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## The prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022792
Article Type:	Research
Date Submitted by the Author:	10-Mar-2018
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Keywords:	LUTS/BPH, Epidemiology < TROPICAL MEDICINE, China

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Manuscripts

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4 **The prevalence of lower urinary tract symptoms**  
5 **suggestive of benign prostatic hyperplasia (LUTS/BPH)**  
6 **in China: results from the China Health and Retirement**  
7 **Longitudinal Study**  
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15 **The prevalence of LUTS/BPH in China**  
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## ABSTRACT

**Objective.** Rapid population aging in China is increasing the prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) among older people and so does the economic burden. Related data in China is insufficient and warranted.

**Design.** Secondary analysis of a cohort sample.

**Setting.** A nationally representative cross-sectional survey—the China Health and Retirement Longitudinal Study (CHARLS) was conducted in 2011 in mainland China.

**Participants.** Community-based individuals were drawn from the CHARLS through multistage probability sampling. Overall, a total of 5888 participants were included in this study.

**Outcome measures.** Self-reported morbid state was obtained using a structured questionnaire. The weighted-prevalence of LUTS/BPH was estimated and stratified by age group, marital status, education levels, economic levels, residing areas and geographic regions. Multivariable weighted logistic regression was used to examine the association of socioeconomic status with the odds of BPH.

**Results.** The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval [CI], 9.36-12.12). Among individuals age over 70 years, the prevalence was 14.67% (95% CI, 11.80-18.09), which increased with aging ( $P<0.05$ ). The prevalence of LUTS/BPH among subjects residing the urban areas was much higher at 13.55% (95% CI, 10.95-16.64) than those living in rural areas at 8.38% (95% CI, 6.90-10.15). The South-Central and South-West had the lowest prevalence of LUTS/BPH, and prevalence was highest among respondent participants living in the North-West region.

**Conclusions.** In this study, we found there was an increasing trend of prevalence with aging and the prevalence varied according to marital status, socioeconomic status and geographic regions.

**Keywords** LUTS/BPH; epidemiology; China

### Strengths and limitations

- Our data is based on the CHARLS, a strict national population survey.
- Prevalence of LUTS/BPH in China is hard to estimate, because not only the huge population but also the diagnostic criteria.
- The CHARLS did not collect the data of weight and height, so we couldn't analyze the relationship of BMI and prevalence of LUTS/BPH, nor obesity with prevalence.
- Testicular androgens are required in the prostate for the development of BPH, which is known.

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3 Benign prostatic hyperplasia (BPH) is one of the most common diseases of mankind and  
4 represents a substantial disease burden. BPH is characterized by a proliferation of both stromal  
5 and epithelial cells of the prostate in the transitional zone surrounding the urethra (1).  
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7 Approximately 50% of men >50 years of age will have pathological evidence of BPH, with this  
8 number increasing to >80% as men reach their eighth decade of life and older (2). And when men  
9 reach their age of 80, this number will increase to 83% (3). As the world population ages, the  
10 incidence and prevalence of BPH have rapidly increased (4). Lower urinary tract symptoms  
11 (LUTS) have been specified by the standardization subcommittee of the International Continence  
12 Society (ICS) in February 2002: "LUTS are the subjective indicators of a disease or change in  
13 conditions as perceived by the patients, carer or partners and may lead him/her to seek help from  
14 health care professionals. Symptoms may either be volunteered or described during the patient  
15 interview. They are usually qualitative" (5). But in 2006, Chapple and Roehrborn emphasized that  
16 the presence of LUTS does not need to be associated with the prostatic pathology only (6). Thus,  
17 LUTS/BPH was used in our study to refer to the symptomatic BPH. Although it is not  
18 life-threatening, LUTS/BPH is associated with serious morbidities and decreases of life quality  
19 (7,8). In America, LUTS/BPH affects more than 20% of American men aged 30 to 79 years, or  
20 roughly 15 million men (9,10). To date, the prevalence of BPH in China is mostly from autopsy  
21 and few of the studies based on the general population, which cannot reflect the actual situation of  
22 the disease (11). And no study has been conducted for LUTS/BPH in China. Thus, there is a  
23 paucity of data on prevalence of LUTS/BPH and its potential risk factors among the elderly in  
24 China.

