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Research Article

Factors influencing nocturia in benign prostatic hyperplasia risk population: Results based on NHANES(2017-2020)

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ABSTRACT

Background: To explore the influencing factors of nocturia in benign prostatic hyperplasia (BPH) risk population. **Methods:** Data from the National Health and Nutrition Examination Survey (NHANES) between the years 2017 and 2020 were analyzed to explore factors influencing nocturia in BPH risk population. After the inclusion of the BPH risk population over 50 years old, the data with incomplete data were excluded, and then univariate logistic regression was used to find the influencing factors for nocturia. Finally, all the influencing factors for nocturia were included for multiple logistic regression. The crucial factors were analyzed by ROC. **Results:** A total of 15,560 is managed. Among these, 1754 men are classified as BPH risk group. Depression rating level, history of elevated blood pressure, obesity, daytime sleepiness, sleep problems, depression, leaked urine during non-exercise, leaked urine before the toilet, leaked urine during exercise, frequency of urine leakage, age and weekday sleep are found to be associated with nocturia by univariate logistic regression（$p < 0.05$). Depression rating level, obesity and leak urine before toilet are risk factors for nocturia by multiple logistic regression（$p < 0.05$). Age (adjusted OR: 1.020, 95% CI 1.006–1.035, $p = 0.006$), PHQ-9 (adjusted OR: 1.100, 95% CI 1.068–1.133, $p = 0.000$), and BMI (adjusted OR: 1.029 95% CI 1.007–1.052, $p = 0.010$) as continuous variables are still risk factors for nocturia ($p < 0.05$). ROC analysis shows that the highest AUX of PHQ-9 is 0.633, frequency of urine leakage 0.571, BMI 0.553, and Age 0.549. **Conclusions:** The nocturia symptoms of the BPH risk population are caused by multiple factors. Among the comprehensive effects of various influencing factors, age, PHQ-9, BMI, and frequency of urine leakage play a major role. The most relevant is PHQ-9, that is, the level of depression score.

Keywords: BPH risk population; Real world study; Nocturia; Logistic Models; NHANES

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Abbreviations

BPH benign prostatic hyperplasia

NHANES National Health and Nutrition Examination Survey

LUTS Lower urinary tract symptoms

ROC receiver operating characteristic

AUC Area under curves

OR adjusted odds ratio

CI confdence interval

FOUL frequency of urine leakage

BMI body mass index

PHQ-9 Patient Health Questionnaire 9

1. Introduction

Benign prostatic hyperplasia (BPH) is a common disease, which mainly occurs in middle-aged and older men. In recent years, with the aggravation of the aging of the population, the incidence of the disease has also increased, which not only affects the physical and mental health of patients but also reduces the quality of life, causing an economic burden on social medical care[1]. BPH is becoming more and more common among men over the age of 50. This is the fourth most common diagnosis for older men[2]. One-quarter of men over 50 years old are affected, one third are affected when they are over 60 years old, and one-half of men over 80 years old are affected[3]. Men over 50 years old are at risk of BPH and become BPH risk population. BPH is a non-malignant enlargement of the prostate. Its clinical manifestations are lower urinary tract symptoms (LUTS) or acute urinary retention (AUR). The management of troublesome LUTS is the main focus of treatment intervention. In some cases, patients with drug treatment failure or worsening symptoms may need minimally invasive or surgical operations[4], which further increases the economic and psychological burden of patients.

The nocturia ≥ two times, which is a common lower urinary tract symptom of BPH, which exceeds the threshold and causes the burden of quality of life[5]. This definition is adopted in this study. Studies has shown that nocturia has a serious impact on the quality of life of patients in the United States and many European countries[6]. The study found that nocturia affects not only the overall health and daytime function but also the total mortality of patients with nocturia who urinate three times or more at night is significantly higher than that of the general population. The risk of falls and injuries at night among people with nocturia is twice that of ordinary people, because frequent nocturia reduces the quality of life, productivity, and may disturb their partners' sleep and affect their health. The lack of sleep caused by nocturia leads to fatigue, mood changes, lethargy, impaired productivity, inattention, and cognitive dysfunction, and is also related to decreased physical health, obesity, diabetes, depression, and heart disease. The annual loss to Americans due to productivity losses and sick leave associated with nocturia is estimated at $62.5 billion[7,8]. Identifying the main influencing factors of nocturia in the BPH risk population is of great significance for further improving the quality of life of this population and reducing the social medical economic burden. This study incorporates the real-world data of NHANES from 2017 to 2020. Statistical analysis was conducted through logistic regression analysis and ROC. The analysis of the influencing factors of nocturia in the BPH risk population can provide a theoretical basis for formulating health education and intervention measures for the BPH risk population.

