol (kcal/day) and diet quality as measured by the simplified *Programme National Nutrition Santé* Guidelines Score 2 (sPNNS-GS2) were assessed using ≥3 24-hour dietary records, which participants complete every 6 months. sPNNS-GS2 measures adherence to French dietary guidelines [23]. Consumption of health-promoting foods (e.g. fruits, vegetables, nuts) positively impacts the total score, while consumption of foods to be consumed with moderation (e.g. salty food, red meat) has a negative impact; higher scores (theoretical range: −17.0 to +13.5 points) reflect better diet quality. The score was modeled on a continuous scale.

For this analysis, we used covariate data provided within a 2.5-year window around baseline. Each covariate except ED contained <5% missing data; participants with incomplete data were excluded while a "missing data" modality was created for ED. Additionally, women who were pregnant at any point during the study period, participants without anthropometric data or with obesity at baseline, those with <2 anthropometric measures during the follow-up, and those with <6 months of follow-up were excluded. Mental morbidity/comorbidity groups were created as follows: (i) neither anxiety nor insomnia (reference), (ii) anxiety alone, (iii) insomnia alone, and (iv) comorbid anxiety and insomnia. Descriptive characteristics, obtained with Chi-squared or Student *t* tests, in the full sample and by sex are presented in Table 1. A comparison of incident obesity rates by baseline mental morbidity group is presented in Table 2, using Cox models adjusted for age (described below).

In the main analysis, we assessed the association between mental morbidity and the incidence of obesity using multivariable Cox proportional hazards models, with age used as the time scale. Participants contributed person-time from their age at baseline (i.e. age at which they completed STAI-T) to their age at obesity onset (defined as the age halfway between the anthropometrics questionnaire where self-reported weight/height corresponding to obesity was first reported, and the previous assessment where BMI did not correspond to obesity), age at last follow-up, age at death, or age as of 1 March 2024, whichever occurred first. The proportional hazards assumption of the Cox model was confirmed using the rescaled Schoenfeld-type residual method. Two different models were computed: Model 1 was adjusted for sex, and Model 2 was further adjusted for marital status, employment, education, sedentariness, physical activity, alcohol consumption, smoking status, depressive symptoms, and ED. Interaction tests by sex were performed, consistent with the secondary hypothesis.

Finally, five sets of sensitivity analyses were conducted to assess the robustness of the findings, using Model 2 as the basis: (i) with further adjustment for medication use that might promote weight gain; (ii) with further adjustment for baseline BMI; (iii) with further adjustment for mean total energy intake and diet quality; (iv) a model with the full sample, imputing missing covariate data using the mode or the mean values; and (v) a model with the full sample, excluding prevalent cases of cancer, diabetes, major cardiovascular disease, or bariatric surgery.

The main tests were two-sided and $P < .05$ was considered as evidence for statistical significance. R version 4.3.1 (R Foundation, Vienna, Austria) was used for the analyses.

Results

A total of 36 474 participants in the NutriNet-Santé cohort had complete data on anxiety and insomnia and were thus eligible for this analysis. The final sample consisted of 23 797 participants who met the inclusion criteria (72% women; mean age = 55.5 ± 12.7 years) (Fig. 1). Baseline characteristics are presented in Table 1. The participants were predominantly female, relatively well educated and non-smoking. Men were older, had higher rates of overweight, were more sedentary, had more depressive symptoms, and had higher alcohol consumption than women (all $P < .001$ except for sedentariness $P < .05$).

Table 2 shows the overall and sex-specific prevalence of mental morbidity according to incident obesity status. In the full sample, 29.1% had anxiety alone, 6.5% had insomnia alone, and 47.6% had neither disorder ($P < .001$). Overall, 16.8% of the participants who developed obesity presented an anxiety-insomnia comorbidity at baseline versus 11.6% of those who did not develop obesity ($P < .001$). Among women who developed obesity, 17.7% had an anxiety-insomnia comorbidity versus 13.7% of women who did not develop obesity ($P < .05$); among men who developed obesity, 14.5% had an anxiety-insomnia comorbidity versus 6.5% of men who did not develop obesity ($P < .001$).

Table 3 presents the results of the multivariable Cox models, with "no anxiety or insomnia" used as reference. During a mean follow-up of 6.2 ± 2.0 years, 733 incident cases of obesity were observed. In Model 1, anxiety-insomnia comorbidity emerged as a significant predictor of incident obesity across sex (HR: 1.58; 95% CI: 1.28, 1.94). In the fully adjusted model (Model 2), this association was no longer significant in the whole sample (HR: 1.12; 95% CI: 0.89, 1.42). Likewise, participants with high anxiety or insomnia did not have

Table 1. Baseline characteristics[a] of participants in the full sample and by sex (NutriNet-Santé cohort, France, 2013–24)

