# The association between lower urinary tract symptoms secondary to benign prostatic hyperplasia and multimorbidity among Chinese middle-aged and elderly males: evidence based on propensity score matching

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**Background:** With the aging population, patients with lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH) often face multiple chronic conditions (multimorbidity), significantly impacting their quality of life. This study aims to determine the relationship between LUTS/BPH, multimorbidity, and various chronic diseases in middle-aged and elderly Chinese populations.

**Methods:** This cross-sectional study utilizes data from the China Health and Retirement Longitudinal Study (CHARLS), involving 6,645 residents aged 45 and above. Data on 14 chronic diseases were collected, with multimorbidity defined based on the presence of 2–5 chronic conditions. The number of chronic conditions was further categorized into five groups. Propensity score matching (PSM) was used to control for 11 confounding factors. Linear regression was employed to analyze the relationship between LUTS/BPH and the number of chronic conditions in middle-aged and elderly Chinese men before and after PSM. Both univariate and multivariate logistic regression analyses were used to explore the association between LUTS/BPH and multimorbidity as well as each chronic disease.

**Results:** The prevalence of multimorbidity was significantly higher among middle-aged and elderly individuals with LUTS/BPH compared to those without. Before PSM, LUTS/BPH was positively correlated with the number of chronic diseases (β=0.175, P<0.001), and the risk of multimorbidity significantly increased, showing a dose-response relationship. The risk of having at least two chronic diseases in patients with LUTS/BPH was 2.39 times higher than in those without LUTS/BPH [odds ratio (OR) =2.39, 95% confidence interval (CI): 2.04–2.80], and the risk of having five chronic diseases was 3.97 times higher (OR =3.97, 95% CI: 3.14–4.99). After PSM, 819 pairs were successfully matched. The positive correlation between LUTS/BPH and multimorbidity still existed, with the risks of having at least two and five chronic diseases being 2.37 times (OR =2.37, 95% CI: 1.94–2.90) and 3.69 times (OR =3.69, 95% CI: 2.62–5.29) higher, respectively. Among them, the risk of emotional/nervous/psychiatric problems was the highest in LUTS/BPH patients (OR =6.58, 95% CI: 2.22–28.13), while the risk of arthritis/rheumatism was the lowest (OR =1.60, 95% CI: 1.30–1.98).

**Conclusions:** In the Chinese population, LUTS/BPH is closely associated with multimorbidity and each of the 14 chronic diseases examined, with a dose-response relationship based on the number of chronic diseases defined within multimorbidity. It is imperative to incorporate LUTS/BPH into multimorbidity research and management. We recommend that clinicians and policymakers consider the increased risk of multimorbidity and various chronic diseases among male LUTS/BPH patients.

## Introduction

Multimorbidity is typically defined as the coexistence of at least two chronic diseases in an individual and has become a significant public health issue globally (1). Due to changes in lifestyle habits, improvements in socioeconomic conditions, advancements in medical diagnostic capabilities, and the increasingly severe problem of population aging, the prevalence of multimorbidity is steadily rising (2). A systematic review and meta-analysis based on worldwide low- and middle-income countries found that multimorbidity's global prevalence is 36.4%, with a prevalence of 29.5% across Asia (3). According to the recent fourth National Urban and Rural Elderly Population Survey (UREP) in China, the prevalence of multimorbidity among Chinese individuals aged 60 and above is as high as 81.1% (4). Multimorbidity not only significantly impacts individual quality of life and imposes substantial economic burdens on families but also increases the utilization and expenditure of medical resources and the overall healthcare burden (5,6). More critically, multimorbidity is associated with premature mortality (7).

Benign prostatic hyperplasia (BPH) is a common urological condition in elderly men, characterized by non-malignant progressive enlargement of stroma and glandular epithelium in the transition zone surrounding the urethra. It is a primary cause of lower urinary tract symptoms (LUTS), which include a range of clinical symptoms such as difficulty urinating, split urine stream, nocturia, increased urinary frequency, and urgency. According to longitudinal studies by Loeb on age-related changes in prostate volume, the prostate volume of elderly male patients increases by 2.5% annually (8). A systematic analysis based on the Global Burden of Disease Study 2019 indicated that men aged 65–74 bear the highest absolute burden of BPH, with the highest prevalence observed in the 75–79 age group, where the prevalence rate is 24.3% (9). Recent studies have found associations between BPH and conditions such as hypertension, diabetes, chronic lung disease, chronic heart disease, dyslipidemia, and thyroid disorders (2,10,11). Chronic diseases are typically not isolated; thus, LUTS/BPH is likely associated with multimorbidity and the number of chronic conditions. However, there is currently limited research on this topic.

Globally, by 2030, one in six people will be aged 60 or above; by 2050, the population of those aged 60 and above is expected to double from 1 billion in 2020 to 2.1 billion (12). Focusing on China, the country is experiencing an unprecedented acceleration in its aging population, with individuals aged 60 and older accounting for approximately 17.8% of the total population in 2020, a figure projected to approach 40% by 2050 (13). LUTS/BPH and multimorbidity are both prevalent among the elderly, indicating that the proportion of patients with

**Highlight box**

**Key findings**
- In the Chinese population, lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH) is closely associated with multimorbidity and each of the 14 chronic diseases examined, with a dose-response relationship based on the number of chronic diseases defined within multimorbidity.