2. Materials and methods

2.1 Study subjects

The population survey data from 2017 to 2020 are obtained from NHANES (https://www.cdc.gov/nchs/nhanes/index.htm), including personnel number SEQN, age, race, country of birth, education level (Education level - Adults 20+), marital status, urine flow rate (mL/min), frequency of urine leakage (How often have urinary leakage?), leak urine during exercise(Leak urine during physical activities?), Leak urine before toilet (Urinated before reaching the toilet?), Leak urine during non-exercise (Leak urine during nonphysical activities), number of nocturia (How many times urinate in night?), Patient Health

Questionnaire (Have little interest in doing things. Feeling down, depressed, or hopeless. Trouble sleeping or sleeping too much. Feeling tired or having little energy. Poor appetite or overeating. Feeling bad about yourself. Trouble concentrating on things. Moving or speaking slowly or too fast. Thoughts you would be better off dead)[9], sleep problems (Ever told doctor had trouble sleeping?), Daytime sleepiness (How often do you feel overly sleepy during the day?), drinking history (Ever had a drink of any kind of alcohol), height (inches), weight (pounds), history of elevated blood pressure (Ever told you had high blood pressure?), history of elevated blood lipids (Doctor told you - high cholesterol level?).

2.2 Data processing

Height and weight were converted into BMI (kg/m^2). The depression scoring items were integrated through the PHQ-9 depression rating scale. At the same time, continuous variables and classified variables were assigned by segments (**Table 1**).

Table 1 - Variable assignment table

Variable	Encode	Classification Description
Sleep problems	0	No
	1	Yes
Age(years)	1	50 - 59
	2	60 - 69
	3	70 - 79
	4	≥80
Race	1	Mexican American
	2	Other Hispanic
	3	Non-Hispanic White
	4	Non-Hispanic Black
	5	Non-Hispanic Asian
	6	Other Race - Including Multi-Racial
Country of birth	0	Non-US
	1	USA
Marital status	1	Married/Living with Partner
	2	Widowed/Divorced/Separated
	3	Never married
Depression rating level	1	Minimal, 0–4
	2	Mild, 5–9
	3	Moderate, 10–14
	4	Moderately severe, 15–19
	5	Severe, 20–27
Drinking history	0	No
	1	Yes
Obesity	0	BMI<30
	1	BMI≥30[10]
History of elevated blood pressure	0	No
	1	Yes
History of elevated blood lipids	0	No
	1	Yes
Nocturia	0	≤2
	1	>2
Urine flow rate level(ml/min)	1	0≤Urine flow rate level<1
	2	1≤Urine flow rate level<2
	3	2≤Urine flow rate level<3
	4	3≤Urine flow rate level<4
	5	4≤Urine flow rate level<5
	6	5≤Urine flow rate level
Daytime sleepy	0	Never
	1	Rarely - 1 time a month
	2	Sometimes - 2-4 times a month
	3	Often- 5-15 times a month
	4	Almost always - 16-30 times a month
Frequency of urine leakage	1	Never
	2	Less than once a month
	3	A few times a month
	4	A few times a week
	5	Every day and/or night
Education level	1	Less than 9th grade
	2	9-11th grade (Includes 12th grade with no diploma)
	3	High school graduate/GED or equivalent
	4	Some college or AA degree
	5	College graduate or above
Depression	0	Normal, PHQ-9<10
	1	Depression, PHQ-9≥10
Weekday sleep(h)	0	Weekday sleep<8h
	1	Weekday sleep≥8h

Table 1 continued

Variable	Encode	Classification Description
Weekend sleep(h)	0	Weekend sleep<8h
	1	Weekend sleep≥8h
Leak urine during exercise	0	No
	1	Yes
Leak urine before toilet	0	No
	1	Yes
Leak urine during non-exercise	0	No
	1	Yes

Data filtering

Data incorporation

Men aged 50 years or older.

