BMC Gastroenterology

RESEARCH

Open Access

Association between gastrointestinal disorders and sleep-related problems: the mediating effect of depression

Shicheng Ye[1,2], Lili Sui[3], Xuan Zeng[1], Zhiwei Dong[3], Zhongqin Liao[1] and Chongzheng Qu[1,2*]

Abstract

Background The relationship between gastrointestinal(GI) diseases and sleep-related problems—such as sleep trouble and sleep disorders—remains insufficiently understood.

Methods Data were derived from the 2005–2014 U.S. National Health and Nutrition Examination Survey (NHANES). Multicollinearity was evaluated using variance inflation factors. Multivariable logistic regression and subgroup analyses were conducted to assess the association between GI diseases and sleep trouble. Mediation analyses explored whether depression mediated the relationships between GI diseases and sleep outcomes, including sleep trouble, sleep disorders, and sleep duration. Sensitivity analyses were performed to evaluate the robustness of the results.

Results In the context of fully adjusted models, individuals afflicted with gastrointestinal diseases exhibited an elevated propensity for experiencing sleep disturbances in comparison with those not affected by such conditions. (adjusted OR = 1.70, 95% CI: 1.41–2.05, $P < .001$). They also showed increased odds of sleep disorders (adjusted OR = 1.80, 95% CI: 1.34–2.41, $P < .001$) and a reduction in sleep duration (adjusted $\beta = -0.15$, 95% CI: −0.29 to −0.01, $P = 0.038$). These associations remained consistent across subgroups, including individuals without hypertension (adjusted OR = 1.69), without diabetes (adjusted OR = 1.72), with no smoking history (adjusted OR = 1.73), those with coronary artery disease (adjusted OR = 1.76), and those with higher DI-GM scores (adjusted OR = 1.81) (all *P*-values < .05). Mediation analysis indicated that depression partially mediated the associations between GI diseases and sleep trouble (Effect = 0.023, 95% CI: 0.022–0.035, $P < .01$), sleep disorders (Effect = 0.010, 95% CI: 0.008–0.014, $P < .01$), and sleep duration (Effect = −0.126, 95% CI: −0.248 to −0.050, $P = 0.040$). These mediation effects remained stable in sensitivity analyses.

Conclusions GI diseases are significantly associated with sleep disturbances, with depression serving as a partial mediator. These findings highlight the importance of addressing both gastrointestinal and psychological health in clinical efforts to improve sleep quality. Further research is needed to guide targeted interventions for this interconnected set of conditions.

Keywords Gastrointestinal diseases, Sleep trouble, Sleep disorders, Sleep time, Depression, Mediating effect, NHANES

*Correspondence:
Chongzheng Qu
873397214@qq.com

Full list of author information is available at the end of the article

Introduction

Sleep disorders and gastrointestinal (GI) diseases are major public health concerns, affecting millions worldwide and placing substantial burdens on healthcare systems. Common sleep disorders—including insomnia, obstructive sleep apnea, and circadian rhythm disruptions—are highly prevalent. Insomnia affects 10%–30% of adults, with higher rates among women (17.6%) than men (10.1%). Sleep-disordered breathing impacts up to 50% of older adults, particularly males [1]. These conditions are associated with reduced productivity, increased the possibility of accidents, and higher rates of chronic diseases such as cardizovascular disease, diabetes, and psychiatric disorders [2]. Economically, sleep deprivation contributes to substantial losses due to increased healthcare utilization and diminished workforce performance [3].

GI diseases, including both functional(e.g., irritable bowel syndrome [IBS]) and organic conditions(e.g., gastroesophageal reflux disease [GERD] and inflammatory bowel disease [IBD]), are similarly widespread, affecting over 40% of the global population [4]. These conditions often present with symptoms such as abdominal pain, bloating, diarrhea, and constipation, significantly impairing quality of life and frequently requiring medical treatment [5]. Their complex etiology involves factors such as dietary patterns(e.g., low fiber intake), psychological stress, infections, autoimmune mechanisms, and medication use(e.g., NSAIDs) [6]. Given their chronic nature and high prevalence, GI diseases warrant strong attention in both clinical practice and public health planning.

Emerging evidence suggests a bidirectional relationship between GI diseases and sleep disorders, whereby dysfunction in one domain may exacerbate the other [7, 8]. Sleep deprivation has been shown to aggravate GI symptoms, while nighttime GI issues—such as acid reflux in GERD—can disrupt sleep patterns [9, 10]. Notably, around 40% of individuals with IBS experience comorbid sleep disturbances, which are associated with more severe GI symptoms and lower quality of life [11]. This interaction may be driven by shared biological pathways, including elevated pro-inflammatory cytokines(e.g., TNF-α, IL-1, IL-6) and changes in gut microbiota that affect the central nervous system via the gut–brain axis [12, 13]. Depression, which frequently co-occurs with both GI diseases and sleep disorders, has been identified as a potential mediator. Studies report higher rates of depression and poorer sleep quality among individuals with IBS and IBD [14, 15]. The gut–brain axis—a bidirectional communication network linking the central and enteric nervous systems through neural, hormonal, immune, and metabolic pathways—may underlie these associations [13]. Despite its importance, the mediating role of depression in the GI–sleep relationship remains underexplored, particularly in large population-based studies.

Although the literature increasingly acknowledges the links between sleep disturbance, GI disorders, and depression, substantial knowledge gaps remain. Many existing studies rely on small clinical samples, limiting external validity. Additionally, while the role of the gut–brain axis, systemic inflammation, and microbiota are well documented, few studies have empirically tested whether depression serves as a mediator using nationally representative data [16]. This study seeks to address these gaps by utilizing data from the National Health and Nutrition Examination Survey (NHANES) to explore the relationship between GI diseases and sleep disturbances, focusing specifically on the mediating role of depression. The use of NHANES enhances the generalizability of the findings and their relevance to public health.

The primary objective of this study was to evaluate the association between GI diseases and sleep outcomes, while clarifying the potential mediating role of depression. By using a large, nationally representative sample, this research aims to provide insights into the complex interactions among gastrointestinal health, mental health, and sleep, ultimately informing the development of integrated interventions to improve sleep quality.

Materials and methods

Study population

The NHANES, administered by the National Center for Health Statistics (NCHS), is a nationally representative program designed to assess the health and nutritional status of the non-institutionalized civilian U.S. population. This study analyzed data from the 2005–2014 NHANES cycles, encompassing 50,965 participants. Exclusion criteria were applied to remove 40,339 individuals for the following reasons: missing data on sleep ($n = 18,869$), gastrointestinal (GI) disease ($n = 4,033$), depression ($n = 1,959$), or key covariates including education, income-to-poverty ratio, BMI, hypertension, smoking, alcohol use, and diabetes ($n = 4,010$). Participants with a cancer diagnosis ($n = 2,305$) or missing data on coronary heart disease, heart failure, stroke, physical activity, HEI-2015, or DI-GM ($n = 9,163$) were also excluded. The final analytical sample consisted of 10,626 participants (Fig. 1).