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42 China is a large country with a population of 1.3 billion. Of them, 25.3% were aged 50 years  
43 or older and 13.26% were greater than 60 years old (12). The project team filed an ethical review  
44 application to Ethical Review Committee (IRB) at Peking University in June 2008. The aging of  
45 the general population means that elderly people now account for a much greater proportion of  
46 patients with BPH. Many modifiable risk factors play roles in pathogenesis of BPH, including sex  
47 steroid hormones, the metabolic syndrome and cardiovascular disease, obesity, diabetes, diet,  
48 physical activity and inflammation. These risk factors cause a large variation of prevalence of  
49 LUTS/BPH in the different regions of China. Epidemiological studies comparing prevalence of  
50 LUTS/BPH according to age, socioeconomic status and geographic region by the same research

method will provide reliable estimates on the understanding of potential risk factors of LUTS/BPH and help for health care plan.

Using data collected from the China Health and Retirement Longitudinal Study (CHARLS), a national random sample of the Chinese population (13), we estimated the prevalence of LUTS/BPH among residents aged 50 years or older in China according to age, marital status, education levels, geographic region and socioeconomic status.

## METHODS

The CHARLS is a survey of the elderly in China, based on a sample of households with members aged 45 years or above and their spouses. Data on the social-economic and health status were collected using standardized questionnaire (13). The baseline survey was conducted in 2011~2012 covering 450 villages/urban communities in 28 provinces. Eligible individuals were selected through four-stage, stratified, cluster sampling. Probabilities proportional to size (PPS) sampling was used in the decision of sample size. Detailed descriptions were provided in the previous publication (14).

### Definitions of LUTS/BPH

BPH is a term used and reserved for the typical histological pattern which defines the disease. However, many men with histological BPH will never seek for medical care nor do they need any treatment for it. The condition goes differently when it is associated with LUTS. Individuals with histologic BPH visit a doctor only when LUTS occurs. Residents, participated in CHARLS and answered positively to the question whether have ever been diagnosed with a prostate illness (excluding prostatic cancer), were symptomatic firstly and diagnosed with BPH. We defined a subject as a LUTS/BPH if he responded positively to this question.

### Data collection and grouping

The households were selected randomly and age-eligibly. All participants had a face-to-face household-interview using a structured questionnaire. Information collected during the household-interview included demographic factors, socioeconomic status and medical history.

Subjects were grouped into 3 strata according to age: 50-59, 60-69 and  $\geq 70$  years old. The

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3 marital status was divided into married and unmarried/separated/widowed. Education level was  
4 divided into 5 categories: no formal education, elementary school, middle school, high school and  
5 college degree or above. Geographic region was divided into rural and urban. The economic level  
6 is defined according to the tertile of GDP. We categorized their living localities into six regions,  
7 i.e., East (7 provinces: Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Anhui, Jiangxi), North (2  
8 cities: Beijing and Tianjin and 3 provinces: Hebei, Shanxi and Inner Mongolia), North-East (3  
9 provinces: Liaoning, Jilin and Heilongjiang), North-West (4 provinces: Shaanxi, Gansu, Qinghai  
10 and Xinjiang), South-Central (5 provinces: Henan, Hubei, Hunan, Guangdong and Guangxi), and  
11 South-West (1 city: Chongqing and 3 provinces: Sichuan, Guizhou and Yunnan). Individuals  
12 living in Hainan, Ningxia, Taiwan and Tibet were not selected in this survey.  
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### 23 Statistical analyses

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25 We used Stata to calculate the overall and age-specific prevalence of LUTS/BPH according  
26 to strata for each factor. The svy: logistic procedure in Stata version 14.2 was used to examine the  
27 association between each risk factor and the prevalence of BPH, adjusting for other potential  
28 confounders including sex, age, area, education, GDP per capita, and region. Both procedures took  
29 into account the complex survey design and the non-response rate for the CHARLS survey when  
30 estimating the prevalence, prevalence odds ratio (OR), and corresponding standard errors.  
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## 38 RESULTS

