# RESEARCH



# Associations of overactive bladder (OAB) with suicidal ideation incidence and all-cause mortality among the U.S. population



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# Abstract

**Background** Few studies have explored the correlation between overactive bladder (OAB) and suicidal ideation. This study aims to investigate the association between OAB and suicidal ideation, as well as the relationship between OAB and all-cause mortality among individuals with suicidal ideation.

**Methods** Data from the 2005–2018 National Health and Nutrition Examination Survey (NHANES) were analyzed using cross-sectional and cohort study designs. Weighted multivariable logistic regression models were used to examine the association between OAB and suicidal ideation. Kaplan-Meier curves and weighted multivariable Cox proportional hazards models assessed the relationship between OAB and all-cause mortality among those with suicidal ideation. Interaction analyses on subgroups were conducted to validate the findings. Mediation analysis was performed to examine the effect of depression on the relationship between OAB and suicidal ideation.

**Results** Among 33,426 participants aged  $\geq$  20 years, 1,290 (3.8%) reported suicidal ideation. After adjusting for potential confounders, participants with OAB were 2.57 times more likely to have suicidal ideation (P < 0.001). Over an average follow-up of 87 months, 197 participants with suicidal ideation died. The Cox model revealed that participants with OAB had a 3.08 times higher risk of death (P = 0.006). Kaplan-Meier curves indicated higher survival rates for non-OAB participants. Mediation analysis indicates that depression significantly mediates the relationship between OAB and suicidal ideation, with a mediation proportion of 75.25% (P < 0.001).

**Conclusions** OAB is positively associated with the incidence of suicidal ideation and all-cause mortality among participants with suicidal ideation. Additionally, the association between OAB and suicidal ideation is mediated by depression.

Keywords ">Overactive bladder, Suicidal ideation, All-cause mortality, NHANES

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# Introduction

Suicide is one of the leading causes of death worldwide, with an estimated 700,000 people dying by suicide each year, making it a significant public health issue [1]. Each suicide is a tragedy, impacting families, communities, and nations, and leaving long-lasting effects on those left behind. Suicidal behavior encompasses a range of actions, including suicidal ideation, planning, attempts, and the act of suicide itself. Suicidal ideation is closely linked to suicide attempts and deaths, serving as a crucial risk factor for future attempts, highlighting the urgent need for early diagnosis and prevention of suicidal thoughts [2]. Suicide often results from feelings of hopelessness, frequently attributed to mental disorders such as major depressive disorder, bipolar disorder, schizophrenia, alcoholism, or substance abuse [3].

According to the International Continence Society, OAB is defined as a symptom syndrome characterized by urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology [4]. OAB is a common and distressing chronic condition that significantly impacts the quality of life and imposes substantial economic burdens [5]. It is estimated that OAB costs developed countries' healthcare budgets and the broader economy billions of dollars [6]. Given the demographic shift towards an aging population and the increasing prevalence of OAB with age, the economic burden of OAB is expected to rise. Additionally, OAB adversely affects occupational and work productivity [7, 8]. Research has suggested a correlation between OAB and increased psychological issues like anxiety and depression [9]. However, a direct link between OAB and suicidal ideation has yet to be established. Additionally, the risk factors and pathogenesis of OAB are not yet fully understood. Although the mechanisms underlying OAB are complex, psychosocial factors such as lifestyle, dietary habits, and personality traits are considered to have the most significant influence on the condition [10]. A population-based study in Taiwan found that OAB patients have significantly higher risks of depression, anxiety, dementia, and psychotic symptoms [11]. Individuals with psychological disorders such as depression have a higher risk of suicide compared to the general population, highlighting the importance and urgency of alleviating OAB symptoms to reduce suicidal ideation. Nonetheless, there is currently a paucity of research exploring the correlation between OAB and suicidal ideation.

This study aims to fill this gap by utilizing a crosssectional analysis of extensive population data from the National Health and Nutrition Examination Survey (NHANES) cycles from 2005 to 2018. It seeks to explore the association between OAB and suicidal ideation among American adults and to determine whether this association is consistent across different demographic groups and comorbid populations. By gaining a clearer understanding of these relationships, the study aims to provide new strategies for the prevention and management of OAB in future clinical practice.

# Methods

The NHANES is designed to assess the nutrition and health of the American population. Data from the NHANES are large-sample, high-quality, and representative to facilitate valuable research on different health conditions in the general population. Since all data are publicly available on the NHANES website (https:// www.cdc.gov/nchs/nhanes/index.htm), there was no requirement for additional ethical approval and informed consent.

# **Study participants**

Among the 70,190 participants in the seven NHANES cycles from 2005 to 2018, 39,749 were aged  $\geq$  20 years. After excluding pregnant women (*n*=708), participants with missing OAB indicator data (*n*=5,319), and those with missing follow-up information (*n*=296), a total of 33,426 participants were included in the study (Fig. 1).

