

# Association between kidney stones and poor sleep factors in U.S. adults

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# Abstract

The purpose of our study is to examine the correlation between sleep factors and the prevalence of kidney stones in US adults. A total of 34,679 participants from the National Health and Nutrition Examination Survey 2007 to 2018 were included in the analyses. Sleep data collection included: presleep factors (difficulty falling asleep, sleep onset latency), intra-sleep factors (risk index of obstructive sleep apnea, restless leg syndrome, difficulty maintaining sleep), post-sleep factors (daytime sleepiness, non-restorative sleep), sleep schedule and duration, and sleep quality. Logistic regression models were used to analyze the correlation between sleep factors and the prevalence of kidney stones. Among the 34,679 participants, the overall incidence of kidney stones was 9.3%. The presence of presleep factors (difficulty falling asleep [odds ratios [OR], 1.680; 95% CI, 1.310–2.150], prolonged sleep onset latency [OR, 1.320; 95% CI, 1.020–1.700]), intra-sleep factors (higher risk index of obstructive sleep apnea [OR, 1.750; 95% CI, 1.500–2.050], restless leg syndrome [OR, 1.520; 95% CI, 1.150–1.990], difficulty maintaining sleep [OR, 1.430; 95% CI, 1.130–1.760]), post-sleep factors (daytime sleepiness [OR, 1.430; 95% CI, 1.220–1.680], non-restorative sleep [OR, 1.400; 95% CI, 1.110–1.760]), short sleep duration (OR, 1.190; 95% CI, 1.080–1.310), mediate sleep quality (OR, 1.140; 95% CI, 1.020–1.290), and poor sleep quality (OR, 1.500; 95% CI, 1.310–1.720) are linked to the occurrence of kidney stones. However, short sleep onset latency, bedtime and wake-up time were not significantly associated with the prevalence of kidney stones. These findings showed positive associations between higher kidney stone prevalence and poor sleep factors.

**Abbreviations:** BMI = body mass index, IQR = interquartile ranges, NHANES = National Health and Nutrition Examination Survey, NRS = non-restorative sleep, ORs = odds ratios, OSA = obstructive sleep apnea, RLS = restless leg syndrome.

Keywords: cross-sectional study, epidemiology, kidney stones, NHANES, sleep

# 1. Introduction

The prevalence of kidney stones has been estimated at 9%,<sup>[1]</sup> with an increasing incidence among adults.<sup>[2]</sup> A common symptom of kidney stones is pain in the kidney area on the back and even down between the legs.<sup>[3]</sup> And sometimes accompanied by hematuria and vomiting.<sup>[4]</sup> The consequences of kidney stones are very serious, causing a heavy burden. However, the pathogenesis of kidney stones is still unclear. Previous studies have reported that many diseases may increase the risk of kidney stones, including systemic metabolic disorders,<sup>[5]</sup> cardiovascular events,<sup>[6]</sup> hypertension, diabetes,<sup>[7]</sup> and obesity.<sup>[8]</sup> Identifying the risk of kidney stones is crucial for preventing and treating these disease factors.

Adequate sleep is crucial for maintaining various physiological processes.<sup>[9]</sup> Poor sleep quality can lead to decreased immunity and increase the risk of some malignant diseases. Sleep duration,<sup>[10]</sup> posture,<sup>[11]</sup> and quality<sup>[12]</sup> have also been reported to play a vital role in kidney stones. Despite this, previous reports on this subject are sparse, and differ in terms of sleep factors. As a result, there is limited evidence to comprehensively reveal the impact of various sleep factors on kidney stones. This study utilized National Health and Nutrition Examination Survey (NHANES) data to investigate the correlation between kidney stones and various sleep factors. These factors included presleep factors (difficulty falling asleep, sleep onset latency), intra-sleep factors (risk index of obstructive sleep apnea [OSA], restless leg syndrome [RLS], difficulty maintaining sleep), post-sleep factors (daytime sleepiness, non-restorative sleep [NRS]), sleep schedule and duration, and sleep quality.

The objective of the present study was to further understand the association between comprehensive sleep factors and kidney stones. We expect this study to provide more detailed

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The datasets generated during and/or analyzed during the current study are publicly available.

The studies involving human participants were reviewed and approved by the NCHS research ethics review board. The patients/participants provided their written informed consent to participate in this study.

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information to aid in the prevention and management of kidney stones.

# 2. Materials and methods

# 2.1. Study population

NHANES is a representative cross-sectional survey designed by the National Center for Health Statistics. The purpose of NHANES is to assess the overall well-being and dietary condition of the American population. The NHANES interview encompassed questions regarding demographics, sleep factors and health status. NHANES used a complex, multistage probabilistic approach to select participants from across the country. The survey methods included interviews at home, conducting health examinations and collecting experimental data at mobile examination centers. In our study, the analysis was restricted to NHANES data collected between 2007 to 2018, and all interviews were conducted during this time period. We selected people aged 20 years or older (n = 34,770). Participants with no kidney stone information (n = 91) or any sleep information (n = 2) were excluded. The final study was 34,679 people. The interviews of this study were asked in the home, by trained interviewers, using the Computer Assisted Personal Interview system. The National Center for Health Statistics research ethics review board granted approval for the survey. Informed consent was obtained from all participants.

#### 2.2. Prevalent kidney stones

Prevalent kidney stones were ascertained by asking participants if they had ever had kidney stones.