Assessment of gastrointestinal disease

GI disease status was determined based on responses from the "Current Health Status"section of the questionnaire. Participants were classified as having a GI disease if they answered "yes"to the question: "During the past 30 days, have you had a stomach or intestinal illness with vomiting or diarrhea?".

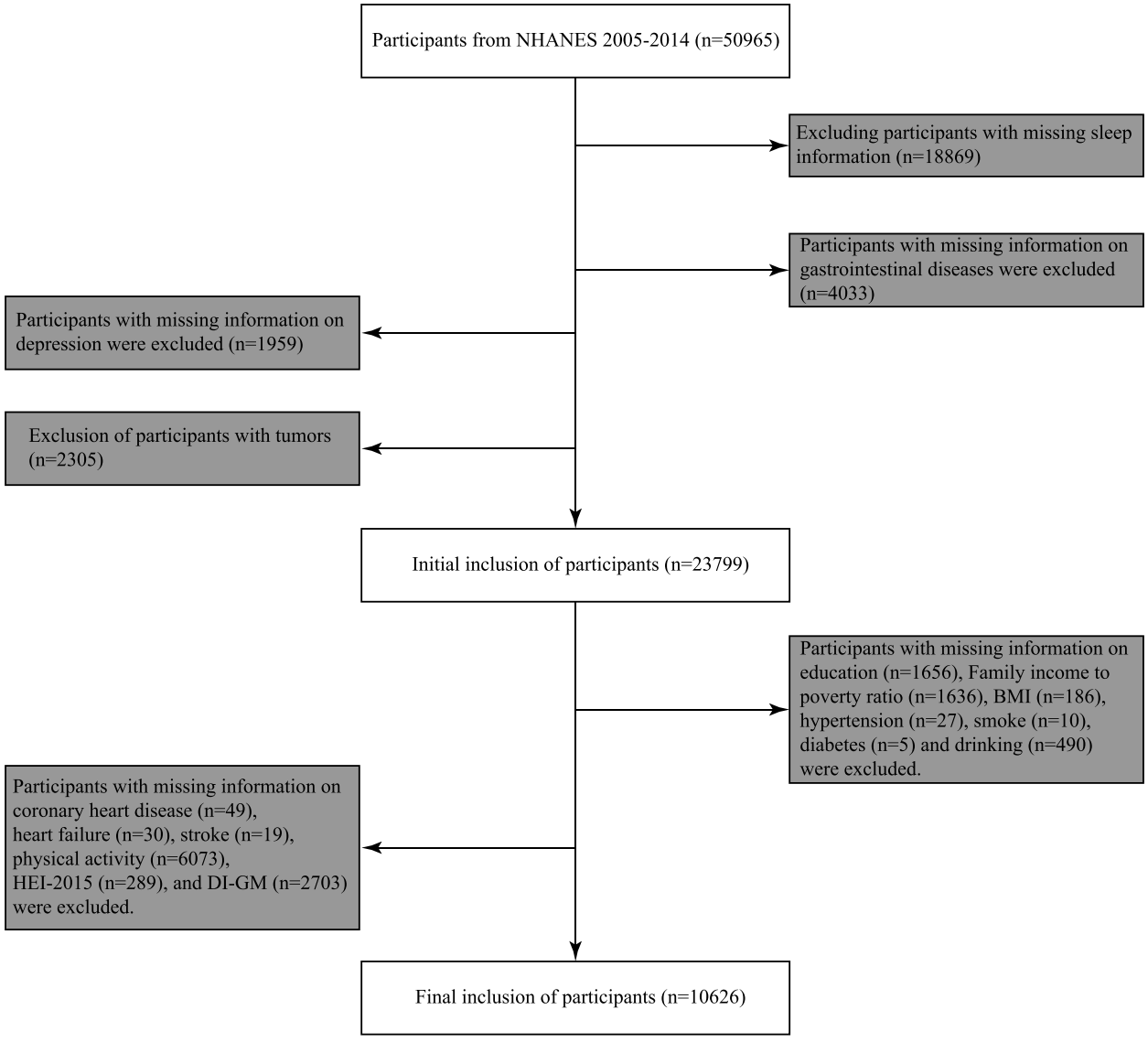

Fig. 1 Flow chart

Assessment of sleep-related factors

Sleep duration was assessed via the question: "On average, how many hours of sleep do you usually get on weekdays or workdays?"Trouble sleeping and sleep disorders were identified through affirmative responses to the questions: "Have you ever been told by a doctor that you had trouble sleeping?" and"Have you ever been told by a doctor that you have a sleep disorder?" [17].

Assessment of depression

Depression was evaluated using the Patient Health Questionnaire-9 (PHQ-9), a validated instrument for assessing depressive symptom severity [18]. The PHQ-9 consists of nine items rated on a 4-point Likert scale (0 = "not at all" to 3 = "nearly every day"), yielding a total score from 0 to 27. A score of ≥ 10 was used to indicate depression [19].

Covariates

Covariates included demographic and clinical variables: age, sex, race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other), education (< 9th grade, 9–11th grade, high school diploma/GED, some college/associate degree, ≥ college graduate), income-to-poverty ratio, BMI, drinking status, smoking status, hypertension, diabetes, physical activity, HEI-2015, DI-GM, caffeine intake, coronary heart disease, heart failure, and stroke. Hypertension was defined as self-reported high blood pressure with current use of antihypertensive medications [20]. Diabetes was defined as physician-diagnosed, fasting glucose ≥ 7.0 mmol/L, or 2-h plasma glucose (OGTT) ≥ 11.1 mmol/L. Prediabetes was defined as fasting glucose 6.1–6.9 mmol/L or OGTT 7.8–11.1 mmol/L, or physician diagnosis [20]. Smoking

status was classified as never smokers (never smoked or quit over a year ago) and current smokers (smoked within the past 30 days or resumed smoking ≥ 2 cigarettes per day) [21]. Drinking status was categorized as never drinkers (< 12 drinks in a lifetime) or current drinkers (≥ 12 drinks per year or ≥ 6 occasions in the past 12 months) [20]. Participants were considered positive for specific cardiovascular conditions if they reported a diagnosis of congestive heart failure, coronary heart disease, angina, myocardial infarction, or stroke [21]. Physical activity was assessed using the Global Physical Activity Questionnaire [18]. Total physical activity was calculated using metabolic equivalent of task (MET) values based on reported frequency and duration. Participants were classified as inactive (< 600 MET-min/week) or active (≥ 600 MET-min/week) [18]. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

