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Joint association of sleep onset time and sleep duration with depression in patients with chronic kidney disease: Insights from the NHANES 2015–2020

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ABSTRACT

Background: The prevalence of depression among patients with chronic kidney disease (CKD) is high and closely related to poor prognosis. However, the association between sleep onset time, sleep duration, and depression in CKD patients has not been thoroughly studied.
Methods: This study utilized cross-sectional data from CKD patients who participated in the National Health and Nutrition Examination Survey from 2015 to 2020, analyzing their sleep onset time, sleep duration, and Patient Health Questionnaire-Nine. Logistic regression models and restricted cubic spline models were used to explore the association between sleep onset time, sleep duration, and depression in CKD patients.
Results: A total of 2141 CKD patients aged 20 and above were included in this study, among whom 246 (11.5 %) had depression. Compared to those reporting optimal sleep onset (22:00–23:59) and sufficient sleep duration (7–8 h), CKD patients with late sleep onset (≥24:00) and either insufficient (<7 h) or excessive (≥9 h) sleep had a significantly higher risk of depression, with adjusted OR of 2.03 (95 % CI:1.29–3.19) and 2.07 (95 % CI:1.07–4.00), respectively. Additionally, the association between sleep onset time, sleep duration, and depression showed a U-shaped pattern, with the inflection point for sleep onset time at 23:00 and for sleep duration at 7.5 h.
Conclusion: Inappropriate sleep onset time and sleep duration are significantly associated with depression in CKD patients. This association may be important to consider in clinical practice for the prevention and management of depressive symptoms in CKD patients.

1. Introduction

Chronic kidney disease (CKD) affects over 10 % of the global population, emerging as a significant public health concern (Global, regional, and national burden of chronic kidney disease, 1990-2017, 2020; KDIGO, 2021). Patients with CKD often experience multiple health issues, including cardiovascular diseases, diabetes, cognitive impairments, and mental health disorders 0(Cogley et al., 2022; Sluiter et al., 2024), further exacerbating the burden of the disease. Depression, one of the most prevalent mental disorders, has a substantial impact on global health. In 2019, depression accounted for the largest share of disability-adjusted life years related to mental disorders, reaching 37.3 %, significantly contributing to the global burden of mental illnesses (Lancet, 2020). In recent years, the global prevalence of depression has risen markedly, increasing from 170.8 million cases in 1990 to 279.6 million in 2019(Collins et al., 2011). In the United States, approximately 9 % of adults experience major depressive disorder each year, with a lifetime prevalence ranging from 17 % to 30 %(Simon et al., 2024). Studies have shown that the prevalence of depression among CKD patients ranges from 10 % to 20 % (Bautovich et al., 2014; Liu et al., 2023),and

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depression is closely associated with disease progression and poor prognosis in CKD(Xu et al., 2024; Zhu et al., 2023).

Given the significant association between depressive symptoms and health outcomes in CKD patients, it is crucial to explore modifiable risk factors for depression. A growing body of evidence suggests that unhealthy lifestyle habits are closely linked to the higher prevalence of depression(Liang et al., 2023; Wang et al., 2024a). Among these factors, sleep quality and patterns, especially sleep duration and sleep disorders, have garnered extensive attention for their association with depression. Previous studies have indicated that both short and long sleep durations, as well as sleep disorders, are strongly associated with depression (Pan et al., 2024; Wang et al., 2024a). Most of these studies focus on adults, adolescents, postpartum women, and the elderly (Didikoglu et al., 2024; Okun, 2015; Roberts and Duong, 2014). While the impact of sleep duration and sleep disorders on depression has been extensively explored in these populations, research on the effect of sleep onset time on depression remains relatively scarce.

Sleep onset time, referring to the time an individual falls asleep, may affect mental health by influencing the circadian rhythm(Lok et al., 2024; Taillard et al., 2021). However, current research on the association between sleep onset time and depression remains limited, particularly among CKD patients. Sleep problems commonly observed in CKD patients, such as poor sleep quality, insomnia, and circadian rhythm disturbances, are closely associated with the high prevalence of depression(Lindner et al., 2015; Lyons, 2024). Studies have shown that sleep-related issues are more prevalent in CKD patients compared to non-CKD populations(Plantinga et al., 2011). Therefore, understanding the association between sleep onset time, sleep duration, and depression, especially in CKD patients, is of great importance. Nevertheless, there is still a significant research gap in this area.

Based on this, the aim of this study is to explore the independent and joint associations between sleep onset time and sleep duration with depression in CKD patients using data from the 2015–2020 National Health and Nutrition Examination Survey (NHANES). We hypothesize that there is a nonlinear association between sleep onset time, sleep duration, and depression.