# 2.3. Presleep factors

Difficulty falling asleep and sleep onset latency were included in presleep factors. Participants who reported having trouble falling asleep 5 to 15 times or 16 to 30 times per month were considered to have difficulty falling asleep. Sleep onset latency was divided into 3 categories: normal (6–30 minutes per night), prolonged (>30 minutes per night), or short ( $\leq$ 5 minutes per night).

### 2.4. Intra-sleep factors

The risk index of OSA, RLS, and difficulty maintaining sleep were included in intra-sleep factors. The risk index of OSA was assessed using an adapted multivariable apnea prediction index, based on NHANES variables. Three symptoms of OSA (noisy snoring, temporary breath cessation, and sudden gasping) was assessed using a Likert scale ranging from 0 to 4. The apnea index was determined by averaging the scores of the symptoms that were not missing. The adapted algorithm included body mass index, age, sex, and a symptom frequency index for apnea to classify participants into low-risk (apnea prediction < 0.5) and high-risk (apnea prediction  $\geq 0.5$ ) groups for OSA. RLS was defined as having frequent leg jerks or cramps, or a selfreported physician diagnosis. Participants who reported having leg jerks or cramps 5 to 15 times or 16 to 30 times per month were considered to have RLS; participants who reported waking up during the night and having trouble getting back to sleep 5 to 15 times or 16 to 30 times per month were considered to have difficulty maintaining sleep.

#### 2.5. Post-sleep factors

Daytime sleepiness and NRS were included in post-sleep factors. Individuals who indicated experiencing excessive

drowsiness during the day 5 to 15 times or 16 to 30 times per month were considered to have daytime sleepiness; Participants who reported feeling unrested during the day 5 to 15 times or 16 to 30 times per month were considered to have NRS.

#### 2.6. Sleep schedule and duration

Sleep schedule was categorized into 3 groups based on wake-up time and bedtime. Wake-up time categories included:  $\leq 06:00$ , 06:01 to 07:00, and > 07:00; bedtime categories included:  $\leq 22:00$ , 22:01 to 23:00, and > 23:00. Participants were asked about their typical sleep duration on weekdays or workdays. The recording time was divided into 3 categories: short (<7 hours), normal (between 7 and 9 hours), and long (more than 9 hours).<sup>[13,14]</sup>

#### 2.7. Sleep quality

Better sleep is considered to be between 7 and 9 hours/night without self-reported trouble sleeping or sleep disorders. Mediate sleep quality was defined as having one of the sleep problems above. Poor sleep quality was defined as experiencing 2 to 3 sleep problems above.

# 2.8. Covariates

Demographic variables and potential confounding variables associated with kidney stones were adjusted. Covariates included age, sex, ethnicity, marital status, level of education, smoking, alcohol intake, poverty income ratio, body mass index (BMI), hypertension, diabetes, and physical activity. Based on self-report questionnaires, race was categorized as nonwhite and white; marital status included married/living with partner, widowed/divorced/separated, or never married; educational level included 2 categories; smoking was divided into <100 or ≥100 cigarettes in life; alcohol drinking was divided into <12 or ≥12 alcohol drinks/year; low, middle, and high income correspond to poverty income ratio ≤1.3, 1.3 to 3.5 and >3.5 respectively; BMI <  $25 \text{ kg/m}^2$ ,  $25-29.9 \text{ kg/m}^2$ , and  $\geq 30 \text{ kg/m}^2$  represent normal weight, overweight, and obesity, respectively; medical conditions included hypertension and diabetes; physical activity was assessed for the presence of vigorous/moderate recreational activities.

#### 2.9. Statistical analysis

Data that follows a normal distribution is represented by the mean with standard deviations, while data that does not follow normal distribution is represented by medians  $\pm$  interquartile ranges (IQR).

Categorical variables are presented as numbers (percentage). We analyzed normally distributed two-group data by the Student *t* test and compared non-normally distributed variables by the Wilcoxon rank-sum test. Analysis of categorical variables with Pearson  $\chi^2$ . Odds ratios (ORs) and 95% confidence intervals were calculated by logistic regression models.

# 3. Results

#### 3.1. Participant characteristics

The characteristics of participants categorized by their kidney stone status are presented in Table 1. The study enrolled a total of 34,679 eligible individuals, of whom 51.5% were male and 48.5% were female. The participants with no kidney stones were 49 years (IQR 34–63), while those with kidney stones was 58