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40 A total of 5,888 participants were involved in our study and the characteristics of the baseline  
41 population are given in Table 1. Five hundred and ninety-nine responded positively. Mean age was  
42 62.78 (standard deviation: 8.56). Most of the participants were married. About a quarter of the  
43 participants didn't receive formal education and half of the rest received elementary or middle  
44 school education. The majority of the respondent participants lived in rural areas. About one third  
45 of respondent characteristics accounted respectively for the three various levels of GDP per capita.  
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51 The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval [CI]:  
52 9.36, 12.12). The weighted results were in Table 2.  
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### 56 Age



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3 Aging men were more likely to be diagnosed with LUTS/BPH, and the weighted prevalence  
4 of LUTS/BPH increased with age. Compared with subjects age <60 years, the adjusted odds ratio  
5 (OR) for the prevalence of LUTS/BPH were 1.50 (95% CI : 1.20, 1.87) for those age 60-69 years  
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7 and 2.09 (95% CI: 1.58, 2.78) for those age  $\geq 70$  years (Table 3).  
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#### 10 11 12 Marital status

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14 The prevalence of LUTS/BPH was slightly higher among married individuals, at 10.80% (95%  
15 CI: 9.61, 12.12) while the prevalence among unmarried/separated/widowed individuals was 9.87%  
16 (95% CI: 6.56, 14.60). The odds of LUTS/BPH in unmarried/separated/widowed individuals was  
17 approximately 0.91 that in married individuals.  
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#### 22 23 Education and economic levels

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25 Variation in the prevalence of LUTS/BPH existed among different education and economic  
26 levels. Prevalence was much higher among individuals with more years-education and it was  
27 highest among individuals with education of college degree or above ( $P < 0.05$ ). The prevalence of  
28 LUTS/BPH was lower among individuals with a low GDP per capita.  
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#### 33 34 Residing areas and regions

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36 The prevalence of LUTS/BPH was higher among subjects residing in urban areas (rural: 8.38%  
37 [95% CI: 6.90, 10.15]; urban: 13.55% [95% CI: 10.95, 16.64]). The odds of LUTS/BPH in urban  
38 residents was 1.5 times that in rural residents. There was a significant difference in the prevalence  
39 of LUTS/BPH according to geographic location. The South-Central and South-West had the  
40 lowest prevalence of LUTS/BPH (9.76% and 9.53%, respectively), followed by the East (10.56%),  
41 North (12.18%), North-East (12.24%) regions; prevalence was highest among respondent  
42 participants living in the North-West region (13.75%). Compared with the East region, the ORs for  
43 LUTS/BPH for the North, North-East, North-West, South-Central, South-West regions were 1.12  
44 (95% CI: 0.75, 1.67), 1.03 (95% CI: 0.76, 1.39), 1.66 (95% CI: 1.12, 2.47), 0.90 (95% CI: 0.53,  
45 1.55), 1.01 (95% CI: 0.66, 1.53), respectively, after adjustment for age, marital status, rural/urban  
46 area, education and GDP per capita (Table 3). The prevalence of each regions can be seen in figure  
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## DISCUSSION

The CHARLS set up a high quality, nationally representative and publicly available micro-database, providing a wide range of information about the households of the elderly and also individual information on the elderly respondents and their spouses. Our research is based on data from the CHARLS. It was known by our research that LUTS/BPH was common among Chinese men age over 50 years. Age had great influence on prevalence of LUTS/BPH from both of our research and previous researches (15).

Rapid population aging in China is increasing the prevalence of LUTS/BPH among older people and so does the economic burden. In our research, adjusted prevalence of LUTS/BPH among men age beyond 50 years reached 10.66% (95% CI: 9.36, 12.12), which could influence on their life quality and bring economic burden on both individuals and society. It was believed that the cost of intervention and treatment of BPH is comprised of direct costs (drugs, procedures, imaging, office visits), indirect costs (lost earnings) and intangible costs (pain and suffering) (16). It is impartial that the costs for LUTS/BPH will continuously increase in the future. Thus, a prevalence study on LUTS/BPH will help formulate policy on public health.