# Data collection

This study primarily focuses on the exposure variable, Overactive Bladder (OAB). Consistent with our previous research [12], OAB positivity is defined as having an Overactive Bladder Symptom Score (OABSS) equal to or greater than 3 (see Table S3 for OABSS scores). The main outcomes assessed are suicidal ideation and allcause mortality. Suicidal ideation is evaluated using the ninth item of the Patient Health Questionnaire 9 (PHQ-9) [13]. Several studies conducted in the past five years have demonstrated that the PHQ-9 consistently shows good internal reliability, with Cronbach's alpha values typically ranging from 0.79 to 0.89 across various settings and populations. For example, a study in Botswana reported a Cronbach's alpha of 0.799, confirming its reliability in a primary healthcare setting [14]. Another study in Lithuania with university students reported high internal consistency with a Cronbach's alpha of 0.86 [15]. Additionally, a systematic review in Uganda highlighted similar reliability scores across diverse cultural contexts [16]. Data on all-cause mortality are obtained from the National Death Index (NDI) up to December 31, 2019 (https://www.cdc.gov/nchs/data-linkage/mortality.htm). A directed acyclic graph (DAG) [17] was created to show the potential correlations between OAB, suicidal ideation, and other variables. Specific definitions of these variables and covariates can be found in Tables S1 to S3. The resulting DAG is presented in Figure S1.



Fig. 1 A flow diagram of eligible participant selection in the national health and nutrition examination survey

#### Statistical analysis

Our study utilized the NCHS-suggested weights to guarantee the national representativeness of data. Then, the fasting subsample 2-year weight (WTSAF2YR) was used as the weighting variable, with the new weights (for 2005–2018) calculated as  $1/7 \times$  WTSAF2YR. While categorical variables are represented as frequencies (percentages), continuous variables are stated as mean±SD. When comparing continuous variables between the OAB and Non-OAB groups, weighted t-tests were employed, while weighted chi-square tests were utilized for categorical variables.

The weighted multiple logistic regression was used in the analysis process to explore the correlation between OAB and suicidal ideation, and the results were presented as an odds ratio (OR) with an accompanying 95% confidence interval (CI). Three models adjusted for covariates were under assessment: Model 1 included no covariates, Model 2 mainly adjusted for demographic characteristics, and Model 3 further adjusted for all covariates. Kaplan-Meier curves were used to describe the mortality rates of participants with suicidal ideation and were compared by the log-rank test. Weighted Cox proportional hazard models were employed to examine the association between OAB and mortality among participants, stratified by the presence of suicidal ideation. Subgroup analyses were subsequently performed to investigate potential interactions.

The direct, indirect, and total effects were evaluated using the R software's "mediation" package [18]. The relationship between OAB and suicidal ideation was examined using a mediation analysis with 1000 bootstrap resamples and variable correction to see if depression mediated the relationship. The mediated fraction was calculated as follows: indirect effect/(indirect impact+direct effect) ×100% [17]. Regression coefficients (Figure S2) represent the overall impact of OAB on suicidal ideation (path C), the direct impact of OAB on suicidal ideation when depression (mediator) is included in the model (path C'), the impact of OAB on depression (path A),

# Result

#### **Baseline characteristics**

In this study, there were a total of 33,426 participants aged 20 years and older (16,723 males and 16,703 females). Baseline characteristics of all participants based on OAB status are shown in Table 1. Baseline characteristics of participants with suicidal ideation are detailed in Supplementary Table S4. The prevalence of OAB was 16%, and the prevalence of suicidal ideation was 3.8%. Over an average follow-up period of 87 months, 197 participants with suicidal ideation died (Table S4). Preliminary assessment indicates that a higher proportion of participants with OAB were female, older, White, married, of higher socioeconomic status, non-smokers, and engaged in regular physical activity. Additionally, to better understand the relationship between OAB and suicidal ideation, as well as the association between OAB and all-cause mortality in individuals with suicidal ideation, baseline characteristics were grouped into the suicidal ideation group and the non-suicidal ideation group (Table S5), and the mortality group and the non-mortality group (Table S6).

### Association of OAB and suicidal ideation

As shown in Table 2, three different models were used to assess the association between OAB and suicidal ideation. In the model adjusting for all covariates, participants with OAB had 2.57 times higher odds of experiencing suicidal ideation compared to those without OAB (OR=2.57, 95% CI [2.02, 3.27], P<0.001). Subgroup analysis results (Fig. 2) also demonstrate a positive association between OAB and suicidal ideation across various demographic groups. In addition, to improve the reliability of this study, we also assessed the relationship between urgency urinary incontinence and suicidal ideation. (Table S9).

Mediation analysis indicates that 75.25% (mediation proportion=indirect effect / (indirect effect+direct effect) \*100%, P<0.001) of the relationship between OAB and suicidal ideation was mediated by depression (indirect effect= $1.52*10^{-2}$ , P<0.001; direct effect= $5.11*10^{-3}$ , P<0.001). As a result, depression may operate as a mediating element in the connection between OAB and suicidal ideation. (Table S7 and S8, Figure S2).

# Correlation between OAB and mortality in participants with suicidal ideation

Among participants with suicidal ideation, 197 deaths occurred. Kaplan-Meier survival curves indicate that participants without OAB had higher survival rates compared to those with OAB (log-rank p<0.05, as shown in Fig. 3). The multivariable Cox regression model in Table 2 demonstrates that the hazard of death is 3.08 times higher in participants with OAB compared to those without OAB (HR=3.08, 95% CI: 1.38, 6.90, P=0.006). Subgroup analyses also support these findings (Fig. 2).