#### Table 1

#### Characteristics of participants by kidney stones.

Characteristics	Non-stone formers (n = 31.445)	Stone formers (n = 3234)	<i>P</i> value
Age median (IOD) y	40 (24, 62)	E9 (42, 60)	< 001
Age, meulan (IQR), y	49 (34, 63)	36 (43, 69)	<.001
Sex, NO. (%)	15,000 (47,700)	1702 (FE 122)	<.001
Male	15,030 (47.796)	1703 (33.133)	
Female Rece No. (%)	16,415 (52.202)	1431 (44.867)	- 001
Race, No. (%)	10 1 40 (00 070)	1510 (40.070)	<.001
NOT-WHILE	19,143 (00.878)	1319 (46.970)	
White	12,302 (39.122)	1715 (53.030)	001
Marital status, NO. (%)			<.001
Married/living with partner	18,308 (58.265)	2026 (62.686)	
Widowed/divorced/separated	7009 (22.306)	879 (27.197)	
Never married	6105 (19.429)	327 (10.118)	
Education level, No. (%)			.170
≤High school	14,977 (47.697)	1582 (48.963)	
>High school	16,423 (52.303)	1649 (51.037)	
Smoking status, No. (%)			
No	17,814 (56.687)	1600 (49.505)	<.001
Yes	13,611 (43.313)	1632 (50.495)	
Alcohol intake, No. (%)			.320
No	6535 (28.621)	711 (29.576)	
Yes	16,298 (71.379)	1693 (70.424)	
PIR, No. (%)		x y	.287
≤1.3	9288 (32,946)	949 (32,268)	
1.3–3.5	10.531 (37.355)	1142 (38.830)	
>3.5	8373 (29,700)	850 (28,902)	
BMI, median (IQR), kg/m <sup>2</sup>		()	< 001
<25	8846 (29,706)	615 (19,974)	
25-30	11 188 (37 571)	1427 (46.346)	
>30	9744 (32 722)	1037 (33 680)	
Hypertension No. (%)	0111(02.122)	1007 (00.000)	< 001
No	18 444 (58 655)	1387 (42 888)	<.001
Vac	13 001(41 345)	1847 (57 112)	
Diabatas No. (%)	13,001(+1.0+3)	1047 (01.112)	< 001
No	26 864 (86 418)	2420 (75 760)	<.001
Voe	20,004 (00.410) 1222 (12 522)	2439 (73.709) 780 (24.221)	
Its	4222 (13.362)	100 (24.231)	- 001
viguruus/mouerate recreational activities, NO. (%)	16 615 (50 840)	1024 (E0.802)	<.001
INU Vee	10,015 (52.843)	1934 (59.802)	
res	14,827 (47.157)	1300 (40.198)	

BMI = body mass index, n = sample size, PRI = poverty income ratio.

years (IQR 43–69 years). Older individuals, males and whites were found to have a higher likelihood of being participants with kidney stones, while a smaller proportion were unmarried. Furthermore, they displayed a greater prevalence of smoking, higher BMI, increased rates of hypertension and diabetes, and lower levels of reported physical activity compared to those without kidney stones.

#### 3.2. Association of presleep factors with kidney stones

First, we examined the correlation between presleep factors and the occurrence of kidney stones by employing a multivariate logistic regression model. Compared to the participants without difficulty falling asleep, participants experiencing difficulty falling asleep were related to a higher occurrence of kidney stones (OR, 1.680; 95% CI, 1.310-2.150) (Fig. 1). Additionally, we observed a positive trend where the risk of kidney stones increased with the severity and frequency of difficulty falling asleep (P for trend <.001). To expand our investigation, we divided the sleep onset latency into 3 categories and found that individuals with prolonged sleep onset latency were related to a greater occurrence of kidney stones (OR, 1.320; 95% CI, 1.020-1.700) than participants with normal sleep onset latency (Fig. 1). Conversely, individuals with short sleep onset latency did not exhibit a significant difference (P > .05)(Fig. 1).

#### 3.3. Association of intra-sleep factors with kidney stones

Our study shows that individuals with a higher risk of OSA (OR, 1.750; 95% CI, 1.500–2.050), RLS (OR, 1.520; 95% CI, 1.150–1.990) and difficulty maintaining sleep (OR, 1.430; 95% CI, 1.130–1.810) were associated with a greater occurrence of kidney stones (Fig. 2). The restricted cubic spline plot revealed a linear association between risk of OSA and prevalence of kidney stones (p for nonlinear = 0.843) (Fig. 3A). Moreover, the likelihood of developing kidney stones increased as the intensity and frequency of difficulty maintaining sleep (P for trend = .005).

# 3.4. Association of post-sleep factors with kidney stones

In this study, we found that individuals with daytime sleepiness (OR, 1.430; 95% CI, 1.220–1.680) and NRS (OR, 1.400; 95% CI, 1.110–1.760) were related to a higher risk of kidney stones (Fig. 4). Furthermore, the likelihood of developing kidney stones rose in correlation with the intensity and frequency of daytime sleepiness (*P* for trend < .001) or NRS (*P* for trend = .007).

# 3. 5. Association of sleep schedule and duration with kidney stones

The association of sleep schedule and duration with kidney stones was further examined. After adjusting for

Pre-sleep factors	n (%)	Model 1 <sup>a</sup> OR (95%Cl)	P value	Model 2 <sup>b</sup> OR (95%Cl)	P value	Model 3 <sup>c</sup> OR (95%Cl)		P Value
Difficulty falling asleep								
No	405/4439 (9.12)	1 [Reference]		1 [Reference]		1 [Reference]		
Yes	134/926 (14.47)	1.780 (1.430-2.200)	<0.001	1.720 (1.350-2.190)	<0.001	1.680 (1.310-2.150)	-	<0.001
Severity of difficulty falling asleep (n/month)								
<5	405/4439 (9.12)	1 [Reference]		1 [Reference]		1 [Reference]		
5-15	67/514 (13.04)	1.580 (1.180-2.080)	0.002	1.560 (1.130-2.110)	0.006	1.510 (1.090-2.060)	-	0.011
>15	67/412 (16.26)	2.040 (1.520-2.700)	<0.001	1.950 (1.390-2.680)	<0.001	1.910 (1.360-2.640)		<0.001
P for trend								<0.001
Sleep onset latency (mi	n)							
<= 5	147/1366 (10.76	8) 1.080 (0.873-1.340)	0.46	1.130 (0.885-1.440)	0.322	1.130 (0.886-1.440) -	<b>•</b>	0.317
5-30	261/2822 (9.24)	1 [Reference]		1 [Reference]		1 [Reference]		
> 30	127/1154 (11.00	) 1.340 (1.070–1.680)	0.011	1.360 (1.050-1.750)	0.018	1.320 (1.020-1.700)	- <b>-</b> -	0.036
						0.5	1 1.5 2 OR	2.5

Figure 1. Association between presleep factors and kidney stones. Adjusted for: <sup>a</sup>Model 1: age, sex, race; <sup>b</sup>Model 2: model 1, marital status, PRI, education level, smoking status, alcohol intake, BMI; <sup>o</sup>Model 2: model 2, hypertension, diabetes, activity.