	Full sample *N* = 23 797	Men *N* = 6779 (28.5%)	Women *N* = 17 018 (71.5%)	*P*-value[b]
BMI, kg/m^2, mean (SD)	23.1 (2.9)	24.3 (2.5)	22.6 (2.9)	<.001
BMI category				<.001
Underweight (<18.5)	1090 (4.6)	69 (1.0)	1021 (6.0)	
Normal weight (18.5–24.9)	16 377 (68.8)	4087 (60.3)	12 290 (72.2)	
Overweight (25.0–29.9)	6330 (26.6)	2623 (38.7)	3707 (21.8)	
Age, years, mean (SD)	55.5 (12.7)	58.2 (13.4)	54.5 (12.2)	<.001
Age category				<.001
<35 years	1753 (7.4)	484 (7.1)	1269 (7.4)	
35–54 years	8741 (36.7)	1935 (28.5)	6806 (40.0)	
55–64 years	6407 (26.9)	1643 (24.2)	4764 (28.0)	
≥65 years	6896 (29.0)	2717 (40.1)	4179 (24.6)	
Educational level				<.001
Less than high school	3729 (15.7)	1136 (16.8)	2593 (15.2)	
High school diploma	4272 (17.9)	1210 (17.8)	3062 (18.0)	
College, undergraduate degree	7566 (31.8)	1698 (25.0)	5868 (34.5)	
Graduate degree	8230 (34.6)	2735 (40.3)	5495 (32.3)	
Professional category[c]				<.001
Manual, blue collar, farmer, office work/administrative staff	7043 (29.6)	1321 (19.5)	5722 (33.6)	
Professional/executive staff	5179 (21.8)	1670 (24.6)	3509 (20.6)	
Retired	9515 (40.0)	3540 (52.2)	5975 (35.1)	
Without professional activity	2060 (8.6)	248 (3.7)	1812 (10.6)	
Marital status				<.001
Living alone (single, divorced, widowed)	5941 (25.0)	1142 (16.8)	4799 (28.2)	
Married, cohabiting	17 856 (75.0)	5637 (83.2)	12 219 (71.8)	
Physical activity level[d]				<.001
Low	4720 (19.8)	1207 (17.8)	3513 (20.6)	
Moderate	9502 (39.9)	2410 (35.6)	7092 (41.7)	
High	9575 (40.2)	3162 (46.6)	6413 (37.7)	
Sedentariness, minutes spent sitting/d[d], mean (SD)	340 (186)	344 (189)	338 (184)	.02
Alcohol use, g ethanol/d, median (first quartile-third quartile)	4.3 (0.7–7.6)	8.6 (2.9–18.6)	2.9 (0.7–5.6)	<.001
Smoking status				<.001
Never smoker	11 851 (49.8)	2921 (43.1)	8930 (52.5)	
Former smoker	9556 (40.2)	3244 (47.9)	6312 (37.1)	
Current smoker	2390 (10.0)	614 (9.0)	1776 (10.4)	
Depressive symptoms[e] (yes)	2631 (11.1)	877 (12.9)	1754 (10.3)	<.001
Eating disorders[f] (yes)	1976 (8.3)	299 (4.4)	1677 (9.9)	<.001
Mean total energy intake[g] (Kcal/day)	1857 (414)	2171 (427)	1725 (328)	<.001
Diet quality index[h] (sPNNS-GS2)	1.68 (3.3)	0.11 (3.5)	2.3 (3.0)	<.001
Use of medications that promote weight gain (yes)	11 679 (49.1)	3261 (48.1)	8418 (49.5)	.06

a: Values represent *n* (%) unless noted otherwise.
b: Obtained by Student *t* tests or Pearson's Chi-squared test, as appropriate.
c: "Without professional activity" includes "homemaker, disabled, unemployed, or student."
d: Assessed with the International Physical Activity Questionnaire-Short Form according to established scoring criteria.
e: Depressive symptomatology was defined as Center for Epidemiologic Studies-Depression Scale, CES-D ≥ 17 in men and CES-D ≥ 23 in women.
f: Eating disorder proneness was assessed with ≥2 affirmative responses on the five-item SCOFF questionnaire; 2954 data points were missing.
g: 7350 data points were missing.
h: The theoretical range of the sPNNS-GS2 is from −17.0 to +13.5 points, with a higher score reflecting better diet quality. 7350 data points were missing.
BMI: body mass index; SD: standard deviation; sPNNS-GS2: simplified *Programme National Nutrition Santé*—Guidelines Score 2.

an increased risk of incident obesity compared with participants without anxiety or insomnia.

As the significance level of the interaction test was $P = .06$, we also performed sex-specific analyses (Table 3). In women ($n = 17\ 018$; $n = 526$ incident obesity cases), similar results for anxiety-insomnia comorbidity were observed as in the full sample (Model 2 HR: 1.00; 95% CI: 0.77, 1.30). In men ($N = 6779$; $n = 207$ incident obesity cases), a significant association between anxiety-insomnia comorbidity and incident obesity was found in both adjusted models (Model 2 HR: 1.71, 95% CI: 1.06, 2.76). Men and women with high anxiety or insomnia did not have an increased risk of incident obesity compared with men and women without these disorders.