# Discussion

In this nationally representative sample study of U.S. adults, we found a significant positive correlation between OAB and suicidal ideation and that depression mediated this association. Furthermore, notably, we observed that among participants with suicidal ideation, OAB significantly increased the risk of mortality. These findings underscore the potential impact of OAB on both the incidence of suicidal ideation and mortality rates among these participants. They highlight the importance of managing and monitoring OAB to mitigate the risk of suicidal ideation and mortality.

Previous research has indicated that urological conditions such as bladder pain syndrome or interstitial cystitis [19] have potentially lethal consequences related to suicide. In a cross-sectional study involving 2,890 men aged 40 and above [20], the association between suicidal ideation and self-reported lower urinary tract symptoms was explored. After adjusting for income-topoverty ratio, BMI, alcohol intake, physical activity, current smoking, and comorbidities, individuals with lower urinary tract symptoms were found to be more likely to experience suicidal ideation. However, this study focused exclusively on men, and since lower urinary tract symptoms were self-reported, there may have been overestimations or underestimations of prevalence rates. In contrast, our study is based on a larger, nationally representative sample of the U.S. population. By adjusting for a broader range of covariates associated with suicidal ideation, we further confirm the robust association between OAB and suicidal ideation. This enhances the reliability of our findings regarding the significant correlation between OAB and suicidal ideation.

Patients with OAB often experience nocturia and urinary incontinence (UI). Data from the Health ABC Study [21] have shown that individuals who experience nocturia three or more times per night have significantly higher mortality rates. Interestingly, no association was found between sleep disturbances (including insomnia, sleep duration, or use of sleep medications) and increased mortality. A meta-analysis of observational studies [22], encompassing 158,456 patients from 19 countries,

# Table 1 Baseline characteristics of all participants were stratified by OAB

Characteristic	Overall, N = 33,426 (100%)	Non-OAB, N = 26,518 (84%)	OAB, N=6,908 (16%)	P Value
Age, n (%)				< 0.001
20–40	11,420 (37%)	10,518 (42%)	902 (16%)	
41–60	11,222 (38%)	9,040 (38%)	2,182 (36%)	
>60	10,784 (25%)	6,960 (20%)	3,824 (48%)	
Gender, n (%)				< 0.001
Male	16,723 (49%)	13,858 (52%)	2,865 (38%)	
Female	16,703 (51%)	12,660 (48%)	4,043 (62%)	
Race, n (%)				< 0.001
Non-Hispanic White	14,366 (68%)	11,569 (69%)	2,797 (65%)	
Non-Hispanic Black	7,191 (11%)	5,212 (10%)	1,979 (17%)	
Other	6,687 (13%)	5,556 (13%)	1,131 (11%)	
Mexican American	5,182 (8%)	4,181 (8%)	1,001 (7%)	
Married/live with partner, n (%)				< 0.001
No	13,599 (37%)	10,296 (36%)	3,303 (42%)	
Yes	19,827 (63%)	16,222 (64%)	3,605 (58%)	
Education level, n (%)				< 0.001
Below high school	8,104 (16%)	5,731 (14%)	2,373 (24%)	
High School or above	25,322 (84%)	20,787 (86%)	4,535 (76%)	
PIR, n (%)				< 0.001
Not Poor	21,156 (79%)	17,343 (81%)	3,813 (71%)	
poor	9,454 (21%)	7,018 (19%)	2,436 (29%)	
Obesity, n (%)				< 0.001
No	20,350 (62%)	16,974 (65%)	3,376 (51%)	
Yes	12,743 (38%)	9,337 (35%)	3,406 (49%)	
Smoking, n (%)				< 0.001
Never	18,236 (55%)	14,894 (56%)	3,342 (48%)	
Former	8,227 (25%)	6,122 (24%)	2,105 (31%)	
Current	6,963 (20%)	5,502 (20%)	1,461 (21%)	
Drinking, n (%)				< 0.001
former	5,345 (13%)	3,763 (12%)	1,582 (22%)	
heavy	6,576 (22%)	5,567 (23%)	1,009 (15%)	
mild	10,892 (37%)	8,903 (37%)	1,989 (34%)	
moderate	4,987 (18%)	4,154 (18%)	833 (15%)	
never	4,579 (10%)	3,446 (10%)	1,133 (14%)	
Physical activity, n (%)				< 0.001
Inactive	5,790 (22%)	4,555 (22%)	1,235 (27%)	
Active	18,869 (78%)	15,797 (78%)	3,072 (73%)	
CCI, n (%)				< 0.001
<1	17,725 (57%)	15,764 (62%)	1,961 (31%)	
$\geq 1$	15,701 (43%)	10,754 (38%)	4,947 (69%)	
Depression, n (%)	3.053 (8%)	1.755 (6.1%)	1.298 (17%)	< 0.001
Suicidal ideation, n (%)			/	< 0.001
No	32,136 (96.2%)	25,738 (97%)	6,398 (93%)	
Yes	1,290 (3.8%)	780 (3%)	510 (7%)	
All-cause mortality, n (%)	3,559 (7.7%)	2,161 (5.9%)	1,398 (17%)	< 0.001