Intra-sleep factors	n (%)	Model 1 <sup>a</sup> OR (95%Cl)	P value	Model 2 <sup>b</sup> OR (95%Cl)	P value	Model 3 <sup>c</sup> OR (95%Cl)		<i>P</i> Value
Risk index of OSA								
<0.5	641/8164 (7.85)	1 [Reference]		1 [Reference]		1 [Reference]	+	
>=0.5	781/4693 (16.64	) 2.070 (1.850-2.310)	<0.001	2.050 (1.770-2.380)	<0.001	1.750 (1.500-2.050 )		<0.001
RLS								
No	405/4472 (9.06)	1 [Reference]		1 [Reference]		1 [Reference]	+	
Yes	92/579 (15.89)	1.650 (1.280-2.100)	<0.001	1.600 (1.210-2.100)	<0.001	1.520 (1.150-1.990)	-	0.003
Difficulty maintaining slee	р							
No	401/4313 (9.30)	1 [Reference]		1 [Reference]		1 [Reference]	+	
Yes	138/1052 (13.12	2) 1.450 (1.170-1.790)	<0.001	1.470 (1.160-1.850)	0.001	1.430 (1.130-1.810)	-	0.003
Severity of difficulty maintaining sleep (n/mont	h)							
<5	, 401/4313 (9.30)	1 [Reference]		1 [Reference]		1 [Reference]	+	
5-15	79/624 (12.67)	1.390 (1.070-1.800)	0.013	1.430 (1.070-1.900)	0.013	1.420 (1.060-1.880)	-	0.017
>15	59/428 (13.79)	1.540 (1.130-2.050)	0.005	1.510 (1.070-2.110)	0.017	1.460 (1.020-2.040)	<b>—</b>	0.032
P for trend								0.005
						1	<u>     </u> 1 15 2	25
						0.5	1 1.5 2 OR	

Figure 2. Association between intra-sleep factors and kidney stones. Adjusted for: <sup>a</sup>Model 1: age, sex, race; <sup>b</sup>Model 2: model 1, marital status, PRI, education level, smoking status, alcohol intake, BMI; <sup>o</sup>Model 3: model 2, hypertension, diabetes, activity. OSA = obstructive sleep apnea, RLS = restless leg syndrome.

confounders, we found that bedtime and wake-up time were not significantly related to the risk of kidney stones (P > .05) (Fig. 5). Subsequently, we analyzed sleep duration. The higher incidence of kidney stones was associated with individuals who had a shorter duration (OR, 1.190; 95% CI, 1.080–1.310) compared to those who had a normal duration (Fig. 5). In addition, the restricted cubic spline plot revealed a nonlinear association between sleep duration and prevalence of kidney stones (p for nonlinear = 0.001) (Fig. 3B). As sleep duration increased to the inflection point, which was equal to 8.12 hours, the risk of kidney stones gradually decreased. Above this point, the risk gradually increased.

# 3.6. Association of sleep quality with kidney stones

Individuals with a mediate sleep quality (OR, 1.140; 95% CI, 1.020–1.290) and poor sleep quality (OR, 1.500; 95% CI, 1.310–1.720) exhibited significant associations with an increased risk of kidney stones when compared to participants with a better sleep quality (Fig. 6).



Figure 3. Restricted cubic spline plots for the relationship between kidney stones and poor sleep factors ([A] risk index of OSA; [B] sleep duration). Adjusted for: age, sex, race, marital status, PRI, education level, smoking status, alcohol intake, BMI, hypertension, diabetes, activity. OSA = obstructive sleep apnea.

# 3.7. Association between kidney stones and poor sleep factors in sex subgroup

According to our findings, poor sleep factors are associated with kidney stones. Since the incidence of kidney stones is different between male and female patients, we conducted a subgroup analysis by sex. As shown in Table 2, we found consistent associations between most poor sleep factors and kidney stones in different sex (*P* for interaction > .05). Interestingly, when we performed analysis of the relationship between NRS and kidney stones, we found that this association existed in different populations (*P* for interaction = .011). The association between NRS and kidney stones was more significant in women (OR, 1.694; 95% CI, 1.195–2.400).

# 4. Discussion

Using an extensive dataset from the population, our study examined how different sleep factors are linked to the occurrence of kidney stones. Our findings indicate a robust association between these sleep factors and the occurrence of kidney stones. presleep disturbances (including difficulty falling asleep and sleep onset latency), intra-sleep disturbances (including risk index of OSA, RLS, and difficulty maintaining sleep), postsleep disturbances (including daytime sleepiness and NRS), disruptions in sleep schedule and duration, and diminished sleep quality may all be significantly associated with an increased prevalence of kidney stones.