As definition of BPH varies, the prevalence varies (17). When responding positively to whether have ever been diagnosed with a benign prostate illness, individual meant that some symptoms of LUTS has happened to him, and he sought for medical care and been diagnosed with a benign prostate illness. Benign prostate illness mainly refers to prostatitis and BPH, which shared a lot of overlap of symptoms. Prostatitis without BPH is a diagnosis of young men, but inflammation in the prostate is also observed in elderly men presenting with BPH. Qian XQ et al (18) clarified that histological prostatitis has affected the clinical progression of BPH because of the inflammation progress. Inflammation is the modifiable risk factors in BPH pathogenesis (15). Patients presenting with BPH may have a component of category IV, asymptomatic prostatitis (19). Thus, in our research, individuals, age over 50 years, responding positively to the question whether have been diagnosed with a benign prostate illness were counted as LUTS/BPH.

BPH increases with age, which has been confirmed by numerous researches. Loeb s et al (20) enrolled 278 men from the Baltimore Longitudinal Study of Aging, reported that the median rate of volume change was 0.6cc per year (range -9.9 to 62.1), corresponding to a median growth rate

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3 of 2.5% per year (range -29.2 to 176.4%). The study was based on autopsy. Although the prostate  
4 volume isn't related to LUTS severity directly, it is a risk factor for it. Claus G et al (21) verified  
5 that larger prostate is associated with increased risks of urinary retention, increased future need for  
6 surgery and clinical progression of BPH. Another study, after following up for 16 years, also  
7 examined the increased incidence and progression of LUTS in men with age, significantly (22). In  
8 our research, LUTS/BPH involved symptoms of LUTS and histological BPH. Individuals age  
9 60-69 years and  $\geq 70$  years has a much higher prevalence of LUTS/BPH, and the adjusted ORs  
10 were 1.5 (95% CI: 1.20, 1.87) and 2.09 (95% CI: 1.58, 2.78) respectively, compared with subjects  
11 age  $< 60$  years ( $p < 0.05$ ).  
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Studies about sex steroid hormones and BPH revealed that androstenediols play a role in  
BPH development (23). Unmarried/separated/widowed individuals accounted 13.20% in all the  
respondent participants, having a lower adjusted prevalence of LUTS/BPH at 9.87% (95% CI:  
6.56, 14.60). These people were usually thought have no or less sexual life compared with married  
men. And married men intended more to visit doctor in case of their illness having a negative  
impact on their spouse and family.

In several studies, socioeconomic status played an important role in progression of  
LUTS/BPH and might vary the results particularly the prevalence and effects of LUTS/BPH (24).  
For example, some researchers found higher rates of BPH in upper income groups, but this may  
due to selection bias, because of higher utilization of medical care (25,26). Using data of Korean  
Community Health Survey performed in 2011, Jo KJ et al made a point that the severity of LUTS  
was associated with several socioeconomic factors, including education level, income level, living  
environment (27). Fowke JH et al confirmed that education of college or more had a lower IPSS  
score (28). Education levels were obtained when people were young, and kept changeless as aging.  
It influenced mainly the understanding of disease and decision-made progress. In our research, we  
analyzed socioeconomic factors including GDP per capita, education levels and geographic region.  
Individuals with education of college degree or above had a high adjusted OR of LUTS/BPH at  
2.67 (95% CI: 1.57, 4.54) ( $P < 0.05$ ). And individuals residing in the urban areas was 1.5 times to  
these in rural. We considered that there was inevitable selection bias, as residents living in urban  
may seek medical care more often than these in rural. Some individuals lack the recognition about  
BPH and hospital visitation is often delayed.

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3 We demonstrated an apparent geographic variation in the prevalence of LUTS/BPH in China.  
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5 Residents in the South-West regions had a much lower prevalence of LUTS/BPH than those living  
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7 in the North-West regions of China. Individuals residing in the north regions, including North,  
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9 North-East and North-West, had a relatively higher prevalence of LUTS/BPH than those living in  
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11 South-Central and South-West. The diet difference may contribute mainly to this discrimination.  
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13 Daily diet of individuals living in north regions contained a lot of milk, dairy product and red meat,  
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15 while individuals living in south regions enjoyed much more fruits and vegetables than those in  
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17 north, which have both been confirmed to increase the risk of LUTS/BPH (29,30). But residents in  
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19 East region didn't show a high prevalence of LUTS/BPH. It was considered that socioeconomic  
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21 development in the East region was, in general, higher than that in other regions, which may  
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23 contribute to the lower prevalence of LUTS/BPH. Besides that mentioned above, the genetic  
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25 susceptibility of BPH was also a factor influencing the prevalence of LUTS/BPH in China.  
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27 Several studies from China reported genetics associated with developing BPH (30), which may be  
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29 one of the factors causing various prevalence of LUTS/BPH in China.