2. Methods

2.1. Study population

This cross-sectional study utilized data from the NHANES, conducted by the Centers for Disease Control and Prevention. NHANES is a continuous, nationwide program in the United States that aims to assess the health and nutritional status of adults and children. The survey uses a stratified, multistage probability sampling method to collect health-related data, including demographic information, questionnaire responses, physical examination results, laboratory findings, and dietary data. The study protocol was approved by the National Center for Health Statistics Ethics Review Board, and all participants provided written informed consent prior to participation. NHANES data are publicly available on the official website (http://www.cdc.gov/nchs/nhanes.htm). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline.

Data from three consecutive NHANES cycles (2015–2016, 2017–2018, and 2019–2020) were used, as sleep onset time and sleep duration were collected in these cycles. We included patients aged 20 years or older with CKD, defined as an estimated glomerular filtration rate (eGFR) of <60 ml/min/1.73 m^2 and/or a urine albumin-to-creatinine ratio $\geq$ 30 mg/g (Warsame et al., 2023). The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation(Levey et al., 2009). Exclusion criteria were: 1) pregnant women; 2) individuals missing data on sleep onset time or sleep duration; 3) individuals missing data on the Patient Health Questionnaire-Nine (PHQ-9).

2.2. Assessment of sleep onset time and sleep duration

Sleep onset time and sleep duration were assessed through self-reported questionnaires. Sleep onset time was obtained by asking participants about "the usual sleep time on weekdays or workdays," and sleep duration was assessed by asking "the number of hours usually sleep on weekdays or workdays." According to the Sleep Research Society and the American Academy of Sleep Medicine recommendations for optimal sleep duration(Watson et al., 2015), sleep duration was categorized into three groups: <7 h (h) (insufficient), 7–8 h (sufficient), and $\geq$ 9 h (excessive). Sleep onset time was classified into three categories: $<22:00$ (early), 22:00–23:59 (optimal), and $\geq$ 24:00 (late).

2.3. Assessment of depression

The severity of depressive symptoms experienced by patients in the past two weeks was assessed using the PHQ-9(Manea et al., 2015). The PHQ-9 consists of nine questions, each with four response options: "not at all," "several days," "more than half the days," and "nearly every day," scored zero, one, two, and three, respectively. Individuals with a total PHQ-9 score of $\geq$10 were classified as having depression. Extensive validation studies have confirmed the reliability of PHQ-9 as a diagnostic tool for depression(Manea et al., 2015). The PHQ-9 aligns with the diagnostic criteria for depression outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Park and Zarate Jr., 2019).

2.4. Covariates

Based on literature and clinical experience(Liu et al., 2024; Wang et al., 2024a; Yin et al., 2023), the following covariates were included: age, sex, race and ethnicity, education level, marital status, poverty income ratio (PIR), body mass index (BMI), smoking status, drinking status, physical activity, obstructive sleep apnea, and comorbid conditions. The detailed definitions and classifications of these variables can be found in the Methods section of the Supplementary Material.

2.5. Statistical analysis

A descriptive analysis was conducted for all participants. Categorical variables are expressed as percentages (%), while continuous variables are presented as means and standard deviations. To compare differences between groups, one-way analysis of variance was performed for normally distributed data, and chi-square tests were used for categorical variables.

Logistic regression analysis using nested models was employed to determine the association between sleep onset time or sleep duration and depression in CKD patients, calculating OR and 95 % CI. Model 1 was unadjusted to establish the preliminary association. Model 2 adjusted for sociodemographic characteristics (age, sex, race/ethnicity, marital status, education level, and PIR) to account for basic demographic confounding. Model 3 further adjusted for BMI, smoking status, drinking status, physical activity and comorbidities, building upon Model 2, to evaluate whether the observed association remained after considering lifestyle and health-related factors, thereby confirming the robustness of the results. Furthermore, the joint effect of sleep onset time and sleep duration on depression in CKD patients was assessed through cross-group analysis, as well as additive and multiplicative interactions, with detailed methods provided in the Supplementary Methods.

To assess potential nonlinear association between sleep onset time, sleep duration, and depression in CKD patients, we employed a multivariable adjusted restricted cubic spline (RCS) model to generate fitting curves for each association. A p-value <0.05 for nonlinearity was regarded as indicative of a nonlinear association. After adjusting for all covariates, we utilized a smoothed piecewise logistic regression model

to analyze the threshold associations between sleep onset time or sleep duration and depression.

To address missing data for covariates, a multivariable single imputation method was employed, using Bayesian ridge regression models as the estimator in each imputation step, implemented through iterative imputation. To further ensure the robustness of our results, we compared the data before (with missing values excluded) and after imputation, and also used K-nearest neighbors imputation as part of the sensitivity analysis.