In this study, we found that difficulty falling asleep, longer sleep onset latency and difficulty maintaining sleep were linked to a greater occurrence of kidney stones. Furthermore, we observed a greater occurrence of kidney stones was associated with daytime sleepiness and NRS. There may be several reasons can explain the strong connection. Firstly, individuals experiencing difficulty falling asleep, longer sleep onset latency and difficulty maintaining sleep often exhibit symptoms of anxiety and depression.<sup>[15]</sup> They may contribute to various neurological and metabolic disorders, such as hyperlipidemia, hypertension, diabetes, and hyperuricemia,<sup>[16-19]</sup> which are also risk factors for kidney stones.<sup>[20-23]</sup> Secondly, daytime sleepiness and NRS often result from chronic sleep deprivation, leading to reduced physical activity. Regular aerobic physical activity can help prevent kidney stone formation by stimulating thirst and increasing water intake. Additionally, anaerobic physical activity contributes to enhanced calcium absorption in bones and reduced urinary calcium excretion,<sup>[24]</sup> further reducing the incidence of kidney stones. In addition, we found that participants with OSA or RLS were positively related to a higher incidence of kidney stones. Hypoxia caused by OSA may contribute to this association. There is considerable evidence that hypoxia may

Post-sleep factors	n (%)	Model 1 <sup>a</sup> OR (95%CI)	P value N	Model 2 <sup>b</sup> OR (95%Cl)	P value	Model 3 <sup>C</sup> OR (95%CI)		P Value
Daytime sleepiness								
Νο	1198/12070 (9.93)	1 [Reference]		1 [Reference]		1 [Reference]	+	
Yes	499/3384 (14.75)	1.520 (1.360-1.700)	<0.001	1.480 (1.260-1.730)	<0.001	1.430 (1.220-1.680)	-	<0.001
Severity of daytime sleepiness (n/month)								
<5	1198/12070 (9.93)	1 [Reference]		1 [Reference]		1 [Reference]	•	
5-15	321/2233 (14.38)	1.480 (1.290-1.690)	<0.001	1.370 (1.130-1.650)	0.001	1.330 (1.100-1.600)	-	0.003
>15	178/1151 (15.46)	1.600 (1.340-1.890)	<0.001	1.710 (1.340-2.170)	<0.001	1.650 (1.290-2.090)		<0.001
P for trend								<0.001
NRS								
No	384/4095 (9.38)	1 [Reference]		1 [Reference]		1 [Reference]	+	
Yes	154/1262 (12.20)	1.490 (1.210-1.830	<0.001	1.440 (1.140-1.800)	0.002	1.400 (1.110-1.760)		0.004
Severity of NRS (n/month)								
<5	384/4095 (9.38)	1 [Reference]		1 [Reference]		1 [Reference]	+	
5-15	86/732 (11.75)	1.430 (1.100-1.830)	0.006	1.400 (1.050-1.830)	0.018	1.380 (1.040-1.820)	<b>_</b>	0.022
>15	68/530 (12.83)	1.580 (1.180-2.080)	0.002	1.500 (1.080-2.060)	0.014	1.430 (1.020-1.960)		0.034
P for trend								0.007
						0.5	1 1 5 2	2.5
						0.0	OR 2	2.0

Figure 4. Association between post-sleep factors and kidney stones. Adjusted for: "Model 1: age, sex, race; "Model 2: model 1, marital status, PRI, education level, smoking status, alcohol intake, BMI; "Model 3: model 2, hypertension, diabetes, activity. NRS = non-restorative sleep.

Sleep schedule and duration	n (%)	Model 1 <sup>a</sup> OR (95%CI)	P value	Model 2 <sup>b</sup> OR (95%Cl)	P value	Model 3 <sup>C</sup> OR (95%CI)	<i>P</i> Value
Wake-up time							
00:01-06:00	582/4829 (12.05)	1.190 (1.020-1.400)	0.029	1.250 ( 0.985-1.600)	0.070	1.250 (0.987-1.600)	0.067
6:01-7:00	248/2449 (10.13)	1 [Reference]		1 [Reference]		1 [Reference]	
07:01-12:00	286/2495 (11.46)	1.130 (0.943-1.350)	0.186	1.100 (0.828-1.470)	0.499	1.080 (0.804-1.440)	0.623
Bedtime							
18:01-22:00	435/4053 (10.73)	0.905 (0.777-1.050)	0.197	0.934 (0.744-1.170)	0.555	0.947 (0.753–1.190) 🔸	0.642
22:01-23:00	331/2816 (11.75)	1 [Reference]		1 [Reference]		1 [Reference]	
23:01-06:00	361/2939 (12.28)	1.120 (0.956-1.320)	0.158	0.933 (0.720-1.210)	0.601	0.931 (0.717–1.210)	0.592
Sleep duration (hours)							
<7	1217/10628 (11.45	) 1.290 (1.190-1.390)	<0.001	1.230 (1.120-1.350)	<0.001	1.190 (1.080-1.310) 🔶	<0.001
7-9	1802/18881 (9.54)	1 [Reference]		1 [Reference]		1 [Reference]	
>9	198/1835 (10.80)	1.050 (0.894-1.220)	0.511	1.160 (0.933-1.420)	0.176	1.090 (0.881-1.340)	0.411
						0.5 1 1.	5 2 2.5 R

Figure 5. Association of sleep schedule and duration with kidney stones. Adjusted for: "Model 1: age, sex, race; "Model 2: model 1, marital status, PRI, education level, smoking status, alcohol intake, BMI; "Model 3: model 2, hypertension, diabetes, activity.