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31 Our research has several strengths. First, our data is based on the CHARLS, a national  
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33 population survey. The interviewers were trained strictly and questionnaires were developed over  
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35 a long and rigorous course. The participants were chosen via strict multistage probability sampling  
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37 procedure. Hence, data from the CHARLS can describe the national condition. Secondly,  
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39 prevalence of LUTS/BPH in China is hard to estimate, because not only the huge population but  
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41 also the diagnostic criteria. Using data from the CHARLS, we avoided both of the questions.

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43 There are still some deficiencies as well. Firstly, the CHARLS did not collect the data of  
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45 weight and height, so we couldn't analyze the relationship of BMI and prevalence of LUTS/BPH,  
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47 nor obesity with prevalence. Secondly, testicular androgens are required in the prostate for the  
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49 development of BPH, which is known. Thirdly, as China is a wide country, although we obey to  
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51 the same principles of diagnosis from China Urology Association (CUA), the diagnosis of  
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53 LUTS/BPH may be slightly different among regions. We cannot be aware of that, since the data of  
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55 CHARLS gives an established diagnosis.

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57 In this study, we looked at the prevalence of LUTS/BPH via the CHARLS data. We found  
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59 that the LUTS/BPH is highly prevalent in older, urban-living men. And the prevalence varied  
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according to marital status, socioeconomic status and geographic regions.

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5 Funding statement

6 This research received no specific grant from any funding agency in the public, commercial or  
7 not-for-profit sectors.  
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12 Competing interest statement

13 None declared.  
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18 Author statement

19 Weiyu Zhang, Hao Hu: Designed the study and drafted the article

20 Haibin Li, Feng Wu: Dealt with the statistics

21 Xiaopeng Zhang, Huanrui Wang, Meishan Zhao: help with data sorting, literature retrieve,  
22 language polish and other chores  
23  
24

25 Kexin Xu: Constructive revision and grasp of the overall situation  
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29  
30 Acknowledgements

31 The authors are full of gratitude to the office of CHARLS for sharing the data. The data can be  
32 accessed at the official website.  
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37 **reference**

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Table 1 The baseline of population

Characteristic	Men (n=5888)
Age, mean (SD)	62.78 (8.56)
Age group, No. (%)	
50-59	2356 (40.01)
60-69	2250 (38.21)
≥70	1282 (21.77)
Marital status, No. (%)	
Married	5111 (86.80)
Unmarried/Separated /Widowed	777 (13.20)
Education levels, No. (%)	
No formal education	1918 (32.84)
Elementary school	1573 (26.93)
Middle school	1426 (24.42)
High school	556 (9.52)
College degree or above	367 (6.28)
Geographic region, No. (%)	
Rural	3742 (63.55)
Urban	2146 (36.45)
GDP per capita, No. (%)	
Low	2114 (35.90)
Middle	1960 (33.29)
High	1814 (30.81)
Region, No. (%)	
East	2506 (42.56)
North	779 (13.23)
North-East	404 (6.86)
North-West	224 (3.80)
South-Central	974 (16.54)
South-West	1001 (17.00)