**What is known and what is new?**
- Propensity score matching (PSM) is a statistical technique used to control for confounding variables in observational studies. This study used PSM to match patients with LUTS/BPH to non-LUTS/BPH patients based on a set of covariates, ensuring balanced groups for an accurate comparison of the association between LUTS/BPH and multimorbidity.
- With the aging population, patients with LUTS/BPH often face multimorbidity, significantly impacting their quality of life.
- This nationwide representative data analysis is the first to use PSM analysis to explore the relationship between LUTS/BPH and the number of chronic diseases, multimorbidity, and up to 14 specific chronic conditions in the Chinese male population. The results indicate that the impact of LUTS/BPH on the number of chronic diseases, multimorbidity, and specific chronic conditions mutually reinforces the reliability of the study.

**What is the implication, and what should change now?**
- It is imperative to incorporate LUTS/BPH into multimorbidity research and management. We recommend that clinicians and policymakers consider the increased risk of multimorbidity and various chronic diseases among male LUTS/BPH patients.

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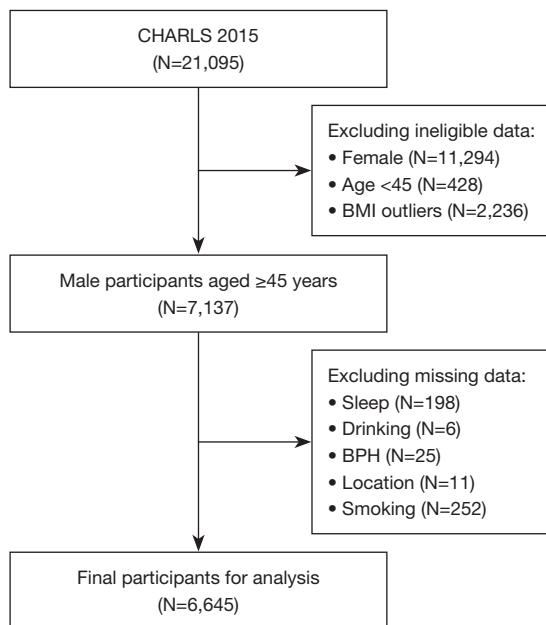
**Figure 1** Flowchart illustrating the data cleaning process in the study. CHARLS, China Health and Retirement Longitudinal Study; BMI, body mass index; BPH, benign prostatic hyperplasia.

LUTS/BPH and multimorbidity will continue to rise in the coming years. Investigating the relationship between LUTS/BPH and multimorbidity, as well as the potential role of LUTS/BPH in the progression of multimorbidity, is crucial for enhancing our understanding of multimorbidity. Such insights are invaluable for preventing multimorbidity, improving the quality of life for those affected, and formulating effective intervention strategies. In light of this, we conducted a study utilizing survey data from the population in China to ascertain the relationship between LUTS/BPH and the number of chronic diseases, multimorbidity, and up to 14 specific chronic conditions. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-268/rc).

## Methods

### Data collection

Our dataset was obtained from the official website of China Health and Retirement Longitudinal Study (CHARLS) (http://charls.pku.edu.cn). All data were collected by trained researchers and include information from middle-aged and elderly individuals across 28 provinces, 150 counties, and 450 villages in China, providing a nationally representative sample. CHARLS offers a high-quality, publicly accessible micro-database encompassing a wide range of socioeconomic and health status data. It is the first comprehensive and diverse aging study database in China, allowing us to explore the relationship between LUTS/BPH, the number of chronic conditions, and multimorbidity. The baseline data for CHARLS primarily comes from 2011, with follow-up surveys conducted every two years, achieving satisfactory response rates each time. On April 28, 2024, we downloaded the CHARLS follow-up questionnaire from 2015. First, we matched and merged data from specific modules within CHARLS. Second, we excluded samples of women, individuals under 45 years of age, and those with abnormal body mass index (BMI) values. Third, we removed records with missing values. Consequently, our final sample comprised 6,645 individuals (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The CHARLS study obtained written informed consent from each participant. Ethical approval for all the CHARLS waves was granted by the Institutional Review Board at Peking University. The Institutional Review Board (IRB) approval number for the main household survey, including anthropometrics, is IRB00001052-11015; the IRB approval number for biomarker collection is IRB00001052-11014.

### Dependent and independent variable

In the CHARLS 2015 Health Status and Functioning questionnaire, each participant's disease information was assessed face-to-face by collecting medical history information. For LUTS/BPH information, male respondents were asked, "Have you ever been diagnosed with a prostate illness, such as prostate hyperplasia (excluding prostatic cancer)?" Researchers also explained the main symptoms of LUTS to the participants. Only those who confirmed having related symptoms were defined as having LUTS/BPH (14,15). For multimorbidity information, respondents were asked, "Have you been diagnosed with (conditions listed below, read one by one) by a doctor?" The list on the screen included 14 chronic diseases: hypertension, dyslipidemia, diabetes or high blood sugar, cancer or malignant tumor, chronic lung diseases, liver disease, heart attack, stroke, kidney disease, stomach or other digestive disease, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism, and asthma. We calculated the number of chronic diseases

each participant had and further categorized them based on the number of chronic conditions: no chronic disease, one chronic disease, two chronic diseases, three chronic diseases, four chronic diseases, and five or more chronic diseases. Participants with at least 2–5 chronic diseases were defined as having multimorbidity.