Results of the sensitivity analyses are presented in Supplementary Table S1. Overall, the findings remained largely unchanged in the full sample. The same sensitivity analyses were then carried out in each sex. In women (Supplementary Table S2), the results were unchanged following further adjustment for use of weight gain-promoting medication, following simple imputation for covariates, and in a reduced sample of $n = 14\ 544$ excluding women with a medical history. In the analysis with $n = 17\ 018$ women (526 incident obesity cases, 163 pure anxiety cases, 33 pure insomnia cases, 93 anxiety-insomnia comorbidity cases) with further adjustment for BMI at baseline, chronic insomnia alone was associated with a lower risk of obesity (HR: 0.69, 95% CI: 0.48, 0.99). Finally, owing to missing data on dietary intake, the sample was reduced to $n = 11\ 576$ women, including 316 incident obesity cases, 106 pure anxiety cases, 14 pure insomnia cases, and 51 anxiety-insomnia comorbidity cases. This analysis included further adjustment for mean total dietary energy intake and diet quality; chronic insomnia was again associated with a lower risk of obesity (HR: 0.56, 95% CI: 0.32, 0.97).

In men (Supplementary Table S3), the anxiety-insomnia comorbidity remained a significant predictor of incident obesity in the

Table 2. General and sex-specific prevalence of each mental morbidity group according to obesity status at follow-up, NutriNet-Santé cohort, France

	Full sample				Men				Women			
	Overall $N = 23\,797$	No incident obesity $n = 23064$	Incident obesity $n = 733$	P[a]	Overall $N = 6\,779$	No incident obesity $n = 6572$	Incident obesity $n = 207$	P[a]	Overall $N = 17\,018$	No incident obesity $n = 16492$	Incident obesity $n = 526$	P[a]
Mental morbidity groups				<.001				<.001				.03
No anxiety or insomnia	12 795 (53.8)	12 446 (54.0)	349 (47.6)		4496 (66.3)	4384 (66.7)	112 (54.1)		8299 (48.8)	8062 (48.9)	237 (45.1)	
High trait anxiety alone[b]	6408 (26.9)	6195 (26.9)	213 (29.1)		1427 (21.1)	1377 (21.0)	50 (24.2)		4981 (29.3)	4818 (29.2)	163 (31.0)	
Chronic insomnia alone	1786 (7.5)	1738 (7.5)	48 (6.5)		399 (5.9)	384 (5.8)	15 (7.2)		1387 (8.2)	1354 (8.2)	33 (6.3)	
Anxiety-insomnia comorbidity	2808 (11.8)	2685 (11.6)	123 (16.8)		457 (6.7)	427 (6.5)	30 (14.5)		2351 (13.8)	2258 (13.7)	93 (17.7)	

Values represent n (%).
a: Obtained by Cox proportional hazards model adjusted for age (time scale).
b: High trait anxiety defined as STAI-T $\geq$ 40. STAI-T, form Y; score range: 20–80 points; higher scores reflect higher proneness to anxiety.