Table 2 The weighted prevalence

Characteristic	Case, No. (%)	Prevalence (%)	95% CI
Total	599 (10.17)	10.66	9.36-12.12
Age group, No. (%)			
50-59	182 (7.72)	8.39	7.01-9.98
60-69	236 (10.49)	10.61	8.67-12.91
≥70	181 (14.12)	14.67	11.80-18.09
Marital status, No. (%)			
Married	522 (10.21)	10.80	9.61-12.12
Unmarried/Separated /Widowed	77 (9.91)	9.87	6.56-14.60
Education levels, No. (%)			
No formal education	162 (8.45)	8.20	6.54-10.23
Elementary school	166 (10.55)	10.69	8.20-13.83
Middle school	130 (9.12)	9.17	6.71-12.40
High school	55 (9.89)	13.99	7.62-24.29
College degree or above	84 (22.89)	21.26	13.55-31.73
Geographic region, No. (%)			
Rural	328 (8.77)	8.38	6.90-10.15
Urban	271 (12.63)	13.55	10.95-16.64
GDP per capita, No. (%)			
Low	203 (9.60)	10.69	8.20-13.83
Middle	232 (11.84)	11.54	10.09-13.16
High	164 (9.04)	9.83	7.44-12.88
Region, No. (%)			
East	244 (9.74)	10.56	8.68-12.81
North	98 (12.58)	12.18	8.63-16.92
North-East	42 (10.40)	12.24	9.11-16.25
North-West	29 (12.95)	13.75	9.92-18.75
South-Central	91 (9.34)	9.76	6.47-14.45
South-West	95 (9.49)	9.53	6.24-14.31

Table 3 The adjusted odds ratio (OR) for the prevalence of LUTS/BPH

Characteristic	Crude OR (95 % CI)	Adjusted OR (95 % CI)	<i>P</i> value
Age group, No. (%)			
50-59	1.00 (reference)	1.00 (reference)	
60-69	1.29 (0.98-1.71)	1.50 (1.20-1.87)	0.001
≥70	1.87 (1.31-2.69)	2.09 (1.58-2.78)	0.000
Marital status, No. (%)			
Married	1.00 (reference)	1.00 (reference)	
Unmarried/Separated /Widowed	0.90(0.59-1.38)	0.91 (0.63-1.30)	0.597
Education levels, No. (%)			
No formal education	1.00 (reference)	1.00 (reference)	
Elementary school	1.34 (0.95-1.88)	1.36 (0.97-1.91)	0.074
Middle school	1.12 (0.79-1.61)	1.30 (0.93-1.82)	0.120
High school	1.82 (0.84-3.92)	2.27 (1.03-4.99)	0.043
College degree or above	3.02 (1.67-5.43)	2.67 (1.57-4.54)	0.000
Geographic region, No. (%)			
Rural	1.00 (reference)	1.00 (reference)	
Urban	1.71 (1.24-2.36)	1.50 (1.71-1.92)	0.002
GDP per capita, No. (%)			
Low	1.00 (reference)	1.00 (reference)	
Middle	1.08(0.77-1.53)	1.23 (0.94-1.62)	0.130
High	0.91(0.58-1.42)	0.99 (0.69-1.42)	0.958
Region, No. (%)			
East	1.00 (reference)	1.00 (reference)	
North	1.17 (0.74-1.84)	1.12 (0.75-1.67)	0.578
North-East	1.18 (0.77-1.79)	1.03 (0.76-1.39)	0.844
North-West	1.35 (0.86-2.11)	1.66 (1.12-2.47)	0.012
South-Central	0.91 (0.55-1.51)	0.90 (0.53-1.55)	0.696
South-West	0.89 (0.53-1.50)	1.01 (0.66-1.53)	0.970

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### The prevalence of clinical BPH in China in 2011