### Covariates

The covariates considered in our analysis encompass age, body mass index (BMI), educational attainment, marital status, nightly sleep duration, residential area, smoking status, alcohol consumption, physical activity, health insurance coverage, and monthly pension amount. BMI is calculated as weight in kilograms divided by height in square meters. Marital status is bifurcated into two categories: the first includes participants living with a spouse (married and unmarried), while the second encompasses those who are married but not living with their spouse, as well as those who are separated, divorced, widowed, or unmarried. Educational attainment is dichotomized into two levels: high school or lower, and college or above. Residential area is classified into rural and urban categories, with rural referring exclusively to villages, and urban encompassing other designations such as main city zone, town center, combination zone between urban and rural, special area, and township central. Smoking status is categorized as either smoker or non-smoker. Alcohol consumption is similarly categorized as drinker or non-drinker. Physical activity is assessed based on whether it is moderate to vigorous, with participants being grouped according to previously established criteria for activity levels (16). To facilitate further subgroup analysis, the following categorizations were made: nightly sleep duration was divided into two categories, ≥7 and <7 hours; BMI was categorized into two groups, ≥24 and <24 kg/m²; monthly pension income was classified into ≥1,000 and <1,000 yuan.

### Statistical analysis

Categorical data were presented as proportions (%) and continuous data as mean ± standard deviation (SD). Differences in baseline characteristics between groups were assessed using *t*-tests or Chi-squared tests, depending on the data type. We removed all missing values. Before propensity score matching (PSM), multivariate linear regression was employed to investigate the relationship between LUTS/BPH and the number of chronic diseases.

Univariate and multivariate logistic regression analyses were conducted to explore the association between LUTS/BPH and multimorbidity and each chronic disease. PSM was then implemented using a nearest neighbor matching method at a 1:1 ratio to balance differences in covariates. To ensure that the matched dataset achieved balance between the treatment and control groups, we verified the balance hypothesis using mean bias and conducting *t*-tests or Chi-squared tests on the two groups. For the matched data, multivariate linear regression was used to further explore the relationship between LUTS/BPH and the number of chronic diseases, while univariate and multivariate logistic regression continued to examine the association between LUTS/BPH and multimorbidity, as well as with each chronic disease. Subgroup analyses were performed to determine the influence of various factors on the relationship between LUTS/BPH and multimorbidity by including interaction variables in the main analysis model. All data analyses were performed using the publicly available RStudio software (version 2023.07.07) and R version 4.3.1. A P value <0.05 was considered statistically significant.

## Results

### Study population characteristics

A total of 6,645 participants were included in this study. The baseline characteristics of the participants are detailed in *Table 1*. The study population was divided into two groups: those with LUTS/BPH (n=819) and those without LUTS/BPH (n=5,826). The average age of the participants was 61.16±9.53 years. There were significant differences in the prevalence of multimorbidity between the two groups (all P<0.001). As the number of chronic diseases defining multimorbidity increased, the prevalence of multimorbidity decreased. The overall prevalence of having at least one chronic disease was 69.29%, with the prevalence of having at least two chronic diseases at 42.62%. The prevalence rates for having at least three, four, and five chronic diseases were 24.05%, 12.25%, and 5.91%, respectively. The prevalence of LUTS/BPH was 12.33%. Among participants with LUTS/BPH, the prevalence of having at least two chronic diseases was 65.32%, while the prevalence of having at least five chronic diseases decreased to 17.95%. Overall, compared to participants without LUTS/BPH, those with LUTS/BPH were older, had higher BMI values and higher education levels, were more likely to be urban residents, were less likely to consume alcohol and smoke, had shorter sleep duration per night, and received higher pensions (all

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**Table 1** Baseline characteristics of 6,645 Chinese middle-aged and elderly Individuals in the CHARLS

| Variable | Overall (n=6,645) | Non-LUTS/BPH (n=5,826) | LUTS/BPH (n=819) | P |
|---|---|---|---|---|
| Age (years) | 61.16±9.53 | 60.64±9.40 | 64.84±9.65 | <0.001 |
| BMI (kg/m²) | 23.45±3.86 | 23.39±3.89 | 23.94±3.58 | <0.001 |
| Education level | | | | <0.001 |
|   College or above | 5,168 (77.77) | 4,491 (77.09) | 677 (82.66) | |
|   High school or lower | 1,477 (22.23) | 1,335 (22.91) | 142 (17.34) | |
| Marital status | | | | 0.22 |
|   Partner or married | 5,765 (86.76) | 5,066 (86.96) | 699 (85.35) | |
|   Widowed or single | 880 (13.24) | 760 (13.04) | 120 (14.65) | |
| Location | | | | <0.001 |
|   Rural | 4,909 (73.88) | 4,403 (75.58) | 506 (61.78) | |
|   Urban | 1,736 (26.12) | 1,423 (24.42) | 313 (38.22) | |
| Smoking | | | | 0.003 |
|   No | 1,009 (15.18) | 856 (14.69) | 153 (18.68) | |
|   Yes | 5,636 (84.82) | 4,970 (85.31) | 666 (81.32) | |
| Drinking | | | | <0.001 |
|   No | 2,777 (41.79) | 2,372 (40.71) | 405 (49.45) | |
|   Yes | 3,868 (58.21) | 3,454 (59.29) | 414 (50.55) | |
| Sleep | 6.54±1.79 | 6.58±1.79 | 6.20±1.78 | <0.001 |
| Physical activity | | | | 0.09 |
|   No | 4,710 (70.88) | 4,108 (70.51) | 602 (73.50) | |
|   Yes | 1,935 (29.12) | 1,718 (29.49) | 217 (26.50) | |
| Insurance | | | | 0.07 |
|   No | 6,184 (93.06) | 5,409 (92.84) | 775 (94.63) | |
|   Yes | 461 (6.94) | 417 (7.16) | 44 (5.37) | |
| Monthly pension | 380.82±1,259.64 | 317.87±1,102.27 | 828.62±2,001.58 | <0.001 |
| Number of chronic conditions | | | | <0.001 |
|   0 | 2,041 (30.71) | 1,910 (32.78) | 131 (16.00) | |
|   1 | 1,772 (26.67) | 1,619 (27.79) | 153 (18.68) | |
|   2 | 1,234 (18.57) | 1,066 (18.30) | 168 (20.51) | |
|   3 | 784 (11.80) | 643 (11.04) | 141 (17.22) | |
|   4 | 421 (6.34) | 342 (5.87) | 79 (9.65) | |
| At least one morbidity | | | | <0.001 |
|   No | 2,041 (30.71) | 1,910 (32.78) | 131 (16.00) | |
|   Yes | 4,604 (69.29) | 3,916 (67.22) | 688 (84.00) | |