Mean (SD) for continuous variables: the *P* value was calculated by the weighted t-tests

Percentages (weighted N, %) for categorical variables: the P value was calculated by the weighted chi-square test

Abbreviation: OAB, overactive bladder; PIR, Ratio of family income to poverty; CCI, Charlson Comorbidity Index

indicated that individuals with urinary incontinence (UI) have a higher risk of mortality. The risk increases with the severity and frequency of urinary leakage events, persisting in adjusted survival regression models for both

men and women. Our study found that individuals with OAB who have suicidal ideation are at a higher risk of mortality. This aligns with the notion that OAB, particularly when accompanied by distressing symptoms like

#### Table 2 Associations between OAB and suicidal ideation

OAB	Model 1 [OR/HR (95% CI)]	<i>p</i> -value	Model 2 [OR/HR (95% CI)]	<i>p</i> -value	Model 3 [OR/HR (95% CI)]	<i>p</i> -value
suicidal ideation						
Non-OAB	1 (ref.)		1 (ref.)		1 (ref.)	
OAB	2.70 (2.28, 3.19)	< 0.001	2.43 (1.98, 2.97)	< 0.001	2.57 (2.02, 3.27)	< 0.001
All-cause mortality in participants with suicidal ideation						
Non-OAB	1 (ref.)		1 (ref.)		1 (ref.)	
OAB	2.58 (1.70, 3.92)	< 0.001	1.76 (1.10, 2.83)	0.019	3.08 (1.38, 6.90)	0.006

Model 1: no covariates were adjusted

Model 2: age, gender, education level, marital, PIR, and race were adjusted

Model 3: age, gender, education level, marital, PIR, race, obesity, smoking, drinking, Physical activity, Depression, and CCI were adjusted Abbreviation: CCI, Charlson Comorbidity Index; PIR, Ratio of family income to poverty; OR, odds ratio; HR, hazard ratio; CI, confidence interval

	Subgroup	OR(95%CI)		P for interaction		Subgroup	HR(95%CI)	P for interaction
. –	Overall	2.57(2.02 to 3.27)				Overall	3.08(1.38 to 6.90)	
A	Age			0.937	В	Age		0.18
	20-40	2.45(1.62 to 3.70)				20-40	4.67(0.65 to 33.55)	<b>→</b>
	41-60	2.52(1.74 to 3.64)				41-60	2.75(1.05 to 7.16)	<b>→</b>
	>60	2.89(1.80 to 4.63)				>60	1.77(0.85 to 3.67)	
	Gender			0.582		Gender		0.347
	Male	2.80(1.94 to 4.04)				Male	1.47(0.71 to 3.07)	
	Female	2.42(1.81 to 3.24)				Female	4.51(1.79 to 11.33)	<b>→</b>
	Race			0.728		Race		0.345
	Mexican American	3.12(1.68 to 5.79)				Mexican American	72.42(8.83 to 593.81)	
	Non-Hispanic White	2.63(1.87 to 3.69)				Non-Hispanic White	3.23(1.61 to 6.51)	<b>→</b>
	Non-Hispanic Black	2.44(1.59 to 3.75)				Non-Hispanic Black	1.00(0.19 to 5.16) < +	
	Other	2.29(1.50 to 3.48)				Other	6.81(1.21 to 38.21)	<b>→</b>
	Marital status			0.056		Marital status		0.073
	No	2.06(1.53 to 2.78)				No	3.67(1.89 to 7.13)	<b>→</b>
	Yes	3.31(2.24 to 4.89)				Yes	1.16(0.40 to 3.32)	
	Education			0.543		Education		0.194
	Below high school	2.51(1.64 to 3.83)				Below high school	1.35(0.49 to 3.73)	
	High School or above	2.63(1.95 to 3.54)				High School or above	3.24(1.66 to 6.31)	
	PIR			0.593		PIR		0.197
	Not Poor	2.69(1.90 to 3.81)				Not Poor	1.65(0.78 to 3.50)	
	poor	2.36(1.70 to 3.28)				poor	4.89(2.14 to 11.18)	<b>→</b>
	Obesity			0.3		Obesity		0.324
	No	2.27(1.65 to 3.11)				No	1.85(0.95 to 3.61)	
	Yes	3.08(2.11 to 4.50)				Yes	4.13(1.42 to 12.05)	
	Smoking			0.7		Smoking		0.197
	Never	3.36(2.30 to 4.91)				Never	4.77(1.42 to 16.04)	<b>→</b>
	Former	2.18(1.29 to 3.69)				Former	1.26(0.41 to 3.82)	
	Current	2.18(1.57 to 3.03)				Current	3.02(1.21 to 7.53)	<b>→</b>
	Drinking			0.855		Drinking		0.307
	former	2.99(1.79 to 4.99)				former	1.05(0.40 to 2.73)	
	heavy	2.43(1.61 to 3.67)				heavy	15.04(1.65 to 137.01)	<b>→</b>
	mild	2.88(1.77 to 4.68)				mild	4.61(1.21 to 17.52)	<b>→</b>
	moderate	2.03(1.03 to 3.99)				moderate	0.00(0.00 to Inf) <	<b>→</b>
	never	2.82(1.27 to 6.25)	· · · · · · · · · · · · · · · · · · ·			never	29.72(0.44 to 2009.28)	<b>→</b>
	Physical activity			0.424		Physical activity		0.661
	Inactive	2.37(1.64 to 3.42)				Inactive	4.14(1.62 to 10.57)	<b>→</b>
	Active	2.68(2.00 to 3.59)				Active	2.28(1.12 to 4.54)	
	CCI			0.965		CCI		0.285
	<1	2.49(1.67 to 3.72)				<1	4.52(1.34 to 15.23)	<b>`</b>
	=1	2.65(1.90 to 3.70)		7		=1	2.14(1.16 to 3.97)	
		0.8	1	6.5			0.4 1	6.5
		protective factor	risk factor	~			protective factor risk factor	