All statistical analyses were conducted using R statistical software (version 4.3.2, http://www.R-project.org, R Foundation) and Free Statistics software (version 2.0, Beijing, China, http://www.clinicalscientists.cn/freestatistics). A two-tailed *p*-value <0.05 was considered statistically significant.

3. Results

3.1. Study population

A total of 2424 patients aged 20 years and older with CKD were included in the study. We excluded pregnant women ($n = 8$), patients with missing data on sleep onset time and sleep duration ($n = 49$), and those with missing depression data ($n = 226$). Ultimately, 2141 CKD patients were included in the analysis for this cross-sectional study. The flowchart for participant enrollment is presented in Fig.1.

3.2. Characteristics of the participants

Table 1 presents the characteristics of the study population stratified by sleep onset time and sleep duration. Among the 2141 CKD patients, there were 1088 males (50.8 %) and 1053 females (49.2 %). Approximately 21.7 % of CKD patients reported an early sleep onset time (<22:00), while 25.5 % reported a late sleep onset time (≥24:00). Furthermore, 24.7 % of participants reported insufficient sleep duration (<7 h), and 27.1 % reported excessive sleep duration (≥9 h). CKD patients with early sleep onset time had an average sleep duration of 8.8 h, whereas those with late sleep onset time had an average sleep duration of 6.8 h. Compared to those with optimal sleep onset time, both late sleepers and early sleepers tended to have higher rates of depression (17.4 % vs. 8.1 % and 12.7 % vs. 8.1 %, respectively). Similarly, participants who reported insufficient or excessive sleep duration also exhibited corresponding trends in depression rates.

3.3. Associations of sleep onset time and sleep duration with depression

The results of the logistic regression model are presented in Table 2. In model 1, both early (<22:00) and late (≥24:00) sleepers had significantly increased risks of depression compared to those with optimal sleep onset time (22:00–23:59), with OR values of 1.65 (95 % CI: 1.16–2.33) and 2.39 (95 % CI: 1.76–3.24), respectively. Compared to individuals with sufficient sleep duration, those with insufficient sleep (<7 h) showed an increased risk of depression (OR = 1.39, 95 % CI: 1.01–1.93), while excessive sleep (≥9 h) was not significantly associated with depression (OR = 1.33, 95 % CI: 0.97–1.83).In the combined grouping of sleep onset time and sleep duration, CKD patients who had late sleep onset time and insufficient (OR = 2.57, 95 % CI: 1.68–3.94) or excessive sleep duration (OR = 2.52, 95 % CI: 1.34–4.73) showed increased depression risks compared to those with optimal sleep onset and sufficient sleep duration. Similarly, CKD patients who had early sleep onset time but excessive sleep duration also had increased depression risk (OR = 2.10, 95 % CI: 1.33–3.31). However, there was no significant association between sleep duration and depression risk in CKD patients with optimal sleep onset.

After adjusting for all covariates, the association between sleep onset time and depression in CKD patients remained significant. Specifically, early (OR = 1.45, 95 % CI: 1.01–2.08) and late (OR = 2.10, 95 % CI: 1.52–2.90) sleepers showed increased risks of depression compared to the reference group (22:00–23:59). In contrast, the association between sleep duration and depression was not significant. The results of the combined grouping of sleep onset time and sleep duration were