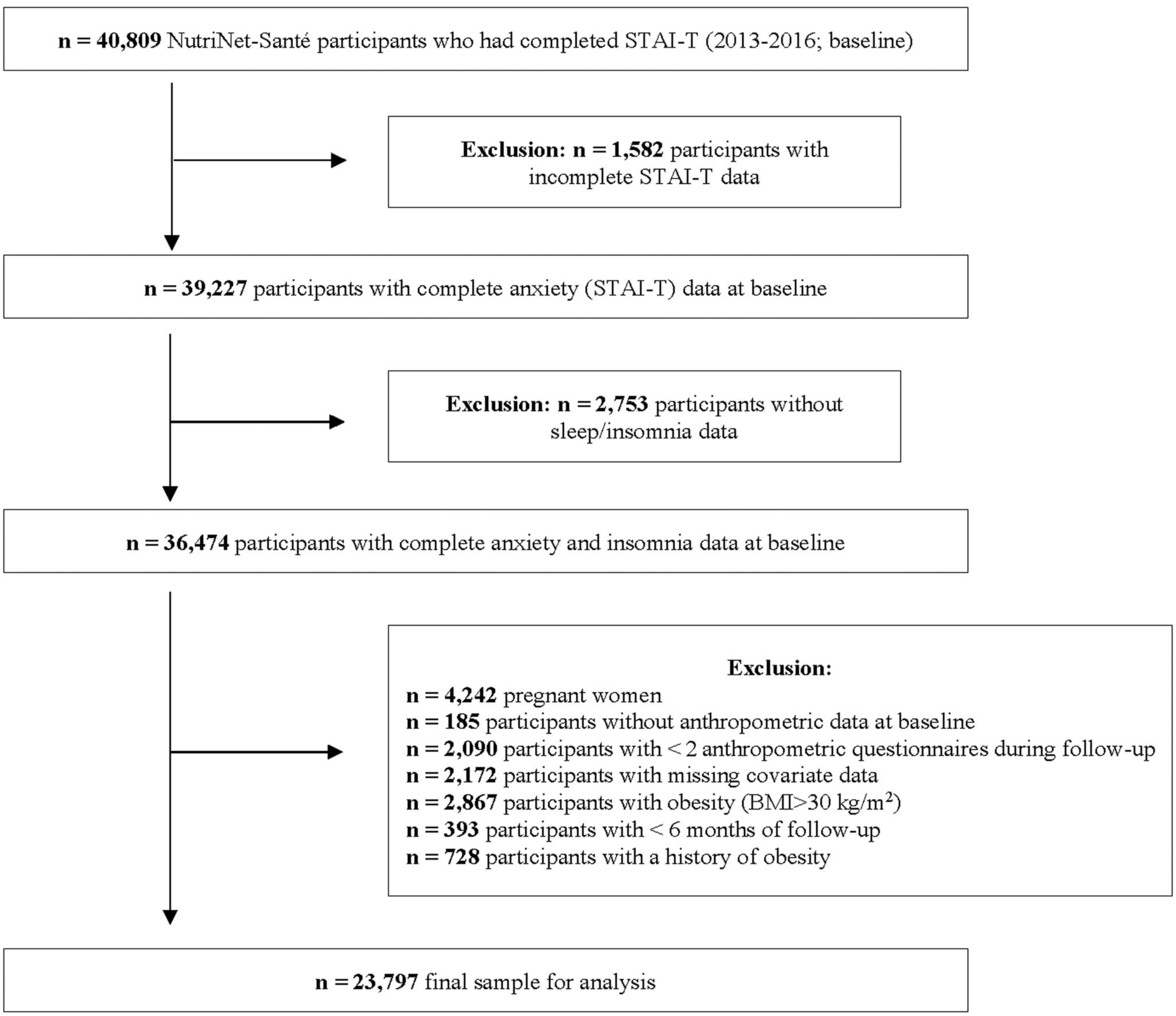

Figure 1. Participant selection flowchart.

following sensitivity analyses: (i) with further adjustment for use of weight gain-promoting medication, (iv) with simple imputation for covariates, and (v) in a reduced sample of $n = 5327$ excluding men with a medical history. Next, for sensitivity analysis (ii), which was further adjusted for baseline BMI, there were $n = 6779$ men (207 incident obesity cases; 50 pure anxiety cases; 15 pure insomnia cases; 40 anxiety-insomnia comorbidity cases), the association was in the hypothesized direction but no longer significant (HR: 1.60, 95% CI: 0.99, 2.61). Finally, owing to missing data on dietary intake, for analysis (iii), the sample was reduced to $n = 4871$ men, including 124 incident obesity cases, 22 cases of pure anxiety, 12 cases of pure insomnia, and 14 cases of anxiety-insomnia comorbidity. This analysis included further adjustment for mean total dietary energy intake and diet quality; the association between anxiety-insomnia comorbidity

Table 3. Associations between mental morbidity and incident obesity in the full sample and by sex, NutriNet-Santé cohort, France (2013–24)

	Full sample ($n = 23\ 797$)						Men ($n = 6779$)						Women ($n = 17\ 018$)					
			Model 1		Model 2				Model 1		Model 2				Model 1		Model 2	
	N cases/ total at risk	Person-years	HR (95% CI)	*P*	HR (95% CI)	*P*	*N* cases/ total at risk	Person-years	HR (95% CI)	*P*	HR (95% CI)	*P*	*N* cases/ total at risk	Person-years	HR (95% CI)	*P*	HR (95% CI)	*P*
No anxiety or insomnia	343/12 795	79 715	*ref*		*ref*		112/4496	28 448	*ref*		*ref*		237/8299	51 267	*ref*		*ref*	
High trait anxiety alone[a]	213/6408	11 061	1.21 (1.02–1.44)	.03	0.98 (0.81–1.17)	.81	50/1427	8863	1.40 (1.00–1.96)	.05	1.11 (0.77–1.61)	.57	163/4981	30 474	1.14 (0.93–1.39)	.21	0.93 (0.75–1.14)	.48
Chronic insomnia alone	48/1786	39 338	1.00 (0.74–1.35)	.97	0.92 (0.68–1.25)	.59	15/399	2510	1.50 (0.88–2.58)	.14	1.36 (0.79–2.34)	.27	33/1387	8551	0.85 (0.59–1.22)	.38	0.79 (0.55–1.14)	.21
Anxiety-insomnia comorbidity	123/2808	17 361	1.58 (1.28–1.94)	<.0001	1.12 (0.89–1.42)	.33	30/457	2933	2.40 (1.60–3.61)	<.0001	1.71 (1.06–2.76)	.03	93/2351	14 429	1.38 (1.08–1.75)	.0009	1.00 (0.77–1.30)	.99

Model 1 is a Cox model adjusted for age (time scale).

Model 2 is a Cox model adjusted for age (time scale), marital status, employment category, educational level, sedentariness, physical activity, alcohol consumption, smoking status, depressive symptoms, and eating disorders.

a: High trait anxiety defined as STAI-T $\geq$ 40. STAI-T, form Y; score range: 20–80 points; higher scores reflect higher proneness to anxiety.