Fig. 2 Subgroup analyses of OAB with suicidal ideation and all-cause mortality in participants with suicidal ideation. (A) the association between OAB and suicidal ideation. (B) the association between OAB and all-cause mortality in participants with suicidal ideation. Analyses were adjusted for age, gender, education level, marital, PIR, race, obesity, smoking, drinking, Physical activity, Depression, and CCI

nocturia and UI, can significantly impact mental health and possibly influence severe outcomes such as suicidal thoughts. Future research should include extensive prospective cohort studies, randomized controlled trials, or animal experiments to determine the underlying mechanisms more conclusively.

There is a positive correlation between OAB and allcause mortality, with underlying mechanisms likely involving psychological health, comorbid chronic conditions, and quality of life impacts. First, OAB patients often experience psychological issues such as depression and anxiety [9], which not only exacerbate the progression of chronic diseases like hypertension and cardiovascular disorders [23, 24] but also directly increase mortality by raising the risk of suicide and other hazardous behaviors. Second, nocturia associated with OAB leads to poor sleep quality [25], which in turn triggers a range of health issues, such as obesity [26], diabetes [27], and the worsening of cardiovascular diseases, thereby increasing the risk of all-cause mortality. Furthermore, frequent urination can cause social impairments and isolation, further diminishing the quality of life for OAB patients, and potentially accelerating disease progression and mortality. These combined mechanisms explain the positive association between OAB and allcause mortality.



Fig. 3 Kaplan–Meier analysis of all-cause mortality in participants with suicidal ideation

In our study, mediation analysis revealed that depression significantly mediates the relationship between overactive bladder (OAB) and suicidal ideation, accounting for 75.25% of the total effect. This suggests that the psychological burden of OAB, characterized by distressing and persistent symptoms, contributes to the onset of depressive symptoms, which in turn elevates the risk of suicidal ideation. The chronic nature of OAB may lead to social isolation, diminished quality of life, and a sense of hopelessness [28], all of which are well-established precursors to depression. Depression, in this context, acts as

a critical psychological pathway, amplifying the impact of OAB on suicidal thoughts by exacerbating feelings of despair and reducing coping mechanisms. These findings underscore the importance of addressing depressive symptoms in patients with OAB to mitigate the heightened risk of suicidal ideation. Mental disorders, particularly anxiety and depression, are significant public health issues affecting both individuals and society and are recognized as important factors increasing the risk of suicidal ideation [29, 30]. OAB is closely associated with depression and anxiety [9, 31], suggesting that depression may influence the strength of the relationship between OAB and suicidal ideation. However, this does not diminish the overall significance of this association. One possible explanation is that OAB can lead to emotional disturbances, thereby further triggering suicidal ideation. OAB and depression share common biological pathways, with serotonin playing a crucial role in the pathogenesis of depression. Evidence indicates that the serotoninergic system plays a significant role in anxiety regulation during development and adulthood [32]. Serotonin also influences bladder function; experimental studies in rats have shown that decreased serotonin levels in the central nervous system (CNS) can lead to increased urinary frequency and overactive bladder muscles [33]. Lower serotonin levels may contribute to depression and play a role in anxiety, which could explain the association between these mental disorders and OAB.

Oxidative stress (OS) refers to an overload of oxidants and free radicals, primarily reactive oxygen species (ROS) such as superoxide anion (O<sup>2-</sup>), hydrogen peroxide  $(H_2O_2)$ , hydroxyl radical (-OH), and reactive nitrogen species (RNS) including nitric oxide (NO) and peroxynitrite (ONOO<sup>-</sup>). ROS and RNS are products of normal cellular metabolism and are recognized to play dual roles of both harmful and beneficial species, as they can exert detrimental or protective effects on biological systems [34]. The onset of OAB may be due to an imbalance between the generation of pro-oxidants such as free radicals and reactive substances, and the protective mechanisms induced by antioxidants to counteract oxidative stress. Hypoxia, excessive oxidative stress, and loss of blood supply play crucial roles in OAB [35]. Studies have indicated that oxidative stress plays a significant role in the pathophysiology of suicide [36, 37], particularly showing a positive correlation between levels of NADPH oxidase (NOX) and advanced oxidation protein products (AOPP) with the intensity of suicidal ideation. This suggests that oxidative stress may play a critical role in the association between OAB and suicidal tendencies and measuring oxidative stress biomarker levels could potentially aid in the early prevention of suicidal behavior.