Statistical analyses

All statistical analyses followed NHANES analytic guidelines. Survey weights were adjusted for the five combined cycles (2005–2014) by dividing the 2-year weight variable (WTMEC2YR) by five. Primary sampling units (SDMVPSU) and strata (SDMVSTRA) were applied to account for the complex sampling design. After weighting, each participant represented 7,826 individuals in the U.S. population. Continuous variables were summarized using means and standard deviations (SD), while categorical variables were expressed as frequencies and weighted percentages. Group comparisons were performed using Student's t-tests for continuous variables and chi-square tests for categorical variables. Variance inflation factors (VIFs) were used to assess multicollinearity. Multivariable logistic regression models were used to examine the association between gastrointestinal disease and trouble sleeping. Model 1 was unadjusted. Model 2 adjusted for sex, age, race/ethnicity, education, and family income-to-poverty ratio. Model 3 additionally adjusted for BMI, drinking status, smoking status, hypertension, and diabetes. Model 4 further included physical activity, HEI-2015, DI-GM, caffeine intake, coronary heart disease, heart failure, and stroke. Subgroup analyses and interaction terms were included to assess effect modification by demographic and health-related variables. Mediation analysis was conducted using the R package mediation to test whether depression mediated the relationship between GI disease and sleep trouble. Direct, indirect, and total effects were estimated using 5,000 bootstrap iterations. Statistical significance was defined by a 95% confidence interval excluding zero. To address missing data, multiple imputation was performed using the R package mice, preserving statistical power and minimizing bias. All analyses were conducted using IBM SPSS Statistics (version 24.0) and R (version 4.3.0). A two-sided P-value < 0.05 was considered statistically significant.

Sensitivity analyses

To evaluate the robustness of the results, additional multivariable linear and logistic regression analyses were conducted to examine the associations between GI disease and both sleep duration and sleep disorder. Unweighted analyses were also performed to assess the consistency of the association between GI disease and trouble sleeping.

Results

Participant characteristics by gastrointestinal disease status

Table 1 summarizes the baseline characteristics of participants with and without gastrointestinal (GI) diseases, including gastric and intestinal disorders, from the 2005–2014 NHANES cycles (n = 10,626). The mean age of participants was 45.56 years (SD = 16.23), with a sex distribution of 50.78% women (n = 5,377) and 49.22% men (n = 5,249). Among them, 6,444,797 participants were identified as having GI diseases, with a similar mean age of 45.60 years (SD = 15.13).

Compared to those without GI diseases, participants with GI conditions had significantly higher body mass index(BMI: 29.89 vs. 29.00, P = 0.007) and a greater prevalence of hypertension (39.26% vs. 29.60%, P < 0.001), diabetes(12.58% vs. 9.36%, P = 0.013), heart failure(4.08% vs. 1.90%, P < 0.001), stroke(4.09% vs. 2.34%, P = 0.010), and depression(20.08% vs. 7.44%, P < 0.001). In addition, they were less likely to engage in regular physical activity(49.62% vs. 58.02%, P < 0.001) and more likely to report a history of smoking(27.15% vs. 21.37%, P = 0.002). Regarding sleep-related outcomes, individuals with GI diseases reported shorter average sleep duration(6.69 vs. 6.85 h, P = 0.047), a higher prevalence of trouble sleeping(37.99% vs. 24.21%, P < 0.001), and a greater frequency of diagnosed sleep disorders(14.99% vs. 8.08%, P < 0.001).

Association between gastrointestinal disease and sleep trouble

As shown in Fig. 2, VIFs for all variables were below 3, indicating no evidence of multicollinearity. Table 2 presents the results of logistic regression models assessing the association between GI diseases and sleep trouble. In the unadjusted model, GI disease was significantly associated with sleep trouble (OR = 1.92, 95% CI: 1.62–2.27, P < 0.001). After adjusting for potential confounders—including sex, age, race/ethnicity, education, family income-to-poverty ratio, BMI, drinking status, smoking status, hypertension, diabetes, physical activity, HEI-2015, DI-GM, caffeine intake, coronary heart disease, heart failure, and stroke, the association remained