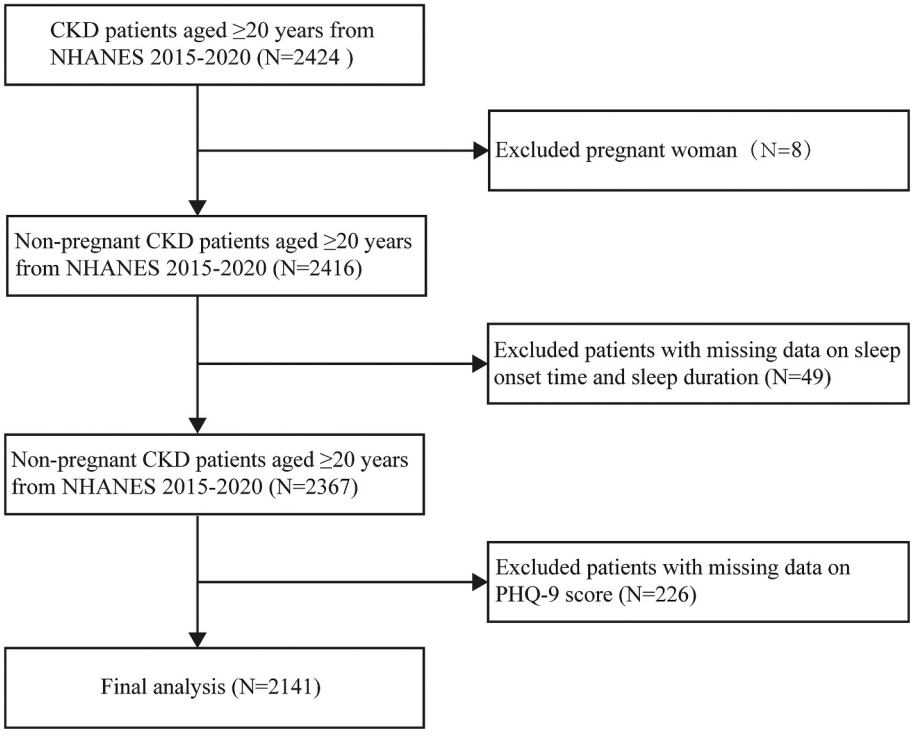

Fig. 1. Flowchart of participant selection among U.S. adults aged 20 years and older with chronic kidney disease from NHANES 2015–2020.
Abbreviations: NHANES, National Health and Nutrition Examination Survey; CKD, chronic kidney disease; PHQ-9, Patient Health Questionnaire-Nine.

Table 1
Descriptive characteristics of U.S. adults aged 20 years and older with chronic kidney disease from NHANES 2015–2020.

Characteristic	Total (n = 2141)	Sleep onset time			Sleep duration		
		<22:00 (n = 464)	22:00–23:59 (n = 1132)	≥24:00 (n = 545)	<7 h (n = 528)	7-8 h (n = 1032)	≥9 h (n = 581)
Age (year), Mean (SD)	61.5 (16.0)	63.5(15.2)	62.1 (16.0)	59.4 (16.5)	60.1(15.1)	61.3(16.0)	63.0(16.5)
Sex							
Male	1088 (50.8)	246 (53.0)	553 (48.9)	289 (53.0)	305(57.8)	517 (50.1)	266(45.8)
Female	1053 (49.2)	218 (47.0)	579 (51.1)	256 (47.0)	223(42.2)	515 (49.9)	315(54.2)
Marital status							
Married or living with a partner	1156 (54.0)	251(54.1)	638 (56.4)	267 (49.0)	276 (52.3)	587 (56.9)	293 (50.4)
Living alone[a]	985 (46.0)	213(45.9)	494 (43.6)	278 (51.0)	252 (47.7)	445 (43.1)	288 (49.6)
Race/ethnicity							
Non-Hispanic white	781 (36.5)	167 (36.0)	433 (38.3)	181(33.2)	151 (28.6)	394 (38.2)	236 (40.6)
Non-Hispanic black	638 (29.8)	144 (31.0)	314 (27.7)	180 (33.0)	184 (34.8)	280 (27.1)	174 (29.9)
Mexican American	275 (12.8)	76 (16.4)	146 (12.9)	53 (9.7)	61 (11.6)	137 (13.3)	77 (13.3)
Others[b]	447 (20.9)	77 (16.6)	239 (21.1)	131 (24.0)	132 (25.0)	221 (21.4)	94 (16.2)
Education level (year)							
< 9	252 (11.8)	77 (16.6)	130 (11.5)	45 (8.3)	52 (9.8)	113 (10.9)	87 (15.0)
9–12	815 (38.1)	208(44.8)	395 (34.9)	212(38.9)	197 (37.3)	369 (35.8)	249 (42.9)
>12	1074 (50.2)	179(38.6)	607 (53.6)	288(52.8)	279 (52.8)	550 (53.3)	245 (42.2)
PIR[c]							
Low	748 (34.9)	201(43.3)	349 (30.8)	198(36.3)	188 (35.6)	329 (31.9)	231 (39.8)
Medium	898 (41.9)	179(38.6)	486 (42.9)	233(42.8)	212 (40.2)	436 (42.2)	250 (43.0)
High	495 (23.1)	84 (18.1)	297 (26.2)	114(20.9)	128 (24.2)	267 (25.9)	100 (17.2)
Smoking status							
Never	1107 (51.7)	231(49.8)	627 (55.4)	249(45.7)	248 (47.0)	557 (54.0)	302 (52.0)
Current	656 (30.6)	150(32.3)	348 (30.7)	158 (29.0)	159 (30.1)	317 (30.7)	180 (31.0)
Former	378 (17.7)	83 (17.9)	157 (13.9)	138(25.3)	121(22.9)	158 (15.3)	99 (17.0)
Drinking status							
No	404 (18.9)	103(22.2)	220 (19.4)	81 (14.9)	84 (15.9)	188 (18.2)	132(22.7)
Yes	1737 (81.1)	361(77.8)	912 (80.6)	464(85.1)	444(84.1)	844 (81.8)	449(77.3)
Body mass index (kg/m^2), Mean (SD)	31.1 (8.0)	30.5(7.9)	30.9(7.6)	31.9(8.9)	32.2(8.6)	30.9(7.6)	30.4(8.1)
Physical activity							
Inactive	1347 (62.9)	304(65.5)	691 (61.0)	352(64.6)	349 (66.1)	609 (59.0)	389 (67.0)
Active	794 (37.1)	160(34.5)	441 (39.0)	193(35.4)	179 (33.9)	423 (41.0)	192 (33.0)
Comorbid condition[d]							
No	677 (31.6)	147(31.7)	373 (33.0)	157(28.8)	147 (27.8)	357 (34.6)	173 (29.8)
Yes	1464 (68.4)	317(68.3)	759 (67.0)	388(71.2)	381 (72.2)	675 (65.4)	408 (70.2)
Sleep duration(hour), Mean (SD)	7.7(1.7)	8.8(1.6)	7.8(1.5)	6.8(1.7)	5.5(0.9)	7.7(0.5)	9.8(1.0)
Obstructive sleep apnea							
No	1046 (48.9)	234 (50.4)	566 (50.0)	246 (45.1)	244 (46.2)	502 (48.6)	300 (51.6)
Yes	1095 (51.1)	230 (49.6)	566 (50.0)	299 (54.9)	284 (53.8)	530 (51.4)	281 (48.4)
Depression							
No	1895 (88.5)	405(87.3)	1040 (91.9)	450(82.6)	458 (86.7)	930 (90.1)	507 (87.3)
Yes	246 (11.5)	59 (12.7)	92 (8.1)	95 (17.4)	70 (13.3)	102 (9.9)	74 (12.7)