Data elimination

Data that do not meet the Data incorporation, incomplete data.

Specific Data filtering process

2017-2020 NHANES data: 15560 persons in total.

7721 males after excluding females.

2465 persons remained after excluding males under 50 years old.

After excluding the following missing items, including the data of urine flow rate, PHQ-9, sleep duration, drinking history, height, weight, history of elevated blood pressure, history of elevated blood lips, and Daytime sleep, there are 1754 people left (**Fig 1**).

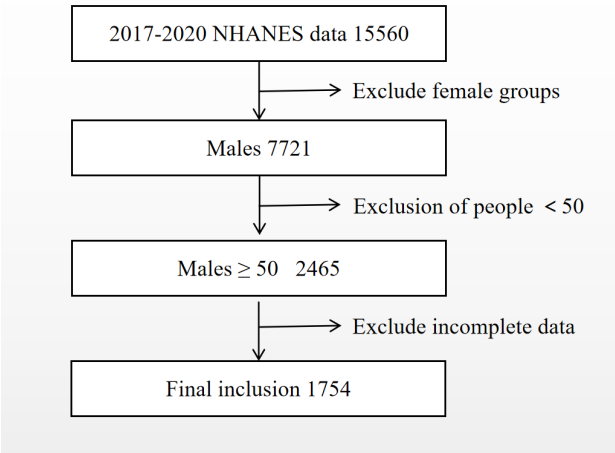

Fig 1 - Data filtering

2.3 Statistical analysis

Statistical analysis was performed using SPSS 26.0 (IBM Corp.). Non-normally distributed data were expressed as median (interquartile range) and compared using the Mann–Whitney U test. Categorical variables were expressed as frequencies and compared using the chi-square or Fisher's exact test. Logistic regression analysis was used to determine what was an independent predictor of nocturia in the total study population. Variables with an unadjusted p-value < 0.05 in the univariate analysis were subsequently evaluated using a multivariate logistic regression model. Receiver operating characteristic (ROC) curves were used to determine the best cut-off values for predicting factors in the study population, respectively. DeLong's test was used to compare the area under curves (AUCs) of the three ROC curves. A p-value < 0.05 is the criteria for statistical significance in this analysis.

Picture processing

The results of logistic regression are plotted with Graph Pad Prism 8 software.

3 Results

3.1 Data characteristics

The data characteristics of NHANES from 2017 to 2020 are shown in **Table 2**.

Table 2. Data characteristics.

Variable	Encode	Nocturia	Normal	p Value
		N=374	N=1380	
Age	1	95	440	0.014
	2	139	521	
	3	83	274	
	4	57	145	
Race	1	35	114	0.174
	2	36	119	
	3	151	598	
	4	111	345	
	5	26	145	
	6	15	59	
Country of birth	0	82	353	0.147
	1	292	1027	

Table 2 continued

Variable	Encode	Nocturia N=374	Normal N=1380	p Value
Education level	1	35	111	0.117
	2	47	142	
	3	102	331	
	4	111	423	
	5	79	373	
Marital status	1	240	960	0.134
	2	104	330	
	3	30	90	
Frequency of urine leakage	1	213	953	0.000
	2	40	130	
	3	41	139	
	4	33	93	
	5	47	65	
Leak urine during exercise	0	322	1290	0.000
	1	52	90	
Leak urine before toilet	0	220	1034	0.000
	1	154	346	
Leak urine during non-exercise	0	316	1261	0.000
	1	58	119	
Sleep problems	0	230	997	0.000
	1	144	384	
Daytime sleepy	0	64	278	0.001
	1	75	373	
	2	121	442	
	3	81	202	
	4	33	85	
Drinking history	0	12	71	0.118
	1	362	1309	
Obesity	0	227	990	0.000
	1	147	390	
History of elevated blood pressure	0	144	660	0.001
	1	230	720	
History of elevated blood lipids	0	163	654	0.190
	1	211	726	
Weekday sleep	0	183	765	0.025
	0	191	615	
Weekend sleep	0	142	580	0.157
	1	232	800	