Table 1 Baseline characteristics of participants

Characteristic	N	Overall *N* = 83,167	No Gastrointestinal disorders *N* = 76,723	Gastrointestinal disorders *N* = 6,444	*p*-value
Sleep time[a], Mean ± SD	10,626	6.84 ± 1.35	6.85 ± 1.34	6.69 ± 1.50	0.047
Sleep trouble [b], n(%)	10,626				< 0.001
No		8,036 (74.72%)	7,506 (75.79%)	530 (62.01%)	
Yes		2,590 (25.28%)	2,276 (24.21%)	314 (37.99%)	
Sleep disorder[b], n(%)	10,626				< 0.001
No		9,744 (91.38%)	9,020 (91.92%)	724 (85.01%)	
Yes		882 (8.62%)	762 (8.08%)	120 (14.99%)	
Demographics					
Sex[b], n(%)	10,626				< 0.001
FeMale		5,377 (50.78%)	4,863 (49.97%)	514 (60.39%)	
Male		5,249 (49.22%)	4,919 (50.03%)	330 (39.61%)	
Age(year)[a], Mean ± SD	10,626	45.56 ± 16.23	45.56 ± 16.32	45.60 ± 15.13	0.641
Race/ethnicity[b], n(%)	10,626				0.346
Mexican		1,808 (8.81%)	1,646 (8.68%)	162 (10.32%)	
Other Hispanic		1,093 (5.19%)	1,003 (5.17%)	90 (5.45%)	
Non-Hispanic White		4,880 (68.36%)	4,505 (68.53%)	375 (66.36%)	
Non-Hispanic Black		2,178 (11.36%)	2,011 (11.28%)	167 (12.23%)	
Other Race		667 (6.28%)	617 (6.33%)	50 (5.65%)	
Education[b], n(%)	10,626				0.631
< 9th grade		1,130 (5.54%)	1,047 (5.58%)	83 (5.09%)	
9–11th grade		1,731 (12.68%)	1,583 (12.60%)	148 (13.66%)	
High school diploma/GED		2,547 (23.71%)	2,341 (23.61%)	206 (24.92%)	
Some College/AA degree		3,101 (31.87%)	2,849 (31.82%)	252 (32.36%)	
≥ College graduate		2,117 (26.21%)	1,962 (26.39%)	155 (23.98%)	
Family income to poverty ratio[a], Mean ±	10,626	2.96 ± 1.65	2.98 ± 1.65	2.77 ± 1.69	0.005
BMI[a], Mean ± SD	10,626	29.07 ± 6.93	29.00 ± 6.88	29.89 ± 7.46	0.007
Lifestyle					
Smoking status[b], n(%)	10,626				0.002
No		8,217 (78.19%)	7,622 (78.63%)	595 (72.85%)	
Yes		2,409 (21.81%)	2,160 (21.37%)	249 (27.15%)	
Drinking status[b], n(%)	10,626				0.299
No		1,460 (10.91%)	1,358 (11.01%)	102 (9.73%)	
Yes		9,166 (89.09%)	8,424 (88.99%)	742 (90.27%)	
HEI-2015[a], Mean ± SD	10,626	52.78 ± 13.13	52.95 ± 13.18	50.76 ± 12.35	0.002
DI-GM[a], Mean ± SD	10,626	5.14 ± 1.74	5.16 ± 1.74	4.89 ± 1.75	0.001
Caffeine[a], Mean ± SD	10,626	183.32 ± 227.10	184.98 ± 229.73	163.54 ± 192.11	0.055
Physical activity[b], n(%)	10,626				< 0.001
No		5,004 (42.63%)	4,558 (41.98%)	446 (50.38%)	
Yes		5,622 (57.37%)	5,224 (58.02%)	398 (49.62%)	
Comorbidities					
Diabetes[b], n(%)	10,626				0.013
No		7,867 (78.60%)	7,283 (79.02%)	584 (73.64%)	
Yes		1,378 (9.61%)	1,245 (9.36%)	133 (12.58%)	
Borderline		1,381 (11.79%)	1,254 (11.62%)	127 (13.78%)	
Hypertension[b], n(%)	10,626				< 0.001
No		6,963 (69.65%)	6,477 (70.40%)	486 (60.74%)	
Yes		3,663 (30.35%)	3,305 (29.60%)	358 (39.26%)	
Coronary heart disease[b], n(%)	10,626				0.130
No		9,924 (94.70%)	9,148 (94.83%)	776 (93.21%)	
Yes		702 (5.30%)	634 (5.17%)	68 (6.79%)	
Heart Failure[b], n(%)	10,626				< 0.001
No		10,319 (97.93%)	9,513 (98.10%)	806 (95.92%)	

Table 1 (continued)

Characteristic	N	Overall *N* = 83,167	No Gastrointestinal disorders *N* = 76,723	Gastrointestinal disorders *N* = 6,444	*p*-value
Yes		307 (2.07%)	269 (1.90%)	38 (4.08%)	
Stroke[b], n(%)	10,626				0.010
No		10,284 (97.53%)	9,477 (97.66%)	807 (95.91%)	
Yes		342 (2.47%)	305 (2.34%)	37 (4.09%)	
Depression[b], n(%)	10,626				< 0.001
No		9,573 (91.58%)	8,929 (92.56%)	644 (79.92%)	
Yes		1,053 (8.42%)	853 (7.44%)	200 (20.08%)	

SD Standard deviation

[a]Student t-test

[b]Chi-square test

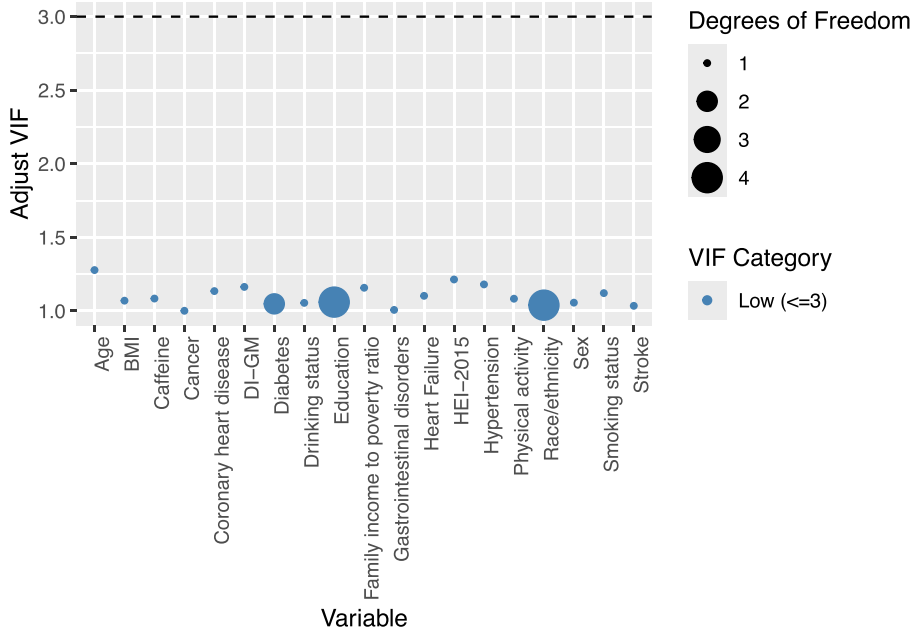

Fig. 2 Variance inflation factor graph

Table 2 Association between gastrointestinal diseases and risk of sleep trouble

Variables	Model 1		Model 2		Model 3		Model 4	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Gastrointestinal diseases								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.92 (1.62 ~ 2.27)	<.001***	1.88 (1.59 ~ 2.24)	<.001***	1.73 (1.44 ~ 2.08)	<.001***	1.70 (1.41 ~ 2.05)	<.001***

Model 1: Crude

Model 2: Adjust: Sex, Age, Race/ethnicity, Education, Family income to poverty ratio

Model 3: Adjust: Sex, Age, Race/ethnicity, Education, Family income to poverty ratio, BMI, Drinking status, Smoking status, Hypertension, Diabetes

Model 4: Adjust: Sex, Age, Race/ethnicity, Education, Family income to poverty ratio, BMI, Drinking status, Smoking status, Hypertension, Diabetes, Physical activity, HEI-2015, DI-GM, Caffeine, Coronary heart disease, Heart failure, Stroke

OR Odds Ratio, *CI* Confidence Interval

****P* <.001,significant difference compared with no GI diseases

significant (adjusted OR = 1.70, 95% CI: 1.41–2.05, $P < 0.001$), indicating a 70% increased possibility of sleep trouble among individuals with GI diseases.