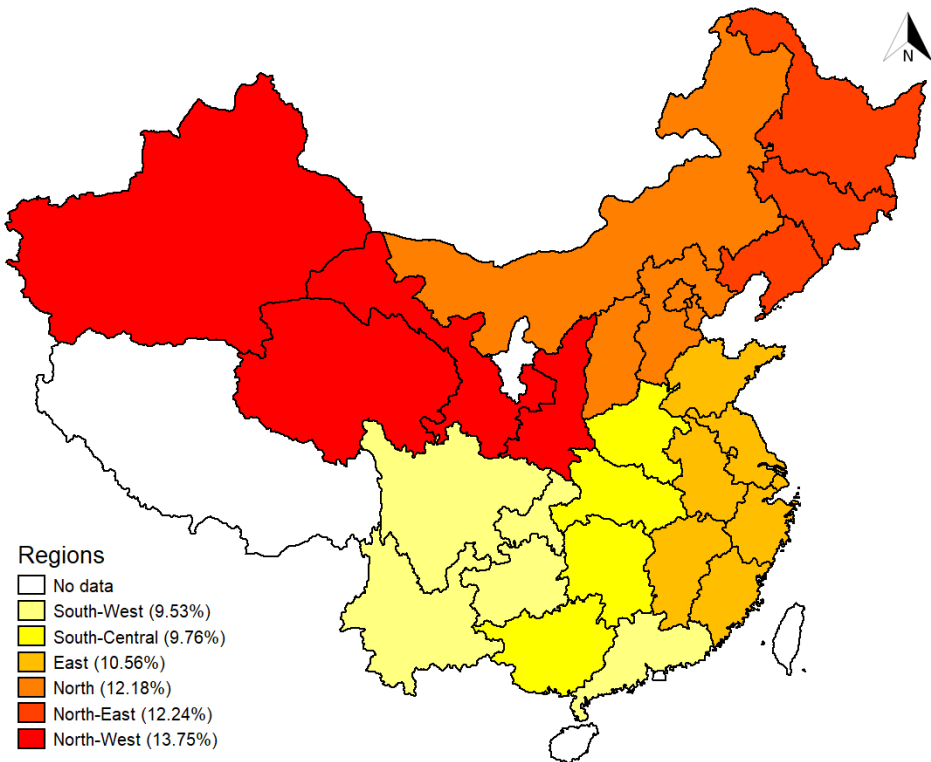


Figure 1. The prevalence of LUTS/BPH in each regions

403x331mm (72 x 72 DPI)

# BMJ Open

## The prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022792.R1
Article Type:	Research
Date Submitted by the Author:	28-Aug-2018
Complete List of Authors:	Zhang, Weiyu; Peking University People's Hospital Zhang, Xiaopeng; Peking University People's Hospital Li, Haibin; Capital Medical University Wu, Feng; Institute for Disease Control and Prevention, Chinese PLA Wang, Huanrui; Peking University People's Hospital Zhao, Meishan; Capital Medical University Affiliated Beijing Friendship Hospital Hu, Hao; Peking University People's Hospital, Urology Xu, Kexin; Peking University People's Hospital
<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health, Urology
Keywords:	LUTS/BPH, Epidemiology < TROPICAL MEDICINE, China

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4 **The prevalence of lower urinary tract symptoms suggestive of benign prostatic**  
5 **hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement**  
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10 **The prevalence of LUTS/BPH in China**

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## ABSTRACT

**Objective.** Rapid population aging in China is increasing the prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) among older people. The associated economic burdens are increasing as well. Relevant data from China is currently insufficient.

**Design.** Secondary analysis of a cohort sample.

**Setting.** A nationally representative cross-sectional survey—the China Health and Retirement Longitudinal Study (CHARLS) was conducted in 2011 in mainland China.

**Participants.** Individuals in the community selected from the CHARLS by multistage probability sampling. A total of 5888 participants aged 50 years and above were included.

**Outcome measures.** Self-reported morbid state was derived from a structured questionnaire. The weighted-prevalence of LUTS/BPH was estimated and stratified by age group, marital status, education levels, economic levels, residential areas and geographic regions. Multivariable weighted logistic regression was used to examine the association of socioeconomic status with the odds of BPH.

**Results.** The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval [CI], 9.36-12.12). Among individuals age over 70 years, the prevalence was 14.67% (95% CI, 11.80-18.09), and it increased with aging ( $P < 0.05$ ). The prevalence of LUTS/BPH among subjects residing the urban areas was higher [13.55% (95% CI, 10.95-16.64)] than those living in rural areas [8.38% (95% CI, 6.90-10.15)]. The prevalence of LUTS/BPH was lowest in the South-Central and South-West and highest the North-West region.

**Conclusions.** We found an increasing trend of prevalence of LUTS/BPH with aging. It varied according to marital status, socioeconomic status and geographic region.

**Keywords** LUTS/BPH; epidemiology; China

### Strengths and limitations

- Our data is based on the CHARLS, a strict national population survey.
- Prevalence of LUTS/BPH in China is difficult to estimate, not only because of the large population but also because of the diagnostic criteria.
- The CHARLS did not collect weights and heights, so we could not analyze the relationship of BMI and obesity with prevalence of LUTS/BP
- Testicular androgens are required in the prostate for the development of BPH.