Sleep quality	n (%)	Model 1 <sup>a</sup> OR (95%CI)	<i>P</i> value	Model 2 <sup>b</sup> OR (95%CI)	<i>P</i> value	Model 3 <sup>C</sup> OR (95%Cl)		<i>P</i> Value
Better sleep	805/10060 (8.00	) 1 [Reference]		1 [Reference]		1 [Reference]		
Mediate sleep	740/7683 (9.63)	1.240 (1.120-1.380)	<0.001	1.180 (1.040-1.320)	0.007	1.140 (1.020-1.290)	•	0.026
Poor sleep	528/3549 (14.88	) 1.760 (1.560-1.980)	<0.001	1.610 (1.410-1.840)	<0.001	1.500 (1.310-1.720)	-	<0.001
						0.5	1 1.5 OR	2

Figure 6. Association between sleep quality and kidney stones. Adjusted for: "Model 1: age, sex, race; "Model 2: model 1, marital status, PRI, education level, smoking status, alcohol intake, BMI; "Model 3: model 2, hypertension, diabetes, activity.

# Table 2

Association between kidney stones and poor sleep factors in sex subgroup.

	Male		Fer		
Variables	OR (95% CI)	P-value	OR (95% CI)	P-value	P for interaction
Presleep factors					
Difficulty falling asleep					.779
No	1 [Reference]		1 [Reference]		
Yes	1.700 (1.210,2.370)	<.001	1.530 (1.060,2.090)	.021	
Sleep onset latency (min)					.092
≤5	1.270 (0.946,1.700)	.108	0.836 (0.521,1.300)	.443	
5–30	1 [Reference]		1 [Reference]		
> 30	1.310 (0.914,1.850)	.135	1.200 (0.810,1.760)	.359	
Intra-sleep factors					.392
Risk index of OSA					
<0.5	1 [Reference]		1 [Reference]		
≥0.5	1.388 (1.055,1.827)	.019	1.313 (0.961,1.795)	.087	
RLS					.061
No	1 [Reference]		1 [Reference]		
Yes	1.230 (0.843.1.796)	.283	1.947 (1.289.2.940)	.002	
Difficulty maintaining sleep			(		.554
No	1 [Reference]		1 [Reference]		
Yes	1.403 (1.018.1.934)	.039	1.407 (0.985.2.009)	.061	
Post-sleep factors		1000	(0.000,2.000)	1001	
Davtime sleepiness					.084
No	1 [Reference]		1 [Reference]		1001
Yes	1 290 (1 030 1 610)	023	1 580 (1 240 1 990)	< 001	
NBS		1020	11000 (112 10,11000)		011
No	1 [Reference]		1 [Reference]		.011
Ves	1 132 (0 824 1 556)	443	1 694 (1 195 2 400)	003	
Sleen schedule and duration	1.102 (0.024,1.000)	.110	1.004 (1.100,2.400)	.000	
Waketime					326
00.01-06.00	1 190 (0 856 1 680)	303	1 310 (0 922 1 880)	140	.020
6:01-7:00	1 [Reference]	.000	1 [Reference]	.140	
07.01-12.00	1 200 (0 798 1 800)	383	1 000 (0 657 1 530)	982	
Bedtime	1.200 (0.700, 1.000)	.000	1.000 (0.007,1.000)	.502	058
18:01-22:00	0 760 (0 553 1 050)	001	1 200 (0 859 1 690)	280	.000
22.00	1 [Reference]	.001	1 [Reference]	.205	
23:01-06:00	0.870 (0.612.1.230)	137	1 010 (0 677 1 500)	966	
Sleen duration (hours)	0.070 (0.012,1.230)	.407	1.010 (0.077,1.300)	.300	737
~7	1 240 (1 000 1 410)	001	1 120 (0 968 1 200)	197	.101
7_9	1 [Reference]	.001	1 [Reference]	.121	
\ \0	1 1/0 (0 838 1 530)	288	1 060 (0 776 1 /10)	710	
Sleen natterns	1.140 (0.030,1.330)	.000	1.000 (0.770, 1.410)	.713	080
Batter clean	1 [Reference]		1 [Beference]		.003
Modiato sloop		259		040	
Poor cleen	1 /30 (1 100 1 720)	.200	1.210 (1.010,1.400) 1.530 (1.250 1.870)	.040	
i uui sieep	1.450 (1.180,1.720)	<.001	1.000 (1.200, 1.070)	<.001	

Adjusted for: age, race, marital status, PRI, education level, smoking status, alcohol intake, BMI, hypertension, diabetes, activity.

NRS = non-restorative sleep, OSA = obstructive sleep apnea, RLS = restless leg syndrome.

cause kidney damage and inflammation, thus accelerating the formation of kidney stones.<sup>[25-27]</sup> Hypercalcemia as a common risk factor for RLS and kidney stones may contribute to their association.<sup>[28,29]</sup> Besides, renal dysfunction is also considered to be one of the risk factors for RLS.<sup>[30]</sup> Renal dysfunction caused by kidney stones may also lead to the association.