**Table 1** (*continued*)

**Table 1** (*continued*)

| Variable | Overall (n=6,645) | Non-LUTS/BPH (n=5,826) | LUTS/BPH (n=819) | P |
|---|---|---|---|---|
| Multimorbidity (≥2) | | | | <0.001 |
| No | 3,813 (57.38) | 3,529 (60.57) | 284 (34.68) | |
| Yes | 2,832 (42.62) | 2,297 (39.43) | 535 (65.32) | |
| Multimorbidity (≥3) | | | | <0.001 |
| No | 5,047 (75.95) | 4,595 (78.87) | 452 (55.19) | |
| Yes | 1,598 (24.05) | 1,231 (21.13) | 367 (44.81) | |
| Multimorbidity (≥4) | | | | <0.001 |
| No | 5,831 (87.75) | 5,238 (89.91) | 593 (72.41) | |
| Yes | 814 (12.25) | 588 (10.09) | 226 (27.59) | |
| Multimorbidity (≥5) | | | | <0.001 |
| No | 6,252 (94.09) | 5,580 (95.78) | 672 (82.05) | |
| Yes | 393 (5.91) | 246 (4.22) | 147 (17.95) | |

Data are presented as mean ± SD or n (%). CHARLS, China Health and Retirement Longitudinal Study; BMI, body mass index; LUTS/BPH, lower urinary tract symptoms/benign prostatic hyperplasia.

P<0.05). Participants with LUTS/BPH had the highest prevalence of having two chronic diseases at 20.51% and the lowest prevalence of having five chronic diseases at 9.65% (P<0.001).

### *Linear and logistic regression results before PSM*

We first used multiple linear regression to analyze the relationship between LUTS/BPH and the number of chronic diseases. Specifically, we used LUTS/BPH as the independent variable and the number of chronic diseases as the dependent variable. The results showed a positive correlation between LUTS/BPH and the number of chronic diseases, regardless of adjusting for age alone or all covariates (Model 1: β=0.188, P<0.001; Model 2: β=0.175, P<0.001, Table S1). We further employed logistic regression to examine how LUTS/BPH influences multimorbidity. Using LUTS/BPH as the independent variable and multimorbidity as the dependent variable, we found that patients with LUTS/BPH had a higher risk of multimorbidity. This association remained robust after adjusting for age alone (Model 1) and for all covariates (Model 2) (all P<0.001, *Table 2*). As the number of chronic diseases defined within multimorbidity increased, the risk of multimorbidity among LUTS/BPH patients also significantly increased. Specifically, the risk of having at least

two chronic diseases was 2.39 times higher in LUTS/BPH patients compared to non-LUTS/BPH individuals [odds ratio (OR) =2.39, 95% confidence interval (CI): 2.04–2.80, P<0.001], and the risk of having at least five chronic diseases was 3.97 times higher (OR =3.97, 95% CI: 3.14–4.99, P<0.001) (*Table 2*). In the multivariable logistic regression analysis, age, BMI, alcohol consumption, living area, education level, nightly sleep duration, health insurance, and monthly pension amount were also significant factors (Table S2). We conducted PSM analysis to further balance the bias introduced by covariates.