Table 2 continued

Variable	Encode	Nocturia N=374	Normal N=1380	p Value
Urine flow rate level	1	248	957	0.000
	2	92	30	
	3	20	76	
	4	9	25	
	5	2	12	
	6	3	10	
Depression	0	320	1307	0.000
	1	54	71	
Depression rating level	1	251	1156	0.000
	2	67	153	
	3	35	57	
	4	14	8	
	5	5	6	

Univariate logistic regression analysis

There are 374 people with nocturia, accounting for 21.32%. Age, Dependence rating level, History of elevated blood pressure, Obesity, Daily sleep, Sleep problems, Dependence, Leak urine during exercise, Leak urine before toilet, Leak urine during non-exercise, Frequency of urine leakage, Weekday sleep are found to be correlated with the presence of nocturia ($p < 0.05$) (**Table 3, Fig 2**).

Table 3 - Univariate logistic regression

Variable	Encode	p Value	OR	95% CI	
Age	NA	0.015	NA	NA	NA
	2	0.153	1.236	0.924	1.652
	3	0.045	1.403	1.008	1.953
	4	0.002	1.821	1.247	2.658
Race	NA	0.179	NA	NA	NA
	2	0.957	0.985	0.579	1.676
	3	0.360	0.822	0.541	1.250
	4	0.833	1.048	0.678	1.619
	5	0.061	0.584	0.332	1.026
	6	0.588	0.828	0.419	1.637
Country of birth	NA	0.147	1.224	0.931	1.608
Education level	NA	0.119	NA	NA	NA
	2	0.850	1.050	0.635	1.736
	3	0.919	0.977	0.629	1.518
	4	0.406	0.832	0.539	1.284
	5	0.084	0.672	0.428	1.054

Table 3 continued

Variable	Encode	p Value	OR	95% CI	
Marital status	NA	0.135	NA	NA	NA
	2	0.083	1.261	0.970	1.638
	3	0.197	1.333	0.862	2.064
Frequency of urine leakage	NA	0.000	NA	NA	NA
	2	0.103	1.377	0.937	2.022
	3	0.151	1.320	0.904	1.927
	4	0.033	1.588	1.039	2.426
	5	0.000	3.235	2.161	4.844
Urine leakage during sports	NA	0.000	2.315	1.611	3.326
Leak urine before toilet	NA	0.000	2.092	1.647	2.657
Leak urine during non-exercise	NA	0.000	1.945	1.388	2.725
Depression	NA	0.000	3.111	2.140	4.524
Sleep problems	NA	0.000	1.630	1.283	2.070
Daytime sleepy	NA	0.001	NA	NA	NA
	1	0.471	0.873	0.605	1.262
	2	0.315	1.189	0.848	1.667
	3	0.004	1.742	1.198	2.533
	4	0.035	1.686	1.038	2.740
Drinking history	NA	0.121	1.636	0.878	3.050

Table 3 continued

Variable	Encode	p Value	OR	95% CI	
Obesity	NA	0.000	1.644	1.295	2.086
History of elevated blood pressure	NA	0.001	1.464	1.159	1.849
History of elevated blood lipids	NA	0.191	1.166	0.926	1.468
Weekday sleep	NA	0.025	1.298	1.033	1.632
Weekend sleep	NA	0.157	1.185	0.937	1.498
Depression Rating Level	NA	0.000	NA	NA	NA
	2	0.000	2.077	1.515	2.847
	3	0.000	2.828	1.817	4.402
	4	0.000	8.060	3.345	19.418
	5	0.027	3.838	1.162	12.674
Urine flow rate level	NA	0.785	NA	NA	NA
	2	0.225	1.183	0.901	1.554
	3	0.953	1.015	0.609	1.694
	4	0.406	1.389	0.640	3.014
	5	0.565	0.643	0.143	2.892
	6	0.825	1.158	0.316	4.238
AGE	continuous variables	0.002	1.020	1.007	1.033
PHQ-9		0.000	1.118	1.089	1.148
BMI		0.000	1.037	1.016	1.058