Host microbiota refers to a community of microorganisms inhabiting various organs of the human body, including the oral cavity, nasal passages, lungs, intestines, skin, and bladder, primarily composed of bacteria, fungi, viruses, and archaea. In recent years, increasing research has highlighted the significant role of host microbiota in the occurrence and development of various human diseases, such as aging, cardiovascular diseases (CVD), and irritable bowel syndrome (IBS) [38, 39]. A recent crosssectional study reported that changes in gut microbiota can influence OAB and daily urgency [40], while other studies suggest that urinary microbiota may play an important role in OAB [41]. In 2023, Kenji Hashimoto and colleagues highlighted the emerging role of host microbiota in neuropsychiatric disorders [42], which are often major contributors to suicidal behavior [43]. Further research in this field could provide valuable insights into the complex relationships among bladder function, suicide, and bladder microbiota.

Approximately 64.1% of the bacterial species in the urinary microbiome have been found to overlap with those in the gut [44], suggesting that many bacteria present in urine may originate from the gastrointestinal tract. Studies have further proposed the existence of a microbiomegut-bladder axis, where gut microbiota may directly or indirectly influence functional urinary disorders, potentially contributing to the onset or exacerbation of OAB symptoms [45, 46]. Longitudinal research indicates that gut microbiota could be linked to an increased risk of OAB symptom progression, possibly through neural crosstalk between the bladder and the gastrointestinal system via parasympathetic and sympathetic pathways [47]. Gut bacteria ferment dietary fiber to produce shortchain fatty acids (SCFAs) such as acetate, propionate, and butyrate. These metabolites exhibit anti-inflammatory properties and may regulate immune responses [48], potentially affecting various organs, including the bladder.

Metabolic syndrome (MetS), defined by a cluster of cardiovascular risk factors such as altered glucose metabolism, abdominal obesity, dyslipidemia, and hypertension [49], is currently believed by scientists to potentially share common pathophysiological features with OAB [50]. A case-control study demonstrated a significantly higher prevalence of OAB among patients with MetS compared to those without [51], possibly due to the autonomic sympathetic overactivity and inflammatory effects associated with MetS. Analysis of longitudinal community-based data suggests a positive association between MetS and its components with suicide risk, after controlling for other factors [52]. Nonetheless, further research is needed to better understand the relationships among metabolic syndrome, OAB, and suicide.

Our study has several strengths. Firstly, we utilized data from the NHANES database, ensuring a representative sample size. We carefully adjusted for covariates such as age, sex, race, and comorbidities, and assessed their stability in various statistical models. Secondly, we relied on a scoring system rather than self-reporting for the diagnosis of OAB, which helps to reduce recall bias and subjective errors. In terms of data handling, we conducted subgroup analyses to validate the robustness of our findings. However, it must be acknowledged that certain limitations remain. (1) The cross-sectional nature of the data limits the ability to conclude causal relationships. Although OAB may affect suicidal ideation through depression, more thorough prospective cohort studies, randomized controlled trials, or animal experiments are required in the future to pinpoint the precise causative process. (2) Even though we included a reasonably high number of covariates based on previous research to improve the robustness of our study results, the limitations of the NHANES database prevent us from eliminating the potential confounding factors' ultimate impact on the study outcomes. It is crucial to carefully and objectively assess the study's findings as a result, underscoring the need for meticulously designed prospective studies in the future to further validate the association between suicide and OAB. (3) The use of questionnaires related to suicidal ideation defined by self-report and OAB defined by urinary incontinence as well as nocturia may bias the results as they may not accurately reflect the diagnosis of the participants. Therefore, the results of this study should be interpreted with caution. (4) In addition, this study utilized the PHQ-9 as an initial screening tool for suicide risk, but it is worth noting that the PHQ-9 may not be able to capture non-fatal suicides, which may not be as sensitive or as comprehensive as dedicated suicide risk assessment tools, and may have underestimated the associations between this study's use of questionnaires and self-reporting to define suicidal ideation as well as OAB and suicidal ideation. In future studies, we will consider incorporating more dedicated suicide risk assessment tools to improve the accuracy of identification of suicidal ideation and associated behaviors.

# Conclusion

In conclusion, there is a significant association between OAB and suicidal ideation. OAB patients at high risk of suicidal ideation should undergo close monitoring and early intervention to reduce suicide rates and mortality.

#### Abbreviations

NHANESNational Health and Nutrition Examination SurveyOABOveractive bladderPHQ-9Patient Health Questionnaire 9K-MCurves Kaplan-Meier curves

# **Supplementary Information**

The online version contains supplementary material available at https://doi. org/10.1186/s12888-024-06107-1.

Supplementary Material 1

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#### Author contributions

H.G. contributed to the original draft, Methodology, Supervision, Project administration, and Formal analysis. S.H. was involved in Writing – review & editing, Supervision, Project administration, and Investigation.

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#### Data availability

The datasets utilized and analyzed in this study are accessible from the corresponding author upon reasonable request.

#### Declarations

#### Ethics approval and consent to participate

The aspects of this study involving human participants, human materials, or human data were conducted following the principles outlined in the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. Written informed consent was obtained from all patients/participants involved in the study.

#### **Consent for publication**

Before their involvement in the study, all participants provided informed consent.