Subgroup analyses

Subgroup analyses evaluated the consistency of the GI disease–sleep trouble association across various population strata (Fig. 3). The association remained significant among participants without hypertension (adjusted OR = 1.69, 95% CI: 1.39–2.05, $P < 0.001$), without diabetes (adjusted OR = 1.72, 95% CI: 1.42–2.09, $P < 0.001$), and without a history of smoking (adjusted OR = 1.73, 95% CI: 1.39–2.14, $P < 0.001$). It also persisted among those with coronary heart disease (adjusted OR = 1.76, 95% CI: 1.13–2.75, $P = 0.016$) and individuals with higher DI-GM scores (adjusted OR = 1.81, 95% CI: 1.29–2.55, $P = 0.001$). Interaction tests indicated no significant effect modification by sex, age or chronic disease status (P for interaction > 0.05).

Mediation analysis

Multicollinearity diagnostics again confirmed acceptable VIFs (< 3) across models (Fig. 2), ensuring robust model performance. Figure 4 shows the mediation results. A significant total effect of GI disease on sleep trouble was observed (Effect = 0.108, 95% CI: 0.069–0.140, $P < 0.01$). After adjusting for depression, the direct effect remained significant (Effect = 0.085, 95% CI: 0.043–0.105, $P < 0.01$), while the indirect effect mediated by depression was also significant (Effect = 0.023, 95% CI: 0.022–0.035, $P < 0.01$). Depression accounted for 21.29% of the total effect. Bootstrap validation confirmed the robustness of these mediation estimates (Fig. 4A).

Sensitivity analyses

Sensitivity analyses using unweighted data (Supplementary Table 1) corroborated the primary findings. In the fully adjusted model, GI disease was associated with a 1.71-fold increased possibility of sleep trouble (adjusted OR = 1.71, 95% CI: 1.47–2.00, $P < 0.001$). Analysis using NHANES-recommended weighted data showed consistent results, with GI disease significantly associated with sleep disorder (adjusted OR = 1.80, 95% CI: 1.34–2.41, $P < 0.001$) (Supplementary Table 2) and reduced sleep duration (adjusted $\beta = -0.15$, 95% CI: −0.29 to −0.01, $P = 0.038$) (Supplementary Table 3). Further mediation analyses demonstrated that depression mediated both the GI disease–sleep disorder and GI disease–sleep duration associations. Specifically, depression accounted for 19.23% of the effect on sleep disorder and 26.68% of the effect on sleep duration (Figs. 4B–C).

Discussion

The present study discovered that, among U.S. adults aged ≥ 20 years, there was a significant relationship between GI diseases and a heightened probability of experiencing sleep disturbances (adjusted OR = 1.70, 95% CI: 1.41–2.05, $P < 0.001$), sleep disorder (adjusted OR = 1.71, 95% CI: 1.47–2.00, $P < 0.001$), and reduced sleep duration (adjusted $\beta = -0.15$, 95% CI: −0.29 to −0.01, $P = 0.038$). These findings suggest that individuals with GI conditions are more likely to experience disrupted sleep patterns and shorter sleep times. Depression was identified as a partial mediator in these relationships.

These results align with growing evidence supporting a bidirectional relationship between GI diseases, sleep disturbances, and depression, potentially mediated by the microbiota–gut–brain axis. Recent studies have highlighted the role of gut microbiota in influencing sleep and mood via neuroendocrine, immune, and metabolic pathways. For instance, a 2024 systematic review by Galie et al. identified shared microbial biomarkers in both sleep disorders and metabolic syndrome, suggesting that gut dysbiosis associated with GI disease may disrupt sleep through altered microbial metabolites [22]. Likewise, Negi al. demonstrated that dietary components—such as fiber and polyphenols—enhance the production of sleep-regulating compounds like serotonin and melatonin, reinforcing the concept of chrononutrition in sleep regulation [23].

The neuro–immune–endocrine axis is also critical. Systemic inflammation, common in many GI diseases, is characterized by elevated levels of pro-inflammatory cytokines such as tumor necrosis factor(TNF), interleukin-1(IL-1), and interleukin-6(IL-6), which have been linked to sleep disturbances [24]. Khanijow et al. documented increased cytokine levels in patients with GERD and IBD, providing a plausible biological explanation for the observed sleep impairments [7]. Additionally, evidence from chrononutrition research suggests that GI-related circadian misalignment—caused by disrupted gut function or irregular meal timing—may further exacerbate sleep issues [25].

Depression was selected as a mediator due to its high comorbidity with both gastrointestinal (GI) diseases and sleep disorders. Biologically, depression can influence GI function via the gut–brain axis, particularly through the vagus nerve and the hypothalamic–pituitary–adrenal(HPA) axis, both of which regulate stress responses and gastrointestinal motility [13]. Psychologically, chronic GI symptoms—such as abdominal pain and bloating—may lead to emotional distress, exacerbate depressive symptoms, and subsequently disrupt sleep [10]. Serotonin, a key neurotransmitter predominantly synthesized in the gut, has been implicated in both depression and sleep regulation [26]. In our mediation

Variables	No n (%)	Yes n (%)	OR (95%CI)	P
Age				
<=50	5406 (92.1%)	497 (7.9%)	1.68 (1.32 ~ 2.14)	<.001***
>50	4376 (92.5%)	347 (7.5%)	1.74 (1.21 ~ 2.48)	0.003**
Sex				
FeMale	4863 (90.8%)	514 (9.2%)	1.58 (1.24 ~ 2.02)	<.001***
Male	4919 (93.8%)	330 (6.2%)	1.84 (1.39 ~ 2.43)	<.001***
Hypertension				
No	6477 (93.2%)	486 (6.8%)	1.69 (1.39 ~ 2.05)	<.001***
Yes	3305 (90.0%)	358 (10.0%)	1.99 (0.69 ~ 5.78)	0.192
Diabetes				
No	7283 (92.7%)	584 (7.3%)	1.72 (1.42 ~ 2.09)	<.001***
Yes	1245 (89.9%)	133 (10.1%)	1.20 (0.49 ~ 2.93)	0.684
Borderline	1254 (90.9%)	127 (9.1%)	1.40 (0.85 ~ 2.30)	0.178
Smoke				
No	7622 (92.8%)	595 (7.2%)	1.73 (1.39 ~ 2.14)	<.001***
Yes	2160 (90.4%)	249 (9.6%)	1.31 (0.59 ~ 2.92)	0.492
Drink				
No	1358 (93.1%)	102 (6.9%)	2.16 (1.70 ~ 2.74)	<.001***
Yes	8424 (92.1%)	742 (7.9%)	1.40 (1.04 ~ 1.89)	0.029*
Physical activity				
No	4558 (90.8%)	446 (9.2%)	1.73 (1.42 ~ 2.11)	<.001***
Yes	5224 (93.3%)	398 (6.7%)	1.84 (1.48 ~ 2.29)	<.001***
BMI				
Underweight	137 (92.4%)	14 (7.6%)	1.51 (1.17 ~ 1.95)	0.002**
Normal	2548 (93.4%)	208 (6.6%)	1.97 (1.53 ~ 2.54)	<.001***
Overweight	3328 (92.5%)	244 (7.5%)	2.04 (1.55 ~ 2.68)	<.001***
Obesity	3769 (91.2%)	378 (8.8%)	1.27 (0.94 ~ 1.73)	0.122
Stroke				
No	9477 (92.4%)	807 (7.6%)	1.87 (1.39 ~ 2.51)	<.001***
Yes	305 (87.2%)	37 (12.8%)	1.53 (1.18 ~ 1.97)	0.002**
Heart failure				
No	9513 (92.4%)	806 (7.6%)	1.46 (1.08 ~ 1.97)	0.016*
Yes	269 (84.7%)	38 (15.3%)	1.99 (1.50 ~ 2.64)	<.001***
Coronary heart disease				
No	9148 (92.4%)	776 (7.6%)	1.41 (0.82 ~ 2.42)	0.211
Yes	634 (90.1%)	68 (9.9%)	1.76 (1.13 ~ 2.75)	0.016*
Caffeine				
<= 101.0	4968 (91.8%)	429 (8.2%)	1.93 (1.47 ~ 2.52)	<.001***
> 101.0	4814 (92.6%)	415 (7.4%)	1.72 (1.32 ~ 2.23)	<.001***
HEI–2015				
<= 52.23	4857 (91.4%)	458 (8.6%)	1.43 (1.07 ~ 1.93)	0.018*
>52.23	4925 (93.2%)	386 (6.8%)	0.45 (int ~ int)	0.999
DI–GM				
<=5	6132 (91.7%)	541 (8.3%)	1.16 (0.74 ~ 1.80)	0.509
> 5	3650 (93.0%)	303 (7.0%)	1.81 (1.29 ~ 2.55)	0.001**