CI: confidence interval; HR: hazard ratio.

and incident obesity was again in the hypothesized direction but no longer significant (HR: 1.17; 95% CI: 0.59, 2.29).

Discussion

In this prospective study of 23 797 adults recruited from the general population, we investigated the association of anxiety, insomnia, and their comorbidity with obesity risk during a mean follow-up of 6.2 years. We compared obesity risk in four morbidity groups established at baseline: no anxiety or insomnia (reference), anxiety alone, insomnia alone, and anxiety-insomnia comorbidity. In the fully adjusted model, no significant association was observed between anxiety-insomnia comorbidity and incident obesity in the overall sample, contrary to our main hypothesis. In turn, our secondary hypothesis was partially confirmed since a borderline significant interaction by sex was observed. A significant association between anxiety-insomnia comorbidity and incident obesity was found only in men, showing that those who had mental comorbidity had a 71% higher risk of developing obesity than their comorbidity-free counterparts. No such associations emerged in women. Our findings are somewhat consistent with those from the population-based HUNT cohort, where an association between anxiety and incident obesity was found only in men [8].

In this study, baseline prevalence of overweight (i.e. persons at risk) varied by sex, being substantially higher in men than in women (38.7% versus 21.8%, respectively). The ratio of the number of cases with mental comorbidity to the total number of persons at risk was likewise twice as high among men than among women (6.5% versus 3.9%, respectively). Taken together, these aspects might partly explain the significant results obtained only in men. The discrepancy between men and women could also be partly due to differences in eating habits and lifestyle. Stress and sleep difficulties likely have a sex-specific impact on food choices, particularly regarding comfort and palatable foods. Men might be more inclined to choose meal-type foods (e.g. hamburgers, steak) whereas women might prefer sweet snacks [24, 25]. Sex-specific differences in multiple components of the hypothalamic-pituitary-adrenal (HPA) axis in response to stress have also been documented. In fact, androgens have been shown to increase and estrogens to decrease HPA activity in adulthood [26]. Chronic stress is a known disruptor of energy homeostasis, leading to deleterious consequences in emotion and metabolism regulation [27]. Women might be more vulnerable to the psychological consequences of stress (e.g. anxiety, depression) while men might have increased vulnerability to the metabolic consequences of stress (e.g. insulin resistance, altered fat distribution) [27, 28].

The present findings also suggest potential differences in the etiology of obesity associated with pure versus comorbid mental disorders. We did not find a significant association between anxiety alone and incident obesity, which contrasts with previous studies. For example, following adjustment for use of antidepressants and antipsychotics, a prospective association was reported between a history of anxiety and risk of obesity among psychiatric patients [7]. Another study carried out in the HUNT cohort found an association between anxiety or depression and obesity, that was adjusted for insomnia symptoms [8]. Individuals with a mental health diagnosis have a significantly higher risk of developing a second mental health disorder compared with their healthy counterparts [29]. In addition, there is a strong association between comorbidity and symptom severity [30]. It is therefore crucial to consider the co-occurrence of ≥2 mental health conditions when identifying populations at high risk and when designing effective public health programs, particularly those aimed at obesity prevention. Presently, public health policy, healthcare systems, and clinical guidelines are largely centered on individual illnesses rather than comorbidity [31].

In the full sample, results remained largely unchanged in the sensitivity analyses. Among men, the results were also mostly unchanged. In models further adjusted for baseline BMI and diet-related variables, respectively, the association between anxiety-insomnia comorbidity and incident obesity were in the hypothesized direction but not significant due to insufficient statistical power (only 14 anxiety-insomnia comorbidity cases). Among women, in analyses with additional adjustment for baseline BMI or total energy intake and diet quality, insomnia emerged as a protective factor for incident obesity. This was an unexpected finding and should be investigated further before attributing it to chance. Whereas baseline BMI was modeled as a confounder, it might also be a mediator of the association, in which case controlling for it might have produced over-adjustment of the models. Future research could also explore the role of sleep duration alongside these mental disorders, which was not possible to address in this study. It has been shown that insufficient sleep or poor sleep quality could heighten food reward sensitivity, leading to increased snacking and a preference for high-fat, high-carbohydrate, energy-dense foods which, over time, increases the risk of weight gain and obesity [2, 32].