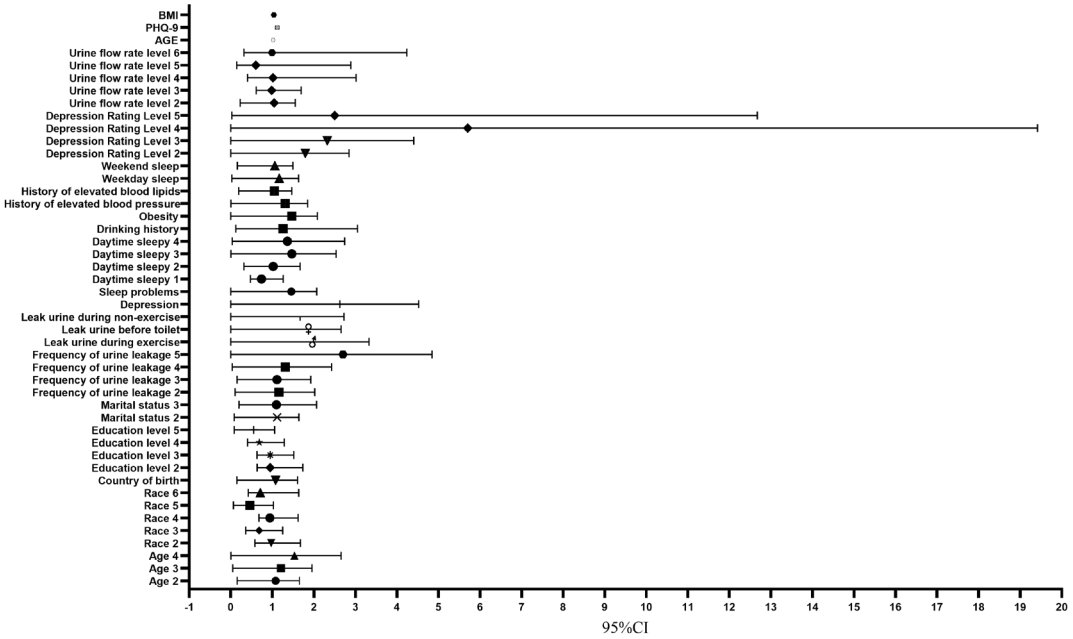

Fig 2 - Univariate logistic regression

(**Fig 2**) Forest plot of univariate logistic regression. Each variable corresponds to a line parallel to the X-axis. Segment length represents 95% CI. Both ends of the line segment represent the low value and high value of 95% CI respectively. Black blocks with different shapes represent OR.

Collinearity

If the Tolerance is less than 0.1 or the Variance Inflation Factor (VIF) is greater than 10, collinearity exists. The results suggest that there is no collinearity between the factors related to nocturia in uni-variate logistic regression (**Table 4**, **Fig 3**). That is to say, the influence of internal doping is small, so multivariate logistic regression analysis can be conducted.

Table 4 - Collinearity

Variable	Group	Tolerance	VIF
Depression Rating Level	1	0.278	3.597
History of elevated blood pressure	2	0.930	1.075
Obesity	3	0.931	1.074
Daytime sleepy	4	0.892	1.121
Sleep problems	5	0.874	1.144
Depression	6	0.295	3.386
Leak urine during non-exercise	7	0.802	1.247
Leak urine before toilet	8	0.762	1.313
Leak urine during exercise	9	0.893	1.120
Frequency of urine leakage	10	0.659	1.516
Age	11	0.876	1.142
Weekday sleep	12	0.970	1.031