### *PSM analysis and balance testing*

We utilized logistic regression to compute propensity scores, which were then used to match suitable subjects to the LUTS/BPH group. Given the variety of matching patterns available for PSM, this study primarily employed the nearest neighbor matching method. Following PSM, 819 pairs were successfully matched using 11 balanced covariates. The results of the PSM matching between the LUTS/BPH group and the non-LUTS/BPH group are detailed in *Table 3*. To validate the reliability of the estimated results, we conducted a balance hypothesis test. The most commonly used method for balance testing is the mean bias, which generally should be less than 10%. After

**Table 2** Univariate and multivariable logistic regression analysis of LUTS/BPH and multimorbidity before PSM

| Regression analysis | Multimorbidity | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | At least one | | At least two | | At least three | | At least four | | At least five | |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| Univariate | 2.56 (2.11–3.12) | <0.001*** | 2.89 (2.48–3.38) | <0.001*** | 3.03 (2.60–3.53) | <0.001*** | 3.40 (2.85–4.04) | <0.001*** | 4.96 (3.98–6.17) | <0.001*** |
| Multivariable | | | | | | | | | | |
| Model 1 | 2.17 (1.79–2.66) | <0.001*** | 2.54 (2.17–2.97) | <0.001*** | 2.66 (2.28–3.10) | <0.001*** | 2.97 (2.48–3.54) | <0.001*** | 4.33 (3.46–5.41) | <0.001*** |
| Model 2 | 2.13 (1.75–2.62) | <0.001*** | 2.39 (2.04–2.80) | <0.001*** | 2.48 (2.11–2.90) | <0.001*** | 2.72 (2.26–3.27) | <0.001*** | 3.97 (3.14–4.99) | <0.001*** |

Model 1 = adjusted for age; Model 2 = adjusted for age, BMI, marital status, education level, residence, smoking, drinking, sleep, health insurance, physical activity and monthly pension. ***, P<0.001. BMI, body mass index; LUTS/BPH, lower urinary tract symptoms/benign prostatic hyperplasia; PSM, propensity score matching; OR, odds ratio; CI, confidence interval.

**Table 3** Balance test results after PSM among 6,645 Chinese middle-aged and elderly population in the CHARLS

| Characteristics | Unmatched/matched | %bias | P value |
| --- | --- | --- | --- |
| Age | Unmatched | 43.6 | <0.001*** |
| | Matched | 4.1 | 0.40 |
| BMI | Unmatched | 15.6 | <0.001*** |
| | Matched | 1.7 | 0.79 |
| Education level | Unmatched | 14.7 | <0.001*** |
| | Matched | 4.2 | 0.44 |
| Marital status | Unmatched | 4.5 | 0.22 |
| | Matched | 1.7 | 0.78 |
| Location | Unmatched | 28.4 | <0.001*** |
| | Matched | 3.5 | 0.51 |
| Smoking | Unmatched | 10.2 | 0.003** |
| | Matched | 5.6 | 0.29 |
| Drinking | Unmatched | 17.5 | <0.001*** |
| | Matched | 0.7 | 0.92 |
| Sleep | Unmatched | 21.5 | <0.001*** |
| | Matched | 4.1 | 0.42 |
| Physical activity | Unmatched | 6.8 | 0.09 |
| | Matched | 1.4 | 0.82 |
| Insurance | Unmatched | 7.9 | 0.07 |
| | Matched | 1.1 | 0.91 |
| Monthly pension | Unmatched | 25.5 | <0.001*** |
| | Matched | 0.2 | 0.70 |

**, P<0.01; ***, P<0.001. PSM, propensity score matching; CHARLS, China Health and Retirement Longitudinal Study; BMI, body mass index.

PSM matching, the mean bias for all covariates significantly decreased; with the exception of the smoking variable, the mean bias was controlled within 5%. Chi-squared tests or *t*-tests revealed no significant differences between the two groups of middle-aged and elderly samples after matching (P>0.05), satisfying the conditional independence assumption.

### PSM adjusted linear and logistic regression results

In the PSM-adjusted dataset, even after adjusting for the age covariate or all covariates, LUTS/BPH remained

positively correlated with the number of chronic diseases (Model 1: β=0.247, P<0.001; Model 2: β=0.245, P<0.001) (Table S1). Both independent logistic regression analyses and those adjusted for age (Model 1) or all covariates (Model 2) consistently showed that LUTS/BPH significantly influenced multimorbidity (all P<0.001). The risk of having at least two chronic diseases was 2.37 times higher in LUTS/BPH patients compared to non-LUTS/BPH individuals (OR =2.37, 95% CI: 1.94–2.90, P<0.001), and the risk of having at least five chronic diseases was 3.69 times higher (OR =3.69, 95% CI: 2.62–5.29, P<0.001) (Table S3).

### Subgroup analysis

To assess whether the impact of LUTS/BPH on the risk of multimorbidity (at least two chronic diseases) varied across different subgroups, we conducted subgroup analyses using logistic regression. The results indicated that the effect of LUTS/BPH on the risk of multimorbidity was consistent across all subgroups. There were no significant interactions between LUTS/BPH and the various factors (all P>0.05) (Figure S1).

### Logistic regression results for LUTS/BPH and each chronic disease

We further conducted logistic regression with LUTS/BPH as the independent variable and each chronic disease as the dependent variable, finding that LUTS/BPH patients had a higher risk of developing each chronic disease (all P<0.05). Even in the PSM-adjusted dataset, regardless of whether age alone (model 1) or all covariates (model 2) were adjusted, the impact of LUTS/BPH on each chronic disease remained robust. The most significant risk was for emotional/nervous/psychiatric problems (OR =6.58, 95% CI: 2.22–28.13, P=0.003), while the lowest risk was for arthritis/rheumatism (OR =1.60, 95% CI: 1.30–1.98, P<0.001) (Table 4).