Abbreviations: NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.
[a] Included widowed, divorced, separated, or never married participants.
[b] Included multiracial participants. NHANES did not provide a detailed list of all races and ethnicities included in this category.
[c] Categorized into three levels: low (PIR ≤ 1.3), medium (1.3 < PIR ≤ 3.5), and high (PIR > 3.5). PIR was calculated by dividing family income by the poverty guidelines, specific to family size, as well as the appropriate year and state.
[d] Comorbid condition was defined as the presence of at least one of the following conditions: diabetes, hypertension, coronary heart disease, or stroke.

consistent with those of the crude model. However, further analysis of the interaction did not find any significant additive or multiplicative interactions (Supplementary Table S1).

The results from the multivariable analysis suggest that the association between sleep onset time, sleep duration, and depression may be nonlinear. The restricted cubic spline model further confirmed a U-shaped association between sleep onset time, sleep duration, and depression (Fig.2, A and B). Threshold analysis indicated that when the sleep onset time was <23:00, the OR for depression in CKD patients was 0.72 (95 % CI: 0.58–0.91), suggesting that delaying sleep onset time by one hour reduces the risk of depression by 28 %. Conversely, when sleep onset time was ≥23:00, the OR for depression was 1.21 (95 % CI: 1.09–1.35), indicating that each hour of delayed sleep increases the risk of depression by 21 % (Table 3). Additionally, when sleep duration was <7.5 h, the OR for depression in CKD patients was 0.79 (95 % CI: 0.65–0.96), implying that each additional hour of sleep duration reduces the risk of depression by 21 %. In contrast, when sleep duration was >7.5 h, the OR for depression was 1.37 (95 % CI: 1.17–1.61), suggesting that each additional hour of sleep increases the risk of depression by 37 % (Table 3).

3.4. Sensitivity analysis

In our sensitivity analysis, we compared the data with missing values excluded and the imputed data, and no statistical differences were found for any characteristics (Supplementary Table S2). Moreover, the results were consistent with our main findings after K-nearest neighbors imputation (Supplementary Table S3).

4. Discussion

In this nationally representative cross-sectional study, we found a nonlinear association between sleep onset time and sleep duration with the risk of depression in patients with CKD. The multivariable logistic regression analysis, adjusted for confounding factors, indicated that the combined effect of sleep onset time and sleep duration significantly increased the risk of depression in CKD patients. Specifically, late sleepers with insufficient or excessive sleep duration show a

Table 2
Logistic regression analysis on the association of sleep onset time and sleep duration with depression in U.S. adults aged 20 years and older with chronic kidney disease from NHANES 2015–2020.