Sleep schedule and duration are also important factors that influence kidney stones. In this study, we have conducted the first investigation of the correlation between sleep schedule, including wake-up time and bedtime, and the occurrence of kidney stones. Our results indicate that there is no higher occurrence of kidney stones among individuals who wake up early (00:01–06:00), wake up late (07:01–12:00), sleep early (18:01–22:00), or sleep late (23:01–06:00), when compared to those with regular wake-up time (6:01–7:00) and bedtime (22:01–23:00). Although previous studies have suggested a potential association between staying up late and various metabolic disorders,<sup>[31–33]</sup> which may contribute to the development of kidney stones, our study did not uncover a significant correlation between staying up late and kidney stones. We speculate that individuals with a tendency for late sleep

may also exhibit late rising patterns, and the schedule of sleep alone may not adequately reflect an individual's sleep characteristics. Furthermore, we analyzed the relationship between sleep duration and kidney stones and found that those with <7 hours of sleep was associated with a greater occurrence of kidney stones, while those who slept more than 9 hours did not. Previous studies have also reported similar findings.<sup>[10]</sup> Our research further suggests that sleep duration, rather than the schedule of sleep, was significantly related to the occurrence of kidney stones. We recommend that the optimal sleep duration is approximately 8 hours because the risk of kidney stones is lowest at this time. The strong correlation between sleep duration and kidney stones may be explained by the following reasons. Firstly, insufficient sleep may lead to endocrine disruption, including deteriorations in glucose homeostasis.<sup>[34]</sup> A sleep deprivation test reported that insufficient sleep also affects the body's inflammatory response.[35] Inflammation and diabetes may lead to an increased risk of kidney stones.<sup>[36,37]</sup> Secondly, the pain and discomfort caused by kidney stones often make it difficult for patients to fall asleep, maintain sleep and wake up early, which may reduce sleep duration.

Moreover, our study expands upon previous findings by examining the association between kidney stones and a comprehensive assessment of sleep quality rather than focusing solely on individual sleep characteristics. Our results demonstrate a significant relationship between poor sleep quality and the occurrence of kidney stones. Genetic factors may explain the significant association. Previous studies on sleep and genetics have demonstrated the presence of a heritable factor in sleep quality.<sup>[38]</sup> As a complex disease, kidney stone also has certain genetic factors.<sup>[39]</sup>

This study utilized repeat cross-sectional data obtained from a nationally representative sample of the adult population in the United States. However, it is important to acknowledge several limitations associated with the present investigation. First, causality cannot be established as a result of the study design's cross-sectional nature. In this study, we found that poor sleep factors were significantly associated with a higher incidence of kidney stones. Metabolic disorders, reduced physical activity, inflammation, and genetic factors may establish this association. However, the typical symptom of kidney stones is pain in the kidney area on the back, which may affect sleep. Second, the assessment of sleep factors relied on self-reported information, introducing the potential for recall bias. It is noteworthy that kidney stones inflict personal discomfort and impose substantial healthcare burdens on communities. Therefore, early identification and reduction of factors related to the incidence of kidney stones play a crucial role in the prevention and treatment of kidney stones.

# 5. Conclusions

Poor sleep factors are correlated with a higher prevalence of kidney stones. These sleep factors include presleep factors (difficulty falling asleep, sleep onset latency), intra-sleep factors (risk index of OSA, restless leg syndrome [RLS], difficulty maintaining sleep), post-sleep factors (daytime sleepiness, non-restorative sleep [NRS]), sleep schedule and duration, and sleep quality. The causality between sleep factors and kidney stones requires further research. Furthermore, it is essential to investigate the mechanism behind this correlation in order to prevent and treat kidney stones.

# **Author contributions**

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Visualization: Benhuang Yan, Jian Yu, Qiang Fang, Linyong Dai.

- Writing original draft: Benhuang Yan.
- Writing review & editing: Yi Zhi, Weibing Li.

# References

 Ferraro PM, Curhan GC, Gambaro G, Taylor EN. Antibiotic use and risk of incident kidney stones in female nurses. Am J Kidney Dis. 2019;74:736–41.