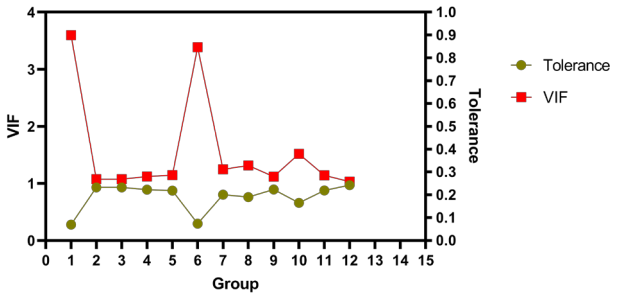

Fig 3- Collinearity

(**Fig 3**) Collinearity. Dark olive green is Tolerance and red is VIF. The left Y axis is the range of VIF. The right Y axis is the range of Tolerance.

Multivariate logistic regression analysis

The results of multivariate logistic regression after collinearity diagnosis suggest that Depression rating level, Obesity, and Leak urine before toilet were related to the occurrence of nocturia ($p < 0.05$) (**Table 5**, **Fig 4**).

Table 5 - Multivariate logistic regression

Variable	Encode	p Value	Adjusted OR	95% CI	
Depression Rating Level	NA	0.002	NA	NA	NA
Depression Rating Level	2	0.002	1.719	1.227	2.408
Depression Rating Level	3	0.795	0.839	0.224	3.143
Depression Rating Level	4	0.241	2.490	0.541	11.448
History of elevated blood pressure	NA	0.379	0.893	0.695	1.148
Obesity		0.005	1.454	1.123	1.882
Daytime sleepy	NA	0.448	NA	NA	NA
Daytime sleepy	1	0.859	1.049	0.617	1.784
Daytime sleepy	2	0.427	0.812	0.486	1.358
Daytime sleepy	3	0.975	1.008	0.620	1.639
Daytime sleepy	4	0.570	1.160	0.695	1.935
Sleep problems	NA	0.149	0.821	0.628	1.073
Leak urine during non-exercise	NA	0.648	1.098	0.735	1.641
Leak urine before toilet	NA	0.007	1.492	1.116	1.994
Leak urine during exercise	NA	0.055	1.488	0.991	2.234
Frequency of urine leakage	NA	0.261	NA	NA	NA
Frequency of urine leakage	2	0.086	0.651	0.399	1.063
Frequency of urine leakage	3	0.152	0.664	0.380	1.162
Frequency of urine leakage	4	0.040	0.565	0.328	0.975

Table 3 continued

Frequency of urine leakage	5	0.052	0.563	0.315	1.005
Age	NA	0.082	NA	NA	NA
Age	2	0.393	1.143	0.841	1.554
Age	3	0.118	1.326	0.930	1.891
Age	4	0.014	1.694	1.114	2.576
Depression		0.172	2.427	0.681	8.657
Weekday sleep	NA	0.070	1.251	0.982	1.595

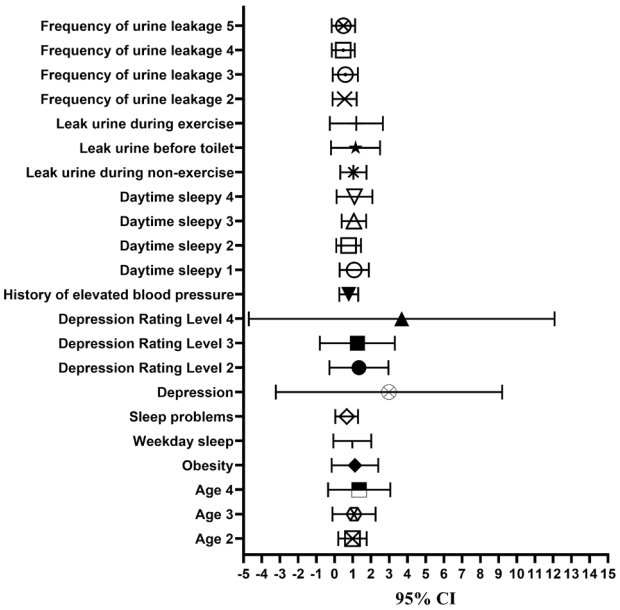

Fig 4 - Multivariate logistic regression

(**Fig 4**) Forest plot of Multivariate logistic regression. Each variable corresponds to a line parallel to the X-axis. Segment length represents 95% CI. Both ends of the line segment represent the low value and high value of 95% CI respectively. Blocks with different shapes represent OR.