This study has some limitations. Chronic insomnia and trait anxiety were measured by self-report questionnaires that included validated scales and criteria widely used in epidemiology, yet these measurements do not replace clinical diagnoses. Individuals with the most severe symptoms of anxiety or insomnia might not have been included in this analysis, potentially reducing variability in the measures and introducing selection bias. Moreover, insomnia was assessed over 6 months (2014), whereas anxiety was assessed over 38 months (2013–16), thus numerous participants had provided anxiety data a few months after providing insomnia data. However, that gap is likely to have a relatively minor impact on the analyses, given the chronicity of both conditions. Next, the dependent variable—BMI—was calculated using self-reported data. Moreover, the studied associations might depend on the obesity measure used, as shown in our previous work [12] or BMI might be a mediator of the association between mental illness and obesity risk. Next, despite the ability to perform sex-specific analyses, the interaction test was borderline significant. Future, sufficiently powered studies using sex-balanced samples are necessary to replicate the analyses and confirm the sex-specific effects. In turn, some residual confounding might have persisted, potentially increasing the risk of biased effect estimates. For example, in order to preserve the available sample sizes for subgroup analyses, we were unable to adjust for sleep duration which is a known dimension of sleep health. It is also important to note that the sensitivity analyses might have produced unstable risk estimates, as few cases of obesity, anxiety, and insomnia were observed, especially in men. Adjustment for dietary variables substantially reduced the sensitivity analysis sample. Finally, the available sample might be considered over-selected, making it somewhat challenging to conclude about the true strength of associations. Participants included in the analysis were generally older, more likely to be retired, to report higher levels of physical activity, and were less likely to be current smokers compared to those who were excluded from the analysis [33, 34]. Moreover, the NutriNet-Santé cohort includes a higher proportion of well-educated individuals with a greater interest in health and nutrition than in the general French population, which might limit the external validity of the findings [35, 36].

Despite the limitations, the study has important strengths. To our knowledge, this is the first study to address a relevant public health question by examining the relationship between anxiety-insomnia comorbidity and obesity incidence. We used a large and diverse sample of French adults, a prospective design, validated mental health, anthropometric, and sociodemographic tools, and extensive covariate adjustment. Another notable strength was the availability of data on multiple mental health conditions (e.g. anxiety, insomnia, depressive symptoms, ED) and physical health status.

The findings advance knowledge about multimorbidity in a public health context and suggest potential sex-specific associations between mental health and obesity risk. Specifically, in this large prospective study, men with anxiety-insomnia comorbidity had a 71% higher 6-year risk of incident obesity than men who had neither anxiety nor insomnia. Further research is needed to better understand the observed sex differences and to replicate the models in different populations. Given the relatively high prevalence of anxiety, insomnia, and obesity in the general population, it is important to decipher their interrelations in order to develop effective obesity prevention strategies.

Acknowledgements

The authors thank Cédric Agaësse (dietary data supervisor), Alexandre De-Sa and Laure Legris (dietitians); Selim Aloui (IT manager), Thi Hong Van Duong, Régis Gatibelza, and Aladi Timera (computer scientists); Julien Allegre, Nathalie Arnault, Laurent Bourhis, Nicolas Dechamp (biostatisticians), and Fabien Szabo de Edelenyi, PhD (biostatistics team leader); Nadia Khemache and Marie Ajanohun (administrative support), Maria Gomes and Mirette Foham (NutriNet-Santé participant support); and Paola Yvroud, MD (health event validator and cohort coordinator) for their technical contribution to the NutriNet-Santé study. The authors would like to thank all the volunteers in the cohort.

Author contributions

V.A.A., C.S., S.C., G.F., and L.K.F. developed the MEMORIES project on which this study is based; E.K.-G., S.H., P.G., and M.T. designed and implemented the NutriNet-Santé cohort study; P.G. and V.A.A. implemented the STAI questionnaire and coordinated anxiety data collection; P.G., D.L., and V.A.A. implemented the sleep questionnaire and coordinated insomnia data collection; V.A.A. and L.K.F. conceptualized the study, designed the analytic strategy, and provided theoretical, empirical, and methodological guidance; M.-C.B. and L.F. K. provided theoretical guidance regarding the etiology of obesity and metabolic disorders; P.D. performed the literature review, statistical analyses, and led the writing; all authors assisted with interpretation of the data, critically revised the manuscript for important intellectual content. All authors approved the final version of the manuscript and its submission.

Supplementary data

Supplementary data are available at *EURPUB* online.

Conflict of interest: The authors have no relevant financial or non-financial interests to disclose.

Funding

The MEMORIES project is funded by the French National Research Agency (Grant No. ANR-21-CE36-0003-01; Dr. Andreeva—PI; P. Duquenne—doctoral studies support). The NutriNet-Santé study is supported by the French Ministry of Solidarity and Health, the National Public Health Agency (Santé Publique France), the National Institute of Health and Medical Research (INSERM), the National Research Institute for Agriculture, Food and the Environment (INRAE), the National Conservatory of Arts and Crafts (CNAM), and Sorbonne Paris Nord University. Florine Berthy was supported by a doctoral fellowship from Sorbonne Paris Nord University—Galilée Doctoral School. The funders had no role in the design of the study; in the collection, analysis, or interpretation of the data; the writing of the manuscript; or in the decision to publish the results.

Data availability

Researchers from public institutions can submit a request for collaboration, including information about their institution and a brief description of the proposed project, to collaboration@etude-nutrinet-sante.fr. All requests are reviewed by the NutriNet-Santé steering committee. If the request is approved, a data access agreement will be required and appropriate authorizations from the competent administrative authorities may be needed. In accordance with existing regulations, no personal data will be accessible. Requests for the statistical programs used to perform the analyses can be addressed to the corresponding author.