- [2] Kittanamongkolchai W, Mara KC, Mehta RA, et al. Risk of hypertension among first-time symptomatic kidney stone formers. Clin J Am Soc Nephrol. 2017;12:476–82.
- [3] Howles SA, Wiberg A, Goldsworthy M, et al. Genetic variants of calcium and vitamin D metabolism in kidney stone disease. Nat Commun. 2019;10:5175.
- [4] Kummer AE, Grams M, Lutsey P, et al. Nephrolithiasis as a risk factor for CKD: the atherosclerosis risk in communities study. Clin J Am Soc Nephrol. 2015;10:2023–9.
- [5] Tasian GE, Ross ME, Song L, et al. Annual incidence of nephrolithiasis among children and adults in South Carolina from 1997 to 2012. Clin J Am Soc Nephrol. 2016;11:488–96.
- [6] Bargagli M, Moochhala S, Robertson WG, et al. Urinary metabolic profile and stone composition in kidney stone formers with and without heart disease. J Nephrol. 2022;35:851–7.
- [7] Ferraro PM, Taylor EN, Eisner BH, et al. History of kidney stones and the risk of coronary heart disease. JAMA. 2013;310:408–15.
- [8] Barghouthy Y, Corrales M, Somani B. The relationship between modern fad diets and kidney stone disease: a systematic review of literature. Nutrients. 2021;13:4270.
- [9] Yang R, Xu XX, Liu H, et al. The impact of morning surgery or afternoon surgery on postoperative sleep quality and melatonin levels of elderly patients: a prospective, randomized study. Nat Sci Sleep. 2022;14:1677–86.
- [10] Yin S, Wang J, Bai Y, Yang Z, Cui J, Wang J. Association between sleep duration and kidney stones in 34 190 American adults: a cross-sectional analysis of NHANES 2007–2018. Sleep Health. 2022;8:671–7.
- [11] Chuang TY, Chiu YC, Fan YH, Hung SC, Cheng WM. Better sleep quality could reinforce the relationship between sleep posture and kidney stone laterality in obstructive sleep apnea patients. Urolithiasis. 2020;48:245–9.
- [12] Sheng W, Xianghong Z, Shi Q, et al. Association between sleep quality and urolithiasis among general population in Western China: a cross-sectional study. BMC Public Health. 2022;22:1787.
- [13] Chunnan L, Shaomei S, Wannian L. The association between sleep and depressive symptoms in US adults: data from the NHANES (2007– 2014). Epidemiol Psychiatr Sci. 2022;31:e63.
- [14] Dong L, Xie Y, Zou X. Association between sleep duration and depression in US adults: a cross-sectional study. J Affect Disord. 2022;296:183-8.
- [15] Chan SH, Lui D, Chan H, et al. Effects of mindfulness-based intervention programs on sleep among people with common mental disorders: a systematic review and meta-analysis. World J Psychiatry. 2022;12:636–50.
- [16] van Reedt Dortland AK, Giltay EJ, van Veen T, Zitman FG, Penninx BW. Longitudinal relationship of depressive and anxiety symptoms with dyslipidemia and abdominal obesity. Psychosom Med. 2013;75:83–9.
- [17] Lim LF, Solmi M, Cortese S. Association between anxiety and hypertension in adults: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2021;131:96–119.
- [18] Harun NSM, Yusoff SSM, Kadir AA, Noor NM, Draman N, Muhammad J. Depression, anxiety, stress, and socio-demographic factors for poor glycaemic control in patients with type II diabetes. J Taibah Univ Med Sci. 2019;14:268–76.
- [19] Tao R, Li H. High serum uric acid level in adolescent depressive patients. J Affect Disord. 2015;174:464–6.
- [20] Huang HS, Liao PC, Liu CJ. Calcium kidney stones are associated with increased risk of carotid atherosclerosis: the link between urinary stone risks, carotid intima-media thickness, and oxidative stress markers. J Clin Med. 2020;9:729.
- [21] Varabei A, Shuleika A, Arlouski Y, Vizhinis E. Peripheral ductal hypertension due to tributaryliths: new reason of abdominalgia for chronic pancreatitis. Pancreatology. 2016;16:S2.
- [22] Le CS, Hong NY. Obstructive uropathy and severe acute kidney injury from renal calculi due to adenine phosphoribosyltransferase deficiency. World J Pediatr. 2016;12:243–45.
- [23] Wang M, Lin X, Yang X, Yang Y. Research progress on related mechanisms of uric acid activating NLRP3 inflammasome in chronic kidney disease. Ren Fail. 2022;44:615–24.
- [24] Hatori M, Hasegawa A, Adachi H, et al. The effects of walking at the anaerobic threshold level on vertebral bone loss in postmenopausal women. Calcif Tissue Int. 1993;52:411–4.
- [25] Wang SY, Luo J, Dong YF, et al. Risk of glomerular filtration rate decline in patients with hypertrophic cardiomyopathy and obstructive sleep apnoea. Sci Rep. 2017;7:17399.

- [26] Ye T, Yang X, Liu H, et al. Theaflavin protects against oxalate calcium-induced kidney oxidative stress injury via upregulation of SIRT1. Int J Biol Sci. 2021;17:1050–60.
- [27] Wang B, Li ZL, Zhang YL, Wen Y, Gao YM, Liu BC. Hypoxia and chronic kidney disease. EBioMedicine. 2022;77:103942.
- [28] Lim LL, Dinner D, Tham KW, Siraj E, Shields R Jr. Restless legs syndrome associated with primary hyperparathyroidism. Sleep Med. 2005;6:283–5.
- [29] Zhou Y, Chu X, Jiang D, et al. Development and validation of a nomogram for risk prediction of nephrolithiasis recurrence in patients with primary hyperparathyroidism. Front Endocrinol (Lausanne). 2022;13:947497.
- [30] Hamed SA, Abdulhamid SK, El-Hadad AF, Fawzy M, Abd-Elhamed MA. Restless leg syndrome in patients with chronic kidney disease: a hospital-based study from upper Egypt. Int J Neurosci. 2023;133:257-68.
- [31] Yan B, Fan Y, Zhao B, et al. Association between late bedtime and diabetes mellitus: a large community-based study. J Clin Sleep Med. 2019;15:1621–7.

- [32] Liu XN, Naduvilath TJ, Wang J, et al. Sleeping late is a risk factor for myopia development amongst school-aged children in China. Sci Rep. 2020;10:17194.
- [33] Su Y, Li C, Long Y, He L, Ding N. Association between bedtime at night and systolic blood pressure in adults in NHANES. Front Med (Lausanne). 2021;8:734791.
- [34] Borel AL, Pépin JL, Nasse L, Baguet JP, Netter S, Benhamou PY. Short sleep duration measured by wrist actimetry is associated with deteriorated glycemic control in type 1 diabetes. Diabetes Care. 2013;36:2902–8.
- [35] Dolgin E. Deprivation: a wake-up call. Nature. 2013;497:S6-7.
- [36] Thongboonkerd V. Roles for exosome in various kidney diseases and disorders. Front Pharmacol. 2019;10:1655.
- [37] Taylor EN, Stampfer MJ, Curhan GC. Diabetes mellitus and the risk of nephrolithiasis. Kidney Int. 2005;68:1230–5.
- [38] Luciano M, Zhu G, Kirk KM, et al. "No thanks, it keeps me awake": the genetics of coffee-attributed sleep disturbance. Sleep. 2007;30:1378–86.
- [39] Oddsson A, Sulem P, Helgason H, et al. Common and rare variants associated with kidney stones and biochemical traits. Nat Commun. 2015;6:7975.