### Discussion

Multimorbidity, described as the coexistence of multiple chronic diseases, has garnered increasing attention in recent years. The definition of multimorbidity varies based on the types, numbers, and assessment methods of chronic diseases, and there is no universally accepted gold standard. The chronic disease data referenced in this study were obtained through questionnaires conducted by professionally trained personnel, covering 14 common diseases. The study sample comprises middle-aged and elderly individuals across China, providing high representativeness. A survey conducted in a prefecture-level city in China reported a prevalence rate of BPH at 10.04% among men over 40 years old, slightly lower than the incidence found in our study (17). This discrepancy could be attributed to our sample population aged 45 years and above. Multimorbidity can occur in middle-aged and elderly populations, with at least two chronic diseases occurring at a rate of 42.62%. A community-based systematic review and meta-analysis indicated that 32.8% of the Asian male population experiences multimorbidity, and this prevalence increases to 51% among individuals over 60 years old (18). These variations might result from differences in study populations and the definitions of multimorbidity used.

Despite variations in the prevalence of BPH across different races and ethnicities, longitudinal trends indicate that population growth and aging significantly impact the global prevalence of BPH (9,19). The prevalence of multimorbidity is also highest among the elderly. Multimorbidity is not only concentrated in older populations but also among individuals with lower socioeconomic status (20). Similarly, income is associated with the presence of moderate to severe LUTS (21). Previous studies have shown that patients with BPH have a poorer quality of life, and multimorbidity negatively affects health-related quality of life (HRQoL), encompassing both physical and psychological factors (22,23). Our study indicates that among Chinese middle-aged and elderly populations aged 45 and above, those with LUTS/BPH are more likely to suffer from multimorbidity. Furthermore, as the number of conditions defined within multimorbidity increases, this likelihood also rises, displaying a dose-response relationship.

We further investigated the associations between LUTS/BPH and various chronic diseases. The results showed that LUTS/BPH was associated with each chronic disease to varying degrees, with the strongest association observed for emotional/nervous/psychiatric problems and the weakest for arthritis/rheumatism. Previous research has also found significant correlations between LUTS/BPH and several chronic diseases. LUTS/BPH may lead to negative emotions such as anxiety and depression. A study based on the National Health Insurance Service-National Sample Cohort (NHIS-NSC) in South Korea showed that BPH even increases the risk of suicide due to mental disorders (24). Wang *et al.* (11) in China discovered

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**Table 4** Univariate and multivariable logistic regression analysis of LUTS/BPH and each chronic disease before and after PSM

| Each chronic disease | Before PSM | | | | | | After PSM | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariable | | | | Univariate | | Multivariable | | | |
| | | | Model 1 | | Model 2 | | | | Model 1 | | Model 2 | |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| Hypertension | 2.28 (1.86–2.80) | <0.001*** | 1.76 (1.51–2.05) | <0.001*** | 1.55 (1.31–1.82) | <0.001*** | 1.57 (1.28–1.93) | <0.001*** | 1.59 (1.29–1.95) | <0.001*** | 1.61 (1.31–1.99) | <0.001*** |
| Dyslipidemia | 2.55 (2.13–3.04) | <0.001*** | 2.57 (2.14–3.08) | <0.001*** | 2.12 (1.75–2.57) | <0.001*** | 1.89 (1.47–2.43) | <0.001*** | 1.88 (1.47–2.42) | <0.001*** | 2.00 (1.54–2.61) | <0.001*** |
| Diabetes/high blood sugar | 2.43 (1.95–3.02) | <0.001*** | 2.34 (1.87–2.91) | <0.001*** | 1.95 (1.54–2.45) | <0.001*** | 1.82 (1.34–2.49) | <0.001*** | 1.82 (1.34–2.49) | <0.001*** | 1.87 (1.37–2.58) | <0.001*** |
| Cancer/malignant tumor | 3.20 (1.82–5.44) | <0.001*** | 2.80 (1.58–4.82) | <0.001*** | 2.54 (1.38–4.50) | 0.002** | 2.77 (1.21–7.11) | 0.02* | 2.79 (1.22–7.18) | 0.02* | 2.94 (1.27–7.64) | 0.02* |
| Chronic lung diseases | 1.81 (1.49–2.17) | <0.001*** | 1.54 (1.27–1.86) | <0.001*** | 1.63 (1.34–1.99) | <0.001*** | 1.64 (1.26–2.13) | <0.001*** | 1.67 (1.28–2.19) | <0.001*** | 1.66 (1.27–2.17) | <0.001*** |
| Liver disease | 2.85 (2.20–3.67) | <0.001*** | 3.09 (2.36–4.00) | <0.001*** | 2.81 (2.14–3.67) | <0.001*** | 2.72 (1.83–4.13) | <0.001*** | 2.71 (1.83–4.11) | <0.001*** | 2.69 (1.81–4.09) | <0.001*** |
| Heart problems | 3.29 (2.75–3.91) | <0.001*** | 2.86 (2.39–3.42) | <0.001*** | 2.46 (2.05–2.96) | <0.001*** | 2.31 (1.80–2.97) | <0.001*** | 2.35 (1.83–3.03) | <0.001*** | 2.41 (1.87–3.12) | <0.001*** |
| Stroke | 2.71 (1.93–3.74) | <0.001*** | 2.40 (1.70–3.34) | <0.001*** | 2.14 (1.50–3.00) | <0.001*** | 2.30 (1.41–3.87) | 0.001** | 2.32 (1.42–3.91) | 0.001** | 2.41 (1.46–4.10) | <0.001*** |
| Kidney disease | 4.73 (3.89–5.75) | <0.001*** | 4.54 (3.72–5.54) | <0.001*** | 4.41 (3.59–5.40) | <0.001*** | 4.22 (3.09–5.85) | <0.001*** | 4.23 (3.10–5.86) | <0.001*** | 4.30 (3.14–5.97) | <0.001*** |
| Stomach/other digestive disease | 1.63 (1.38–1.91) | <0.001*** | 1.63 (1.382–1.92) | <0.001*** | 1.71 (1.44–2.02) | <0.001*** | 1.67 (1.33–2.09) | <0.001*** | 1.67 (1.33–2.10) | <0.001*** | 1.70 (1.35–2.14) | <0.001*** |
| Emotional/nervous/psychiatric problems | 3.23 (1.86–5.42) | <0.001*** | 3.10 (1.76–5.25) | <0.001*** | 3.22 (1.81–5.55) | <0.001*** | 6.84 (2.33–29.10) | 0.002** | 6.87 (2.34–29.25) | 0.002** | 6.58 (2.22–28.13) | 0.003** |
| Memory-related disease | 3.74 (2.51–5.51) | <0.001*** | 2.98 (1.98–4.42) | <0.001*** | 2.81 (1.84–4.21) | <0.001*** | 3.37 (1.81–6.77) | <0.001*** | 3.44 (1.84–6.92) | <0.001*** | 3.40 (1.81–6.86) | <0.001*** |
| Arthritis/rheumatism | 1.56 (1.34–1.81) | <0.001*** | 1.45 (1.24–1.69) | <0.001*** | 1.54 (1.32–1.81) | <0.001*** | 1.57 (1.27–1.93) | <0.001*** | 1.57 (1.27–1.93) | <0.001*** | 1.60 (1.30–1.98) | <0.001*** |
| Asthma | 2.11 (1.63–2.72) | <0.001*** | 1.71 (1.31–2.22) | <0.001*** | 1.76 (1.34–2.30) | <0.001*** | 1.76 (1.22–2.55) | 0.003** | 1.80 (1.25–2.63) | 0.002** | 1.78 (1.23–2.61) | 0.003** |