Variable	Model 1 OR (95 %CI)	Model 2 OR (95 %CI)	Model 3 OR (95 %CI)
Sleep onset time			
<22:00	1.65 (1.16–2.33)	1.45 (1.02–2.08)	1.45 (1.01–2.08)
22:00–23:59	1.00	1.00	1.00
≥24:00	2.39 (1.76–3.24)	2.32 (1.69–3.19)	2.10 (1.52–2.90)
Sleep duration			
<7 h	1.39 (1.01–1.93)	1.41 (1.01–1.96)	1.26 (0.90–1.77)
7–8 h	1.00	1.00	1.00
≥9 h	1.33 (0.97–1.83)	1.19 (0.86–1.64)	1.17 (0.84–1.62)
Sleep onset time and sleep duration			
<22:00 and < 7 h	1.71 (0.64–4.56)	1.95 (0.71–5.30)	1.65 (0.60–4.55)
<22:00 and 7–8 h	1.13 (0.64–1.99)	0.97 (0.54–1.72)	0.93 (0.52–1.67)
<22:00 and ≥ 9 h	2.10 (1.33–3.31)	1.72 (1.08–2.76)	1.69 (1.05–2.73)
22:00–23:59 and < 7 h	0.93 (0.53–1.62)	0.90 (0.51–1.59)	0.85 (0.48–1.50)
22:00–23:59 and 7–8 h	1.00	1.00	1.00
22:00–23:59 and ≥ 9 h	1.05 (0.63–1.75)	0.94 (0.56–1.59)	0.87 (0.51–1.48)
≥24:00 and < 7 h	2.57 (1.68–3.94)	2.47 (1.59–3.84)	2.03 (1.29–3.19)
≥24:00 and 7–8 h	2.10 (1.31–3.35)	2.04 (1.26–3.29)	1.82 (1.12–2.97)
≥24:00 and ≥ 9 h	2.52 (1.34–4.73)	2.12 (1.11–4.05)	2.07 (1.07–4.00)

Model 1: Unadjusted.
Model 2: Adjusted for age, sex, marital status, race/ethnicity, education level and PIR.
Model 3: Adjusted for the variables in Model 2 + smoking status, drinking status, body mass index, physical activity, comorbid condition and obstructive sleep apnea.
Comorbid condition was defined as the presence of at least one of the following conditions: diabetes, hypertension, coronary heart disease, or stroke.
Abbreviations: NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.

significantly higher risk of depression.

In this study, the overall prevalence of depression among patients with CKD was 11.5 %, which is slightly higher than the previously reported prevalence of 9 % among American adults(Simon et al., 2024). Research indicates that this phenomenon may be related to comorbidities such as cardiovascular diseases and diabetes in CKD patients (Hedayati et al., 2009; Pu et al., 2020). Compared to previous studies on sleep and depression risk(Ortiz de la Rosa et al., 2022), we reached similar conclusions: both insufficient and excessive sleep duration are associated with a higher prevalence of depression compared to adequate sleep duration. However, studies on sleep onset time and its association with depression in CKD populations is relatively limited.

Our research further indicates a significant association between sleep onset time and depression in CKD patients, with both early and late sleepers exhibiting a higher prevalence of depression, particularly among late sleepers. In contrast, a retrospective cross-sectional study conducted on patients with delayed sleep phase syndrome (DSPS) found no association between self-reported sleep onset and depressive symptoms(Abe et al., 2011). Another case-control study reported that adolescents with earlier sleep onset and longer sleep duration showed a significant reduction in depressive symptoms compared to the control group(Dewald-Kaufmann et al., 2014). However, our multivariable analysis showed that compared to the reference group (22:00–23:59 and 7–8 h), early sleep combined with excessive sleep duration (<22:00 and ≥ 9 h) increased the risk of depression in CKD patients. The discrepancies between these two studies and our findings may be attributed to differences in the study populations and age. The first study involved Japanese DSPS patients with an average age of 27.1 ± 9.2 years, while the second study focused on Dutch adolescents with an average age of 15.44 years. Additionally, both studies had relatively small sample sizes of 90 and 55, respectively, whereas our study included a larger sample of 2141 American CKD patients with an average age of 61.5 ± 16 years. Furthermore, we hypothesize that, although sleep onset time before 22:00 helps regulate the circadian rhythm and improves sleep quality, excessive sleep duration may disrupt the biological clock and increase systemic inflammation(Leone et al., 2020; Satyanarayanan et al., 2020), contributing to depressive symptoms(Dowlati et al., 2010). Moreover, excessive sleep duration is often linked to reduced physical activity, which has been shown to increase the risk of depression(Wassink-Vossen et al., 2014). Our study also found that CKD patients with sleep duration ≥9 h tend to have inactive physical activity, which may further increase the risk of depression. Nevertheless, caution is warranted when generalizing our findings to other populations.