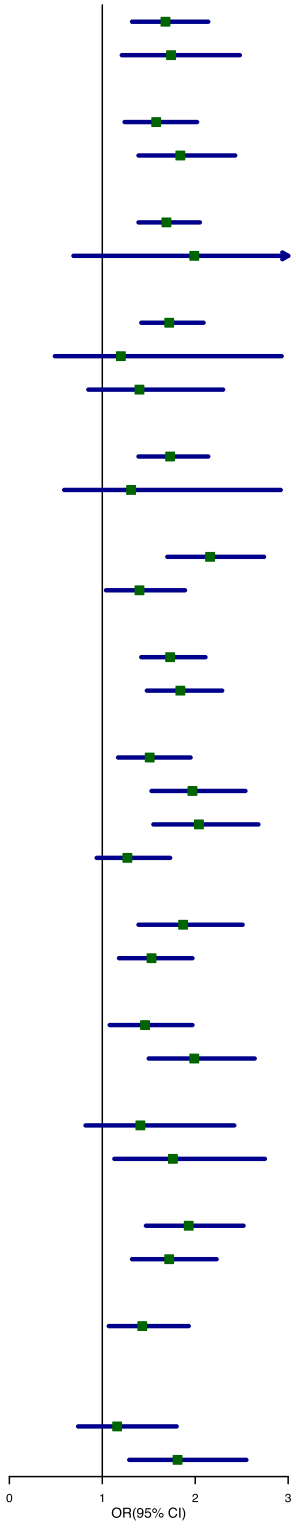

Fig. 3 Sylvan chart

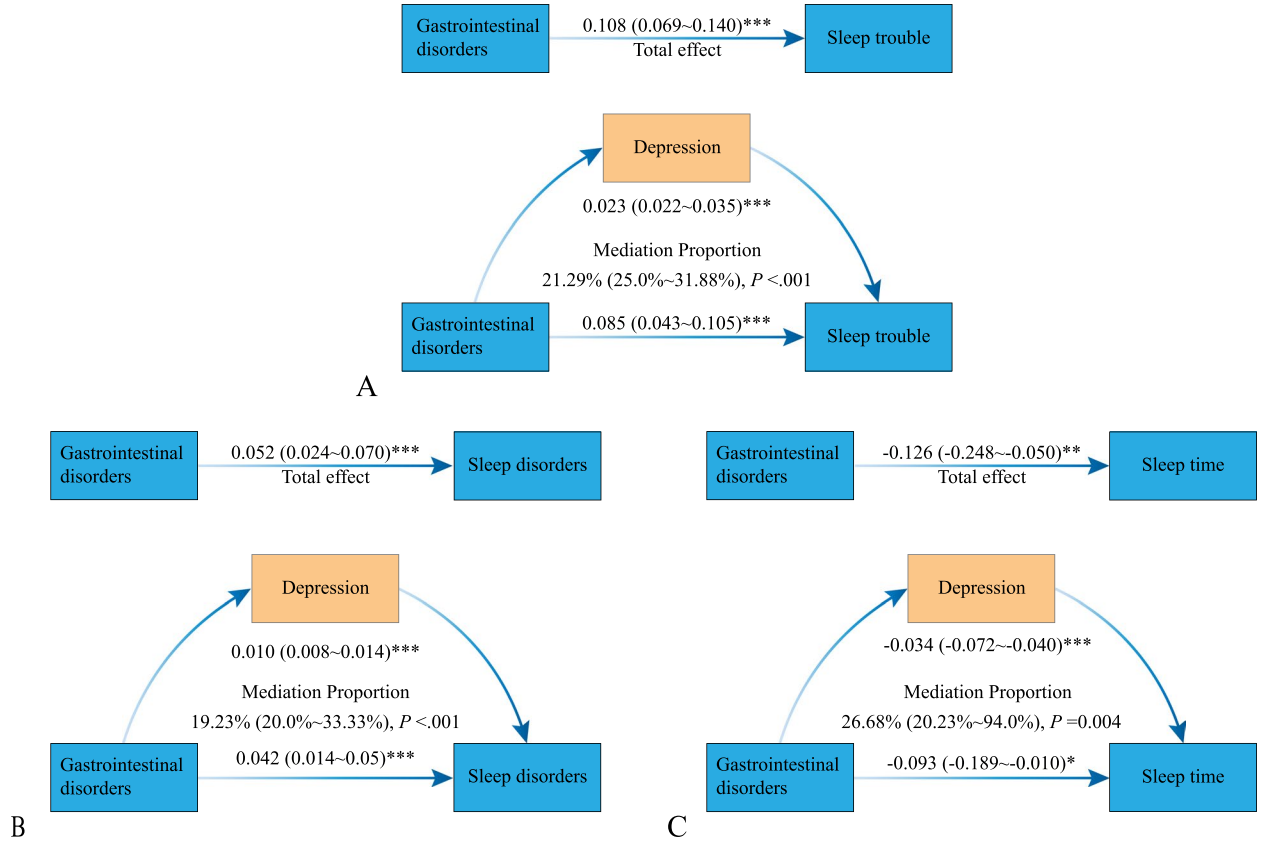

Fig. 4 Intermediary graph

analysis, depression accounted for approximately 30% of the observed association between GI disease and sleep disturbance, suggesting it plays a significant but not exclusive mediating role.