Ethics approval

The NutriNet-Santé cohort study is conducted in accordance with the principles outlined in the Declaration of Helsinki. It has been approved by the Institutional Review Board of the French Institute for Health and Medical Research (INSERM # 00000388FWA00005831) and by the National Commission on Informatics and Liberty (CNIL # 908450 and # 909216). NutriNet-Santé is registered at: https://clinicaltrials.gov/ct2/show/NCT03335644. Informed consent was obtained in an electronic format from all volunteers prior to enrollment in the cohort.

Key points

- Prospective data from 23 797 adults from the ongoing NutriNet-Santé general-population cohort were used to investigate the association between pure and comorbid anxiety and insomnia as risk factors for incident obesity.
- Men with anxiety-insomnia comorbidity had a 71% higher risk of developing obesity over an average of 6 years compared to their counterparts free of mental disorders at baseline.
- No associations were observed between anxiety alone or insomnia alone and incident obesity.
- This large prospective study advances public health knowledge about multimorbidity in the context of public health and can help inform preventive action.

References

1 Palagini L, Miniati M, Caruso V *et al.* Insomnia, anxiety and related disorders: a systematic review on clinical and therapeutic perspective with potential mechanisms underlying their complex link. *Neurosci Appl* 2024;**3**:103936. https://doi.org/10.1016/j.nsa.2024.103936

2 St-Onge MP, Shechter A. Sleep disturbances, body fat distribution, food intake and/or energy expenditure: pathophysiological aspects. *Horm Mol Biol Clin Investig* 2014;**17**:29–37. https://doi.org/10.1515/hmbci-2013-0066

3 Dymek A, Zielińska M, Englert-Bator A *et al.* Generalized anxiety disorder and obesity: overlapping neuroendocrine, metabolic, and behavioral pathways. *Nutrients* 2025;**17**:2835. https://doi.org/10.3390/nu17172835

4 Bacaro V, Ballesio A, Cerolini S *et al.* Sleep duration and obesity in adulthood: an updated systematic review and meta-analysis. *Obes Res Clin Pract* 2020;**14**:301–9. https://doi.org/10.1016/j.orcp.2020.03.004

5 Fatima Y, Doi SAR, Mamun AA. Sleep quality and obesity in young subjects: a meta-analysis. *Obes Rev* 2016;**17**:1154–66. https://doi.org/10.1111/obr.12444

6 Chan WS, Levsen MP, McCrae CS. A meta-analysis of associations between obesity and insomnia diagnosis and symptoms. *Sleep Med Rev* 2018;**40**:170–82. https://doi.org/10.1016/j.smrv.2017.12.004

7 Perez-Pinar M, Mathur R, Foguet Q *et al.* Cardiovascular risk factors among patients with schizophrenia, bipolar, depressive, anxiety, and personality disorders. *Eur Psychiatry* 2016;**35**:8–15. https://doi.org/10.1016/j.eurpsy.2016.02.004

8 Brumpton B, Langhammer A, Romundstad P *et al.* The associations of anxiety and depression symptoms with weight change and incident obesity: the HUNT study. *Int J Obes (Lond)* 2013;**37**:1268–74. https://doi.org/10.1038/ijo.2012.204

9 Soehner AM, Harvey AG. Prevalence and functional consequences of severe insomnia symptoms in mood and anxiety disorders: results from a nationally representative sample. *Sleep* 2012;**35**:1367–75. https://doi.org/10.5665/sleep.2116

10 Coste J, Valderas JM, Carcaillon-Bentata L. Estimating and characterizing the burden of multimorbidity in the community: a comprehensive multistep analysis of two large nationwide representative surveys in France. *PLoS Med* 2021;**18**:e1003584. https://doi.org/10.1371/journal.pmed.1003584

11 Duquenne P, Samieri C, Chambaron S *et al.* Chronic insomnia, high trait anxiety and their comorbidity as risk factors for incident type 2 diabetes mellitus. *Sci Rep* 2024;**14**:11927. https://doi.org/10.1038/s41598-024-62675-y

12 Andreeva VA, Torres MJ, Druesne-Pecollo N *et al.* Sex-specific associations of different anthropometric indices with acute and chronic insomnia. *Eur J Public Health* 2017;**27**:1026–31. https://doi.org/10.1093/eurpub/ckx123

13 National Research Agency (ANR). *Mental Health Status as a Determinant of Nutrition-Related Chronic Diseases—MEMORIES.* Paris: ANR, 2021. https://anr.fr/Project-ANR-21-CE36-0003

14 Hercberg S, Castetbon K, Czernichow S *et al.* The NutriNet-Santé study: a web-based prospective study on the relationship between nutrition and health and determinants of dietary patterns and nutritional status. *BMC Public Health* 2010;**10**:242. https://doi.org/10.1186/1471-2458-10-242

15 Lassale C, Peneau S, Touvier M *et al.* Validity of web-based self-reported weight and height: results of the Nutrinet-Sante study. *J Med Internet Res* 2013;**15**:e152. https://doi.org/10.2196/jmir.2575

16 Bruchon-Schweitzer M, Paulhan I. *STAI-Y: Inventaire d'anxiété etat-trait Forme Y/C. D. Spielberger*. Paris: Éditions du Centre de Psychologie Appliquée, 1993.