Model 1 = adjusted for age; Model 2 = adjusted for age, BMI, marital status, education level, residence, smoking, drinking, sleep, health insurance, physical activity and monthly pension. *, P<0.05; **, P<0.01; ***, P<0.001. BMI, body mass index; LUTS/BPH, lower urinary tract symptoms/benign prostatic hyperplasia; PSM, propensity score matching; OR, odds ratio; CI, confidence interval.

that men with LUTS/BPH are 1.43 times more likely to have cardiovascular diseases (CVDs) compared to their healthy counterparts, although this likelihood decreases in individuals aged 60 and above. Other cross-sectional and cohort studies have shown that BPH may be related to hypertension, diabetes, chronic lung disease, chronic heart disease, dyslipidemia, rheumatoid arthritis, asthma, non-alcoholic fatty liver disease (NAFLD), kidney disease, inflammatory bowel disease, and memory loss (2,25-31). However, to date, no studies have explored the relationship between LUTS/BPH and cancer/malignancies. Although LUTS may be closely associated with prostate cancer, this does not necessarily imply a connection with systemic cancers. Cancer patients often have multiple chronic diseases, and LUTS is associated with systemic chronic conditions such as asthma, heart disease, irritable bowel syndrome, recurrent urinary tract infections, arthritis, neurological disorders, vitamin D deficiency, chronic anxiety, depression, and sleep disturbances (32). Therefore, these findings should be interpreted cautiously, and future research should include more covariates to further explore the relationship between LUTS/BPH and cancer/malignancies.

The mechanisms underlying the relationship between BPH and multimorbidity and various chronic diseases are not well-defined but may involve hormone levels, inflammatory factors, and sympathetic nervous activity. Firstly, sex hormones significantly influence prostate disease. Androgen reduction and estrogen regulation imbalance can lead to prostate enlargement and inflammation, and hypogonadism, which is common in older adults, increases the risk of multimorbidity due to androgen deficiency (33-35). Secondly, insulin is a key factor affecting prostate disease. Both hyperinsulinemia and insulin resistance are risk factors for BPH (36). Insulin resistance is not only a major contributor to diabetes but has also been linked to neurodegenerative and neurodevelopmental disorders in animal studies (37). Thirdly, the presence of inflammatory factors is associated with the symptoms of LUTS in prostate enlargement, playing a crucial role in the onset and progression of BPH (33,38). Data from the Survey of Mid-Life in the United States (MIDUS) indicate that circulating levels of inflammatory factors increase linearly with the number of chronic diseases (39). Fourthly, LUTS can cause patients to wake frequently and suffer from sleep disturbances, leading to increased sympathetic nervous activity, which may contribute to chronic kidney disease

(CKD), chronic obstructive pulmonary disease (COPD), and CVDs (40,41). A systematic review based on global community-dwelling populations also suggests that sleep is a modifiable risk factor for preventing multimorbidity (42). In conclusion, the association between LUTS/BPH and multimorbidity and chronic diseases is well-documented and not merely coincidental.