Beyond depression, other mechanisms may contribute to the GI–sleep association, including systemic inflammation, visceral hypersensitivity, and metabolic dysregulation. Inflammation is a well-established pathway, evidence suggests that sleep deprivation increases pro-inflammatory cytokine levels, creating a feedback loop that sustains both sleep and GI disturbances [24]. Visceral hypersensitivity—frequently observed in functional GI disorders such as IBS—can amplify pain perception and impair sleep quality [27]. Metabolic impairments, such as altered nutrient absorption in GI diseases, may also disrupt the synthesis of sleep-regulating hormones like melatonin [28]. Together, these biological pathways underscore the complex interplay underlying the GI–sleep relationship.

Although our findings are broadly consistent with existing literature, discrepancies remain regarding the strength and directionality of associations between GI disorders and sleep outcomes. For example, Ballou et al. found variable associations between constipation and depression severity, suggesting that different GI symptoms may have distinct effects on psychological health and sleep quality [10]. Such inconsistencies may stem from differences in study populations, methodological approaches or the specific GI conditions examined. Additionally, some studies adjusting for socioeconomic and lifestyle factors have reported attenuated associations, indicating that contextual variables may modulate these relationships [29, 30]. Further sources of variability include unmeasured confounders, inconsistent definitions of sleep disorders, and the inherent limitations of cross-sectional designs in establishing causality. Although our use of the nationally representative NHANES dataset enhances generalizability, further research is needed to resolve these inconsistencies.

The persistent association between GI diseases and sleep disturbances among individuals with CHD and higher DI-GM scores suggests that comorbid conditions and gut-related factors may modulate this relationship. CHD is characterized by chronic systemic inflammation, including elevated levels of C-reactive protein and IL-6, which may amplify the inflammatory effects of GI diseases on sleep physiology [31, 32]. Patients with CHD frequently have other comorbidities such as obesity and diabetes, both independently associated with GI dysfunction and sleep disruption, potentially creating synergistic

adverse effects [7] This cumulative inflammatory and disease burden likely contributes to the stronger associations observed in this subgroup.

Interestingly, higher DI-GM scores—typically indicative of a healthier gut microbiome—did not mitigate the association between GI disease and sleep disturbances. This suggests that even with favorable microbiota composition, pathological processes such as visceral hypersensitivity or chronic low-grade inflammation may override the potential benefits [33]. Normally, a healthy gut microbiome supports the synthesis of sleep-modulating compounds, such as short-chain fatty acids and serotonin [23]. However, the presence of GI disease, with its associated pain, dysmotility, and psychological stress, may negate these benefits, resulting in persistent sleep problems [27]. These findings highlight the multifactorial and bidirectional nature of the gut–sleep axis and support the need for integrated interventions addressing both microbiome health and GI pathology.

Limitations

This study has several limitations. First, although the sample size was sufficient for conventional regression analyses, it may have been underpowered for machine learning models, potentially limiting their ability to detect complex, non-linear relationship. Second, the reliance on self-reported data for GI diseases, sleep outcomes, and CHD may introduce misclassification bias and residual confounding, which could affect the precision of our findings [34]. Third, the cross-sectional design precludes causal inference, making it unclear whether GI disease leads to sleep disturbances or vice versa. Fourth, reverse causality is plausible, as disrupted sleep may worsen GI symptoms, creating a bidirectional feedback loop [35]. Fifth, in the assessment of GI diseases and sleep disorder, due to data limitations, functional and organic gastrointestinal diseases could not be combined and sleep apnea could not be assessed separately.Sixth, due to missing or inconsistent data in NHANES, factors such as obstructive sleep apnea, chronic pain, and hypnotic drug use cannot be adjusted.Finally, recall bias and underreporting—particularly for conditions like CHD—could have influenced the accuracy of subgroup analyses.

Despite these limitations, our findings offer valuable insights. The strong associations observed in a large, nationally representative sample emphasize the need for integrated clinical strategies that address both gastrointestinal and psychological health to improve sleep quality. Future longitudinal studies are necessary to determine causal pathways and to investigate additional mediators, including inflammatory and metabolic factors. Interventions targeting the gut microbiome, chrononutrition, and systemic inflammation may offer promising avenues to alleviate sleep disturbances in individuals with GI disorders.

Conclusions

This study identifies a significant association between gastrointestinal diseases and sleep disturbances, with depression partially mediating this relationship. These findings underscore the importance of addressing both psychological and gastrointestinal factors in clinical practice to improve sleep health. Continued research is needed to clarify causal mechanisms and to develop targeted, multidimensional interventions for this interconnected triad of health concerns.

Abbreviations

NHANES	National Health and Nutrition Survey
PHQ-9	The Patient Health Questionnaire-9
CHD	Coronary heart disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04180-8.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

Acknowledgements

Thank you to the editors and reviewers for taking the time and energy to provide feedback on our manuscripts and making insightful comments and valuable improvements. Thank you to Ms Sui Li Li, my future wife, for the support and companionship she has been through a lot of difficulties. Thank my good friends, Dong Zhiwei, Zeng Xuan, Liao Zhongqin for their help in the article. Thank my tutor, Professor Qu Chongzheng, for his guidance in life and study.

Authors' contributions

Shicheng Ye, Lili Sui and Zhiwei Dong wrote the main manuscript text, and Shicheng Ye, Xuan Zeng, Zhongqin Liao prepared and analyzed figures and tables. The whole process guidance is given by Chongzheng Qu. All authors reviewed the manuscript.

Funding

No funding.

Data availability

All data generated or analyzed during this study are included in this paper [and its supplementary information file].