17 Kose J, Cheung A, Fezeu LK *et al.* A comparison of sugar intake between individuals with high and low trait anxiety: results from the NutriNet-Santé study. *Nutrients* 2021;**13**:1526. https://doi.org/10.3390/nu13051526

18 American Academy of Sleep Medicine (AASM). *International Classification of Sleep Disorders—Third Edition (ICSD-3).* Darien: AASM, 2014.

19 American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders (DSM–5).* Washington: APA, 2013.

20 Craig CL, Marshall AL, Sjostrom M *et al.* International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;**35**:1381–95. https://doi.org/10.1249/01.MSS.0000078924.61453.FB

21 Fuhrer R, Rouillon F. The French version of the CES-D (Center for Epidemiologic Studies-Depression Scale). *Eur Psychiatry* 1989;**4**:163–6. https://doi.org/10.1017/S0767399X00001590

22 Garcia FD, Grigioni S, Allais E *et al.* Detection of eating disorders in patients: validity and reliability of the French version of the SCOFF questionnaire. *Clin Nutr* 2011;**30**:178–81. https://doi.org/10.1016/j.clnu.2010.09.007

23 Chaltiel D, Adjibade M, Deschamps V *et al.* Programme National Nutrition Sante – Guidelines Score 2 (PNNS-GS2): development and validation of a diet quality score reflecting the 2017 French dietary guidelines. *Br J Nutr* 2019;**122**:331–42. https://doi.org/10.1017/S0007114519001181

24 Wansink B, Cheney MM, Chan N. Exploring comfort food preferences across age and gender. *Physiol Behav* 2003;**79**:739–47. https://doi.org/10.1016/S0031-9384(03)00203-8

25 Kose J, Fezeu LK, Touvier M *et al.* Dietary macronutrient intake according to sex and trait anxiety level among non-diabetic adults: a cross-sectional study. *Nutr J* 2021;**20**:78. https://doi.org/10.1186/s12937-021-00733-1

26 Goel N, Workman JL, Lee TT *et al.* Sex differences in the HPA axis. *Compr Physiol* 2014;**4**:1121–55. https://doi.org/10.1002/j.2040-4603.2014.tb00575.x

27 Krolick KN, Shi H. Estrogenic action in stress-induced neuroendocrine regulation of energy homeostasis. *Cells* 2022;**11**:879. https://doi.org/10.3390/cells11050879

28 Jeong IK. The role of cortisol in the pathogenesis of the metabolic syndrome. *Diabetes Metab J* 2012;**36**:207–10. https://doi.org/10.4093/dmj.2012.36.3.207

29 McGrath JJ, Lim CCW, Plana-Ripoll O *et al.* Comorbidity within mental disorders: a comprehensive analysis based on 145 990 survey respondents from 27 countries. *Epidemiol Psychiatr Sci* 2020;**29**:e153. https://doi.org/10.1017/S2045796020000633

30 Kessler RC, Chiu WT, Demler O *et al.* Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry* 2005;**62**:617–27. https://doi.org/10.1001/archpsyc.62.6.617

31 Makovski TT, Cuschieri S, Valderas JM *et al.* Preventing multimorbidity: moving beyond the single disease lens. *Int J Public Health* 2025;**70**:1608880. https://doi.org/10.3389/ijph.2025.1608880

32 Zuraikat FM, Wood RA, Barragan R *et al.* Sleep and diet: mounting evidence of a cyclical relationship. *Annu Rev Nutr* 2021;**41**:309–32. https://doi.org/10.1146/annurev-nutr-120420-021719

33 Kose J, Paz Graniel I, Peneau S *et al.* A population-based study of macronutrient intake according to mental health status with a focus on pure and comorbid anxiety and eating disorders. *Eur J Nutr* 2022;**61**:3685–96. https://doi.org/10.1007/s00394-022-02923-x

34 Andreeva VA, Torres MJ, Leger D *et al.* Major change in body weight over 5 years and total sleep time: investigation of effect modification by sex and obesity in a large e-cohort. *Int J Behav Med* 2017;**24**:493–500. https://doi.org/10.1007/s12529-017-9635-6

35 Andreeva VA, Salanave B, Castetbon K *et al.* Comparison of the sociodemographic characteristics of the large NutriNet-Sante e-cohort with French census data: the issue of volunteer bias revisited. *J Epidemiol Community Health* 2015;**69**:893–8. https://doi.org/10.1136/jech-2014-205263

36 Andreeva VA, Deschamps V, Salanave B *et al.* Comparison of dietary intakes between a large online cohort study (Etude NutriNet-Santé) and a nationally representative cross-sectional study (Etude Nationale Nutrition Santé) in France: addressing the issue of generalizability in epidemiology. *Am J Epidemiol* 2016;**184**:660–9. https://doi.org/10.1093/aje/kww016

European Journal of Public Health, 2026, 36, 1–8
https://doi.org/10.1093/eurpub/ckag049
Original Manuscript