Multivariate logistic regression analysis (continuous variables)

Continuous variables of PHQ-9, BMI, Age are used for univariate logistic regression. Age, as a continuous variable, also has an impact on nocturia in the univariate logistic region. Age is also included in this analysis to determine the specific impact of these indicators on nocturia. Age (adjusted OR: 1.020, 95% CI 1.006–1.035, p = 0.006), PHQ-9 (adjusted OR: 1.100, 95% CI 1.068–1.133, p = 0.000), and BMI (adjusted OR: 1.029 95% CI 1.007–1.052, p = 0.010), Frequency of urine leakage (p = 0.025) and weekday sleep (adjusted OR: 1.276, 95% CI 1.002-1.625, p = 0.048) are related to nocturia and are risk factors for nocturia (p < 0.05) (**Table 6**, **Fig 5**).

Table 6 - Multivariate logistic regression(continuous variables)

Variable	Encode	p **Value**	**Adjusted OR**	**95% CI**	
Age	continuous variables	0.006	1.020	1.006	1.035
PHQ-9		0.000	1.100	1.068	1.133
BMI		0.010	1.029	1.007	1.052
Frequency of urine leakage	NA	0.025	NA	NA	NA
	2	0.001	0.487	0.315	0.753
	3	0.081	0.616	0.358	1.061
	4	0.014	0.511	0.299	0.874
	5	0.034	0.539	0.305	0.954
History of elevated blood pressure	NA	0.423	0.902	0.701	1.161
Daytime sleepy	NA	0.431	NA	NA	NA
	1	0.872	1.044	0.616	1.771
	2	0.447	0.821	0.494	1.365
	3	0.943	1.018	0.629	1.648
	4	0.515	1.183	0.714	1.962
Sleep problems	NA	0.325	0.873	0.667	1.143
Weekday sleep	NA	0.048	1.276	1.002	1.625

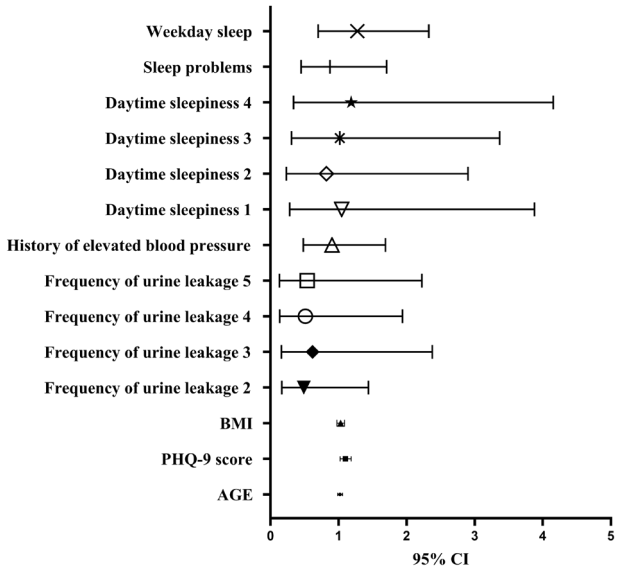

Figure 5 - Multivariate logistic regression (continuous variables)

(**Fig 5**) Forest plot of multivariate logistic regression (continuous variables). Each variable corresponds to a line parallel to the X-axis. Segment length represents 95% CI. Both ends of the line segment represent the low value and high value of 95% CI respectively. Black blocks with different shapes represent OR.

3.2 ROC analysis

Age, BMI, Frequency of urine leakage, and PHQ-9 are used for ROC analysis to predict the relationship with nocturia. The larger the AUX in ROC analysis, the more accurate the prediction result of this factor. The analysis results show that the highest AUX of PHQ-9 is 0.633. AUX of Frequency of urine leakage is 0.571. AUX of BMI is 0.553, and AUX of Age is 0.549. It shows that PHQ-9 is the most relevant among the comprehensive factors (**Table 7**, **Fig 6**).