In addition, our study found that CKD patients with late sleep onset and adequate sleep duration (≥24:00 and 7–8 h) did not reduce the depression risk (OR = 1.82, 95 % CI: 1.12–2.97) compared to those reporting optimal sleep onset and sufficient sleep duration (22:00–23:59 and 7–8 h). While the sleep duration in this group meets the recommended 7–8 h, we believe that sleeping after midnight is commonly associated with an evening chronotype, which tends to be accompanied by circadian rhythm disturbances, higher psychological stress, and poor sleep quality, thereby potentially increasing the risk of depression (Merikanto and Partonen, 2021; Ong et al., 2007; Wang et al., 2024b). Although we observed joint effects between sleep onset time and sleep duration, further analysis revealed no significant multiplicative interactions. However, it is interesting to note that both RERI and AP were close to the null value, and SI was greater than one (though not significant). This suggests that, due to limitations in sample size or outcome events, a positive additive interaction may still exist despite the lack of statistical significance in this study. Considering the joint effects mentioned above, we recommend that CKD patients maintain a regular sleep schedule and avoid going to bed too late, particularly after midnight. An optimal sleep duration is 7–8 h, and excessive sleep duration (≥9 h) should be avoided, as it may elevate the risk of depression. Maintaining a healthy sleep pattern could help reduce the risk of depression and improve overall health in CKD patients.

Through the adjustment of confounding factors in the RCS curve fitting analysis, we found a U-shaped association between sleep onset time, sleep duration, and the risk of depression in CKD patients. This finding is consistent with previous cohort studies involving Chinese adolescents and rural adults, which also indicated a U-shaped association between sleep duration and depressive symptoms(Jiang et al., 2020; Liu et al., 2020). Further threshold analysis revealed that the inflection points for sleep onset time and sleep duration were 23:00 and 7.5 h, respectively. Delaying sleep before 23:00 was associated with a reduced risk of depression, while delaying sleep after 23:00 increased the risk. Additionally, for those with sleep durations shorter than 7.5 h, increasing sleep duration was linked to a lower risk of depression, whereas extending sleep beyond 7.5 h was associated with an increased risk. This finding aligns with the recommendation by the American Academy of Sleep Medicine and the Sleep Research Society, which suggests that adults should get seven to eight hours of sleep each night (Watson et al., 2015).

The underlying mechanisms linking sleep onset time and sleep duration to depression in patients with CKD remain unclear, but may be related to several factors. First, delayed sleep onset and insufficient sleep may affect melatonin secretion, thereby disrupting circadian rhythms and regulating inflammatory cytokines (such as interleukin-6, interleukin-1β, and tumor necrosis factor-alpha) (Landgraf et al., 2016;