#### Institutional review board statement

Institutional Review Board permission was not required as the NHANES database is publicly accessible.

#### Conflict of interest

The authors declare no relevant financial or non-financial conflicts of interest.

#### **Competing interests**

The authors declare no competing interests.

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#### References

- Lovero KL, Dos Santos PF, Come AX, Wainberg ML, Oquendo MA. Suicide in Global Mental Health. Curr Psychiatry Rep. 2023;25:255–62.
- Harmer B, Lee S, Rizvi A, Saadabadi A. In: StatPearls, editor. Suicidal ideation. Treasure Island (FL): StatPearls Publishing; 2024.
- 3. Hawton K, van Heeringen K. Suicide Lancet. 2009;373:1372–81.
- 4. Henderson E, Drake M. Overactive bladder. Maturitas. 2010;66:257-62.
- Gibson S, Ellsworth P. Emerging therapies for overactive bladder: preclinical, phase I and phase II studies. Expert Opin Investig Drugs. 2024;:1–12.
- Wagner TH, Hu T. Economic costs of urinary incontinence. Int Urogynecol J. 1998;9:127–8.
- Meng E, Lin W, Lee W, Chuang Y. Pathophysiology of overactive bladder. LUTS. 2012;4:48–55.
- Milsom I, Kaplan SA, Coyne KS, Sexton CC, Kopp ZS. Effect of Bothersome overactive bladder symptoms on Health-related quality of life, anxiety, Depression, and treatment seeking in the United States: results from EpiLUTS. Urology. 2012;80:90–6.
- Zhang Y, Wu X, Liu G, Feng X, Jiang H, Zhang X. Association between overactive bladder and depression in American adults: a cross-sectional study from NHANES 2005–2018. J Affect Disord. 2024;356:545–53.
- Jin Z, Zhang Q, Yu Y, Zhang R, Ding G, Li T, et al. Progress in overactive bladder: novel avenues from psychology to clinical opinions. PeerJ. 2023;11:e16112.
- Tzeng N-S, Chang H-A, Chung C-H, Kao Y-C, Yeh H-W, Yeh C-B, et al. Risk of Psychiatric disorders in overactive bladder syndrome: a Nationwide Cohort Study in Taiwan. J Investig Med. 2019;67:312–8.
- 12. Feng G, Huang S, Zhao W, Gong H. Association between life's essential 8 and overactive bladder. Sci Rep. 2024;14:11842.
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606–13.
- Molebatsi K, Motlhatlhedi K, Wambua GN. The validity and reliability of the Patient Health Questionnaire-9 for screening depression in primary health care patients in Botswana. BMC Psychiatry. 2020;20:295.
- Pranckeviciene A, Saudargiene A, Gecaite-Stonciene J, Liaugaudaite V, Griskova-Bulanova I, Simkute D, et al. Validation of the patient health questionnaire-9 and the generalized anxiety disorder-7 in Lithuanian student sample. PLoS ONE. 2022;17:e0263027.

- Huang S, He Q, Wang X, Choi S, Gong H. Associations of the planetary health diet index (PHDI) with asthma: the mediating role of body mass index. BMC Public Health. 2024;24:2305.
- Wu R, Gong H. The association between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio and chronic obstructive pulmonary disease: the mediating role of dietary inflammatory index. Front Nutr. 2024;11.
- Hepner KA, Watkins KE, Elliott MN, Clemens JQ, Hilton LG, Berry SH. Suicidal ideation among patients with bladder Pain Syndrome/Interstitial cystitis. Urology. 2012;80:280–5.
- Breyer BN, Kenfield SA, Blaschko SD, Erickson BA. The Association of Lower Urinary Tract Symptoms, Depression and suicidal ideation: data from the 2005–2006 and 2007–2008 National Health and Nutrition Examination Survey. J Urol. 2014;191:1333–9.
- Endeshaw YW, Schwartz AV, Stone K, Caserotti P, Harris T, Smagula S, et al. Nocturia, insomnia symptoms and mortality among older men: the Health, Aging and Body Composition Study. J Clin Sleep Med. 2016;12:789–96.
- 22. John G, Bardini C, Combescure C, Dällenbach P. Urinary incontinence as a predictor of death: a systematic review and Meta-analysis. PLoS ONE. 2016;11:e0158992.
- 23. Rubio-Guerra AF, Rodriguez-Lopez L, Vargas-Ayala G, Huerta-Ramirez S, Serna DC, Lozano-Nuevo JJ. Depression increases the risk for uncontrolled hypertension. Exp Clin Cardiol. 2013;18:10–2.
- 24. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: a clinical review. Eur Heart J. 2014;35:1365–72.
- 25. Ancoli-Israel S, Bliwise DL, Nørgaard JP. The effect of nocturia on sleep. Sleep Med Rev. 2011;15:91–7.
- 26. Beccuti G, Pannain S. Sleep and obesity. Curr Opin Clin Nutr Metab Care. 2011;14:402–12.
- 27. Darraj A. The Link between sleeping and type 2 diabetes: a systematic review. Cureus 15:e48228.
- Przydacz M, Golabek T, Dudek P, Skalski M, Sobanski J, Klasa K, et al. Overactive bladder symptoms negatively affect sleep quality of patients with Depression. Int Neurourol J. 2021;25:59–68.
- Zhang J, Liu X, Fang L. Combined effects of depression and anxiety on suicide: a case-control psychological autopsy study in rural China. Psychiatry Res. 2019;271:370–3.
- Nepon J, Belik S-L, Bolton J, Sareen J. The relationship between anxiety disorders and suicide attempts: findings from the national epidemiologic survey on Alcohol and related conditions. Depress Anxiety. 2010;27:791–8.
- Melotti IGR, Juliato CRT, Tanaka M, Riccetto CLZ. Severe depression and anxiety in women with overactive bladder. Neurourol Urodyn. 2018;37:223–8.
- Gordon JA, Hen R. The serotonergic system and anxiety. NMM. 2004;5:027–40.
  Lee K-S, Na Y-G, DEAN-MCKINNEY T, Klausner AP, Tuttle JB, Steers WD. Altera-
- tions in voiding frequency and cystometry in the Clomipramine Induced Model of endogenous depression and reversal with fluoxetine. J Urol. 2003;170:2067–71.
- Valko M, Leibfritz D, Moncol J, Cronin MTD, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol. 2007;39:44–84.
- Wu Y-H, Chueh K-S, Chuang S-M, Long C-Y, Lu J-H, Juan Y-S. Bladder hyperactivity Induced by oxidative stress and bladder ischemia: a review of treatment strategies with antioxidants. Int J Mol Sci. 2021;22:6014.