Table 7 - ROC analysis results

Variable	AUC	95%CI	p Value
Frequency of urine leakage(FOUL)	0.571	0.541- 0.600	0.000
Age	0.549	0.516- 0.583	0.004
PHQ-9	0.633	0.601-0.665	0.000
BMI	0.553	0.518- 0.587	0.003

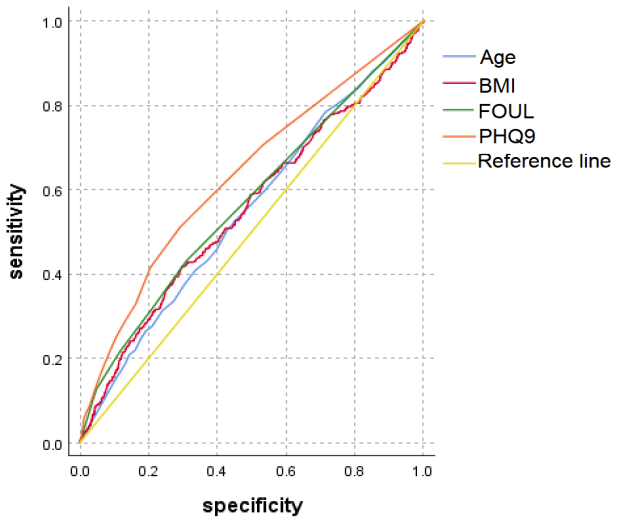

Fig 6 - ROC analysis results

(**Fig 6**) ROC analysis results. Orange is PHQ-9, deep sky blue is Age, green is Frequency of urine leakage, yellow is Reference line. The area size under different color lines represents the prediction effect on nocturia.

Conclusions

To sum up, nocturia is affected by many factors. In the multiple logistic regression, Depression, BMI, or Obesity are the most important influencing factors, and Age and sleep are the secondary influencing factors. As BPH is an aging disease, the incidence rate and prevalence rate will increase with the growth of men's age[11]. This may be the reason why age plays a role in nocturia in the BPH risk population. Larger body sizes, especially obesity, may promote BPH/LUTS through several possible mechanisms. Obesity increases the ratio of estrogen to testosterone and its metabolites, so it may promote the natural increase of men with age[12], which may be the reason why obesity or BMI increases the risk of nocturia in the BPH risk population. BPH mostly occurs in middle-aged and older adults. Because of their own age, this group is also prone to poor sleep quality. In addition, lower urinary tract symptoms induced by glandular hyperplasia, such as frequent nocturia, lead to sleep disorders and form a vicious circle. Through the analysis of this real-world data, among the BPH risk population, the impact on nocturia can be attributed to the gradual growth of age, weight gain caused by various factors, and depression or sleep deprivation caused by various reasons. PHQ-9 is found to play an important role in nocturia by ROC analysis. Therefore, while focusing on nocturia symptoms, we should pay special attention to the mental health problems of the BPH risk population. The comprehensive coordination of the living environment of nocturia patients can achieve the goal of reducing the incidence of the disease.

Data Availability

The datasets generated and analyzed during the current study are available in the "https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Questionnaire&Cycle=2017-2020"

Authors' contributions

C. Zhang and H. J. Gao conceived and designed the study. B. T. Tang, C. J. Shang, X. J. Ye, M. Zhu conducted data analysis. Q. Y. Yang, Y. S. Zhang, X. B. Rong, Z. S. Lin and Y. X. Chen carried out data collation. Z. C. Zhang, Y. Chen and S. P. Huang wrote the paper. P. Jiang, F. Hu and S. P. Huang reviewed and edited the manuscript. All authors approved the final version of the article. Z. C. Zhang, Y. Chen, B. T. Tang, X. J. Ye, S. P. Huang contributed equally to this work and are co-first authors.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethics Statement

there were no ethical considerations taken into account during this research.

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