Declarations

Ethics approval and consent to participate

All survey procedures are supervised and approved by the NCHS Ethics Review Board, and each survey respondent provides written consent. These publicly available data are de-identified, so further institutional review committee approval is exempted. The NHANES survey protocol has received approval from the Ethics Review Board of the National Center for Health Statistics, and all participants have provided written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]The Third Clinical Medical College of Guangzhou University of Chinese Medicine, Guangzhou 510378, China
[2]The Third Affiliated Hospital of Guangzhou University of Chinese Medicine, No. 261 Longxi Avenue, Liwan District, Guangzhou City, Guangdong Province 510378, China
[3]Guangzhou University of Chinese Medicine, 510405 Guangzhou, China

Received: 6 February 2025 / Accepted: 18 July 2025
Published online: 19 August 2025

References

1. Jaqua E, Hanna M, Labib W, et al. Common sleep disorders affecting older adults. Permanente J. 2023;27(1):122–32.
2. Chattu V, Manzar M, Kumary S, et al. The global problem of insufficient sleep and its serious public health implications. Healthcare (Basel, Switzerland). 2018;7(1):1.
3. Hafner M, Stepanek M, Taylor J, et al. Why sleep matters-the economic costs of insufficient sleep: a cross-country comparative analysis. Rand Health Quarterly. 2017;6(4):11.
4. Sperber A, Bangdiwala S, Drossman D, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of rome foundation global study. Gastroenterology. 2021;160(1):99–114.
5. Hawley J, Forster S, Giles E. Exercise, the gut microbiome and gastrointestinal diseases: therapeutic impact and molecular mechanisms. Gastroenterology. 2025;169(1):48–62.
6. Peery A, Murphy C, Anderson C, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2024. Gastroenterology. 2025;168(5):1000–24.
7. Khanijow V, Prakash P, Emsellem H, et al. Sleep dysfunction and gastrointestinal diseases. Gastroenterol hepatol. 2015;11(12):817–25.
8. Cremonini F, Camilleri M, Zinsmeister A, et al. Sleep disturbances are linked to both upper and lower gastrointestinal symptoms in the general population. Neurogastroenterol Motil. 2009;21(2):128–35.
9. El Hage CN, Fu Y, Ghoneim S, et al. Association between obstructive sleep apnea and gastroesophageal reflux disease: a systematic review and meta-analysis. J Gastroenterol Hepatol. 2023;38(8):1244–51.
10. Ballou S, Katon J, Singh P, et al. Chronic diarrhea and constipation are more common in depressed individuals. Clin Gastroenterol Hepatol. 2019;17(13):2696–703.
11. Tu Q, Heitkemper M, Jarrett M, et al. Sleep disturbances in irritable bowel syndrome: a systematic review. Neurogastroenterol Motil. 2017;29(3). https://doi.org/10.1111/nmo.12946.
12. Nakhal M, Yassin L, Alyaqoubi R, et al. The microbiota-gut-brain axis and neurological disorders: a comprehensive review. Life (Basel, Switzerland). 2024;14(10):1234.
13. Appleton J. The gut-brain axis: influence of microbiota on mood and mental health. Integr Med. 2018;17(4):28–32.
14. Chen D, Zhang Y, Huang T, et al. Depression and risk of gastrointestinal disorders: a comprehensive two-sample Mendelian randomization study of European ancestry. Psychol Med. 2023;53(15):7309–21.
15. Marinelli C, Savarino E, Marsilio I, et al. Sleep disturbance in inflammatory bowel disease: prevalence and risk factors - a cross-sectional study. Sci Rep. 2020;10(1):507.
16. Zhang J, Yu S, Zhao G, et al. Associations of chronic diarrheal symptoms and inflammatory bowel disease with sleep quality: a secondary analysis of NHANES 2005–2010. Front Neurol. 2022;13:858439.
17. Yin J, Gong R, Zhang M, et al. Associations between sleep disturbance, inflammatory markers and depressive symptoms: Mediation analyses in a large NHANES community sample. Prog Neuropsychopharmacol Biol Psychiatry. 2023;126:110786.
18. Liang J, Huang S, Jiang N, et al. Association between joint physical activity and dietary quality and lower risk of depression symptoms in US adults: cross-sectional NHANES study. JMIR Public Health Surveill. 2023;9:e45776.
19. Liu X, Liu X, Wang Y, et al. Association between depression and oxidative balance score: National Health and Nutrition Examination Survey (NHANES) 2005–2018. J Affect Disord. 2023;337:57–65.
20. Jiang J, Zhao H, Chen J, et al. The association between dietary creatine intake and cancer in U.S. adults: insights from NHANES 2007–2018. Front Nutr. 2024;11:1460057.
21. Jia Y, Zhang S, Liu J. Exploring BMI's mediating influence on cardiovascular risk correlations with the triglyceride-glucose index: using NHANES and CHARLS cohorts. Front Cardiovasc Med. 2025;12:1593413.
22. Dos Santos A, Galiè S. The microbiota-gut-brain axis in metabolic syndrome and sleep disorders: a systematic review. Nutrients. 2024;16(3):390.
23. Singh A, Negi PS. Appraising the role of biotics and fermented foods in gut microbiota modulation and sleep regulation. J Food Sci. 2025;90(1):e17634.
24. Irwin M, Olmstead R, Carroll J. Sleep disturbance, sleep duration, and inflammation: a systematic review and meta-analysis of cohort studies and experimental sleep deprivation. Biol Psychiat. 2016;80(1):40–52.
25. Matenchuk B, Mandhane P, Kozyrskyj A. Sleep, circadian rhythm, and gut microbiota. Sleep Med Rev. 2020;53:101340.
26. Yano J, Yu K, Donaldson G, et al. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell. 2015;161(2):264–76.
27. Oh A, Koehler A, Yonker M, et al. Sleep disorders and chronic pain syndromes in the pediatric population. Semi Pediatr Neurol. 2023;48:101085.
28. Konturek P, Brzozowski T, Konturek S. Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options. J Physiol Pharmacol. 2011;62(6):591–9.
29. Banker H, Goel A, Kumawat S, et al. Cognitive impairment in IBS: a narrative overview. J Gastrointestin Liver Dis. 2025;34(1):122–7.
30. Levenstein S. The very model of a modern etiology: a biopsychosocial view of peptic ulcer. Psychosom Med. 2000;62(2):176–85.
31. Luc G, Empana J, Morange P, et al. Adipocytokines and the risk of coronary heart disease in healthy middle aged men: the PRIME Study. Int J Obes. 2010;34(1):118–26.
32. Ridker P, Rifai N, Stampfer MJ, et al. Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. Circulation. 2000;101(15):1767–72.
33. Snelson M, Kellow N, Coughlan MT. Modulation of the gut microbiota by resistant starch as a treatment of chronic kidney diseases: evidence of efficacy and mechanistic insights. Adv Nutr. 2019;10(2):303–20.
34. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. J Multidiscip Healthc. 2016;9:211–7.
35. Ananthakrishnan A, Long M, Martin CF, et al. Sleep disturbance and risk of active disease in patients with Crohn's disease and ulcerative colitis. Clin Gastroenterol Hepatol. 2013;11(8):965–71.

Publisher's Note