- Koweszko T, Gierus J, Zalewska A, Maciejczyk M, Waszkiewicz N, Szulc A. The relationship between suicide and oxidative stress in a Group of Psychiatric inpatients. J Clin Med. 2020;9:3462.
- Loo JL, Mohamad Kamal NA, Goon JA, Ahmad Damanhuri H, Tan JAC, Abdul Murad NA, et al. The role of oxidative stress in suicidal Behaviour among Bipolar patients: a cross-sectional study in a Malaysian sample. Front Psychiatry. 2021;12:698911.
- Matsumoto H, Shiotani A, Katsumata R, Fukushima S, Handa Y, Osawa M, et al. Mucosa-Associated Microbiota in patients with irritable bowel syndrome: a comparison of subtypes. Digestion. 2021;102:49–56.
- Yin J, Liao S, He Y, Wang S, Xia G, Liu F, et al. Dysbiosis of gut microbiota with reduced Trimethylamine-N-Oxide level in patients with large-artery atherosclerotic stroke or transient ischemic attack. JAHA. 2015;4:e002699.
- Okamoto T, Hatakeyama S, Imai A, Yamamoto H, Yoneyama T, Mori K, et al. Altered gut microbiome associated with overactive bladder and daily urinary urgency. World J Urol. 2021;39:847–53.
- Antunes-Lopes T, Vale L, Coelho AM, Silva C, Rieken M, Geavlete B, et al. The role of urinary microbiota in lower urinary tract dysfunction: a systematic review. Eur Urol Focus. 2020;6:361–9.
- Hashimoto K. Emerging role of the host microbiome in neuropsychiatric disorders: overview and future directions. Mol Psychiatry. 2023;28:3625–37.
- 43. Brådvik L. Suicide risk and Mental disorders. Int J Environ Res Public Health. 2018;15:2028.
- 44. Dubourg G, Morand A, Mekhalif F, Godefroy R, Corthier A, Yacouba A et al. Deciphering the urinary microbiota repertoire by Culturomics reveals mostly anaerobic Bacteria from the gut. Front Microbiol. 2020;11.
- Worby CJ, Schreiber HL, Straub TJ, van Dijk LR, Bronson RA, Olson BS, et al. Longitudinal multi-omics analyses link gut microbiome dysbiosis with recurrent urinary tract infections in women. Nat Microbiol. 2022;7:630–9.
- Choi HW, Lee KW, Kim YH. Microbiome in urological diseases: Axis crosstalk and bladder disorders. Investig Clin Urol. 2023;64:126–39.
- 47. Shen C, Fang M, Zhang X, Zhu Z, Chen J, Tang G. Causal effects of gut microbiota on risk of overactive bladder symptoms: a two-sample mendelian randomization study. Front Microbiol. 2024;15.
- Smith PM, Howitt MR, Panikov N, Michaud M, Gallini CA, Bohlooly-Y M, et al. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. Science. 2013;341:569–73.
- Swarup S, Ahmed I, Grigorova Y, Zeltser R. In: StatPearls, editor. Metabolic syndrome. Treasure Island (FL): StatPearls Publishing; 2024.
- Hsu L-N, Hu J-C, Chen P-Y, Lee W-C, Chuang Y-C. Metabolic syndrome and overactive bladder syndrome may share common pathophysiologies. Biomedicines. 2022;10:1957.
- Saratlija Novakovic Z, Tesija RA, Puljak L. Association between metabolic syndrome and overactive bladder: a case–control study. Scandinavian J Urol. 2017;51:470–3.
- Chang J-C, Yen AM-F, Lee C-S, Chen SL-S, Chiu SY-H, Fann JC-Y, et al. Metabolic syndrome and the risk of suicide: a community-based integrated screening samples cohort study. Psychosom Med. 2013;75:807–14.

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