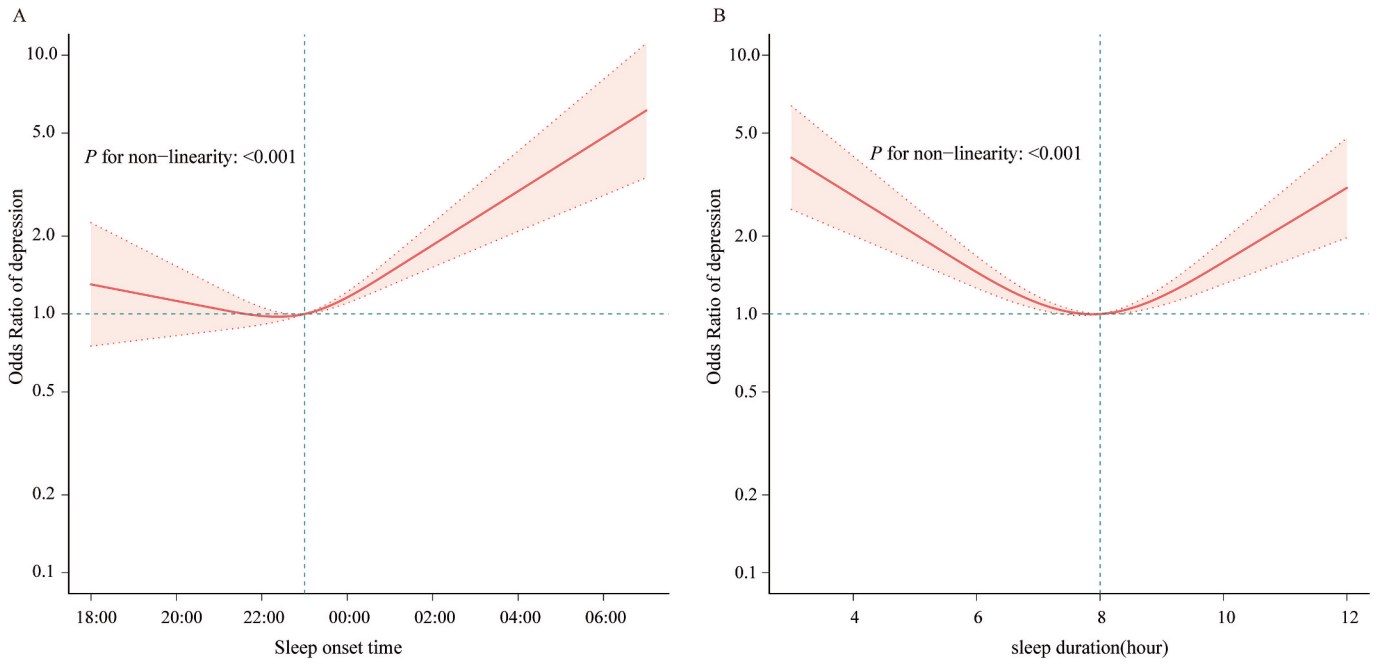

Fig. 2. Restricted cubic spline analysis of the association between sleep onset time (A) and sleep duration (B) with depression in U.S. adults aged 20 and older with chronic kidney disease from NHANES 2015–2020.
Note: The restricted cubic spline model was adjusted for age, sex, marital status, race/ethnicity, education level, poverty income ratio, smoking status, drinking status, body mass index and physical activity, comorbid condition and obstructive sleep apnea. Only 99 % of the data is displayed.

Table 3
Threshold effect analysis of sleep onset time and sleep duration on depression in U.S. adults aged 20 years and older with chronic kidney disease from NHANES 2015–2020.

Variable	Adjusted[a] OR (95 %CI)
Sleep onset time	
< 23:00	0.72 (0.58–0.91)
≥ 23:00	1.21 (1.09–1.35)
Likelihood Ratio test *p*-value	<0.001
Sleep duration	
<7.5 h	0.79 (0.65–0.96)
≥7.5 h	1.37 (1.17–1.61)
Likelihood Ratio test *p*-value	<0.001

Comorbid condition was defined as the presence of at least one of the following conditions: diabetes, hypertension, coronary heart disease, or stroke.
Abbreviations: NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.
[a] Adjusted for age, sex, marital status, race/ethnicity, education level, PIR, smoking status, drinking status, body mass index and physical activity, comorbid condition and obstructive sleep apnea. Only 99 % of the data is displayed.

Satyanarayanan et al., 2020). Previous studies have shown a significant association between these factors and depressive symptoms (Dowlati et al., 2010; Gimeno et al., 2009). Furthermore, due to reduced melatonin levels in CKD patients and elevated inflammatory cytokine levels (Garibotto et al., 2006; Koch et al., 2010), there may be an increased risk of depression and heightened sensitivity to sleep issues.

Our study has several limitations. First, since the findings are based on cross-sectional data, we cannot establish causal association between sleep onset time, sleep duration, and depressive symptoms. Future longitudinal studies are needed to verify these associations. Second, we collected information on sleep duration and sleep onset time through self-reports, which may introduce reporting and recall biases. However, in large-scale studies, objectively measuring sleep information can be challenging, and self-reported methods have been widely adopted in many studies(Hu et al., 2024; Zhou et al., 2020). Additionally, existing research has demonstrated good consistency between self-reported sleep assessments and data obtained through actigraphy(Lockley et al., 1999). In the future, we plan to conduct longitudinal studies to explore the causal association between sleep issues and depression in patients with CKD.

5. Conclusion

In conclusion, among American CKD patients, a U-shaped association was observed between sleep onset time, sleep duration, and the prevalence of depression, with inflection points at 23:00 for sleep onset time and 7.5 h for sleep duration. CKD patients who sleep late and have either insufficient or excessive sleep duration exhibit a higher prevalence of depression. This study offers new insights into the prevention and intervention of depression in CKD patients, emphasizing the importance of sleep management in reducing depression risk.

Ethics approval and consent to participate

Study protocols for NHANES were approved by the National Center for Health Statistics Ethics Review Board (Protocol #2011–17, https://www.cdc.gov/nchs/nhanes/irba98.htm). All the participants signed the informed consent before participating in the study. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Kaiying He: Writing – original draft, Methodology, Formal analysis. **Shiwan Guo:** Methodology, Formal analysis. **Juan Zhu:** Visualization, Data curation. **Zhihui Wang:** Validation, Data curation. **Shun Chen:** Validation. **Jiewei Luo:** Writing – review & editing, Supervision. **Li Chen:** Writing – review & editing, Supervision, Conceptualization. **Li Zhang:** Writing – review & editing, Supervision. **Jing Wu:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2025.103006.

Data availability

These survey data are free and publicly available, and can be downloaded directly from the NHANES website (http://www.cdc.gov/nchs/nhanes.htm) by users and researchers worldwide.

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