The association between LUTS/BPH and multimorbidity underscores the shared characteristics among different chronic diseases, often non-specific in nature. Early identification of comorbid chronic diseases in patients with LUTS/BPH is crucial for effectively screening and managing chronic conditions. The current healthcare model predominantly focuses on specialized treatment for individual diseases, posing significant challenges when dealing with multimorbidity. Treating certain chronic diseases often simultaneously alleviates LUTS/BPH symptoms. Previous studies have shown that metabolic syndrome is closely related to BPH/LUTS, and improving metabolic syndrome can prevent the progression of BPH within five years (43). Recent studies also indicate that psychological care interventions applied to LUTS/BPH patients can effectively reduce negative emotions, thereby improving patients' quality of life (44). However, some reports suggest that oral 5α-reductase inhibitors (5α-RIs) for treating LUTS/BPH may increase the risk of NAFLD, type 2 diabetes mellitus (T2DM), and potential renal dysfunction (45,46). Additionally, patients treated with a combination of 5α-RIs and α-receptor blockers have also been reported to have an increased risk of heart disease (47). Similarly, when performing transurethral surgery for LUTS/BPH, the impact of other chronic diseases must also be considered, which is a matter of particular clinical concern. Patients with LUTS/BPH may have concomitant bladder dysfunction (often caused by diabetes or neurological disorders), which may reduce the therapeutic effect of transurethral surgery for BPH. This is not a reason to refuse surgical treatment based on current knowledge. A recent meta-analysis shows that transurethral surgery can improve symptoms in BPH patients with bladder dysfunction, demonstrating advantages over drug therapy (48). Therefore, during patient consultation, it is essential to fully inform patients of the risk that they may only partially benefit from the treatment (49). For patients who refuse transurethral surgery, other alternative treatment options should be considered. In conclusion, we should not only pay attention to the epidemiological association

between LUTS/BPH and other chronic diseases, but also consider that treating one chronic disease may affect or be affected by other chronic diseases. It is crucial for urologists to collaborate with geriatricians and general practitioners to assess the multimorbidity risks in male patients with BPH and take appropriate preventive measures.

Our study provides a new reference for the current research on multimorbidity patterns in China. Given the diverse types and combinations of chronic diseases, it is impractical to study the incidence and treatment outcomes of LUTS/BPH combined with other chronic diseases individually. Our research indicates that LUTS/BPH, as a common chronic condition, warrants further exploration in the context of multimorbidity with other chronic diseases. Based on real-world data, a Spanish study conducted cluster analysis and identified eight multimorbidity patterns among the elderly, with urogenital, mental, and musculoskeletal system diseases predominating in men (50). A nationwide survey in Japan examined the relationship between multimorbidity patterns and self-rated health (SRH), identifying three patterns associated with poor SRH outcomes, including a group where urological diseases clustered with malignant tumors, digestive system diseases, and hematological diseases (51). In the UK, a nationwide study based on individual electronic health records found that diseases co-occurring with BPH included depression, erectile dysfunction, abdominal hernia, and substance abuse (52). However, several recent studies on multimorbidity patterns have not included LUTS/BPH as part of the chronic disease combinations (53,54). The differences in comorbidity patterns among studies may be attributed to variations in the ethnicity, socioeconomic status, lifestyle, and behavioral factors of the study populations (20). Given China's large population and significant aging demographic, incorporating LUTS/BPH as part of the multimorbidity patterns in Chinese research is crucial.

To our knowledge, this nationwide representative data analysis is the first to use PSM analysis to explore the relationship between LUTS/BPH and the number of chronic diseases, multimorbidity, and up to 14 specific chronic conditions in the Chinese male population. The results are mutually supportive, and the subgroup analyses further enhance the reliability of the findings. However, several limitations are unavoidable. First, the prevalence of LUTS/BPH may be underestimated since many individuals regard it as a natural part of aging, and only a tiny proportion seek medical help, potentially leading to misclassification. Second, while this study addresses a broad range of chronic diseases and adjusts for various risk factors, other confounding factors might still exist. Third, as a cross-sectional study, it cannot establish a causal relationship between LUTS/BPH and multimorbidity; further cohort studies are needed to confirm longitudinal associations. This research represents a preliminary step in exploring multimorbidity involving the urinary and other systems. Future studies should investigate multimorbidity patterns and related interdisciplinary fields, such as uro-cardiology (10).

## Conclusions

In the Chinese population, LUTS/BPH was found to be closely associated with multimorbidity and up to 14 specific chronic diseases, with a dose-response relationship based on the number of chronic conditions defined within multimorbidity. It is imperative to include LUTS/BPH in the study and management of multimorbidity. Policymakers and urologists need to recognize the significant link between LUTS/BPH and multimorbidity, as this will enhance the understanding of these chronic conditions. Health assessments for high-risk multimorbidity screening should be conducted among LUTS/BPH patients, as treating LUTS/BPH may influence or be influenced by other chronic diseases. Further research into the potential pathophysiological mechanisms and interactions of BPH in developing multimorbidity and various chronic diseases is necessary to improve the overall or personalized treatment of multimorbidity.

## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-268/rc

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-24-268/coif). The authors

have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The CHARLS study obtained written informed consent from each participant. Ethical approval for all the CHARLS waves was granted by the Institutional Review Board at Peking University. The IRB approval number for the main household survey, including anthropometrics, is IRB00001052-11015; the IRB approval number for biomarker collection is IRB00001052-11014.

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