For peer review only

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3 Benign prostatic hyperplasia (BPH) is a common disease of men, representing a  
4 substantial disease burden. BPH is characterized by a proliferation of both stromal  
5 and epithelial cells of the prostate in the transitional zone surrounding the urethra  
6 (1). Approximately 50% of men >50 years of age have pathological evidence of BPH,  
7 increasing to >80% as men reach their eighth decade of life and older (2). When men  
8 reach 80 years, this number increases to 83% (3). As the world population aged, the  
9 incidence and prevalence of BPH have rapidly increased (4). Lower urinary tract  
10 symptoms (LUTS) have been specified by the standardization subcommittee of the  
11 International Continence Society (ICS) in February 2002: "LUTS are the subjective  
12 indicators of a disease or change in conditions as perceived by the patients, carer or  
13 partners and may lead him/her to seek help from health care professionals.  
14 Symptoms may either be volunteered or described during the patient interview. They  
15 are usually qualitative" (5). However, in 2006, Chapple and Roehrborn emphasized  
16 that the presence of LUTS does not need to be associated with prostatic pathology  
17 only (6). Therefore, LUTS/BPH in our study referred to symptomatic BPH. Although it  
18 is not life-threatening, LUTS/BPH is associated with serious morbidities and  
19 decreases quality of life (7,8). In America, LUTS/BPH affects more than 20% of  
20 American men aged 30 to 79 years, or roughly 15 million men (9,10). The prevalence  
21 of BPH in China is currently determined from autopsy data and a few studies based  
22 on the general population that cannot accurately reflect the current status of the  
23 disease (11). No study has been conducted for LUTS/BPH in China. Therefore, there is  
24 a paucity of data regarding prevalence of LUTS/BPH and its potential risk factors  
25 among the elderly in China.  
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47 China has a population of 1.3 billion, 25.3% aged 50 years or older and 13.26% aged  
48 more than 60 years (12). The aging of the general population means that elderly  
49 people now account for a much greater proportion of patients with BPH. Many  
50 modifiable risk factors play roles in pathogenesis of BPH, including sex steroid  
51 hormones, the metabolic syndrome cardiovascular disease, obesity, diabetes, diet,  
52 physical activity and inflammation. These risk factors cause a large variation of  
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3 prevalence of LUTS/BPH in various regions of China. Epidemiological studies  
4 comparing prevalence of LUTS/BPH according to age, socioeconomic status and  
5 geographic region by the same research method will provide reliable estimates on  
6 the understanding of potential risk factors of LUTS/BPH and help design health care  
7 plans.  
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12 Using data collected from the China Health and Retirement Longitudinal Study  
13 (CHARLS), a national random sample of the Chinese population (13), we estimated  
14 the prevalence of LUTS/BPH among residents aged 50 years or older in China  
15 according to age, marital status, education levels, geographic region and  
16 socioeconomic status.  
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21 The project team filed an ethics review application to Ethical Review Committee (IRB)  
22 at Peking University in June 2008.  
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## 26 27 METHODS

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31 The CHARLS is a survey of the elderly in China, based on a sample of households with  
32 members middle-aged and elderly and their spouses. Individuals aged 50 years and  
33 above were included in this study. Data on social-economic and health status were  
34 collected using standardized questionnaire (13). The baseline survey was conducted  
35 in 2011–2012 covering 450 villages/urban communities in 28 provinces. Eligible  
36 individuals were selected through four-stage, stratified cluster sampling. Probabilities  
37 proportional to size (PPS) sampling were used in the determination of sample size.  
38 Detailed descriptions were provided in a previous publication (14).  
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### 46 47 Definitions of LUTS/BPH

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49 BPH is a term reserved for the typical histological pattern that defines the disease.  
50 However, many men with histological BPH never seek medical care, nor do they  
51 require treatment for it. The condition proceeds differently when it is associated with  
52 LUTS. Individuals with histologic BPH visit a doctor only when LUTS occurs. Residents  
53 who participated in CHARLS were asked whether they have ever been diagnosed  
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3 with a prostate illness (excluding prostatic cancer). We defined him as a subject with  
4 LUTS/BPH if he responded positively to this question.  
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#### 8 Patient and Public Involvement 9

10 The households were selected randomly and age-eligibly. All participants had a  
11 face-to-face household-interview using a structured questionnaire. Information  
12 collected during the household-interview included demographic factors,  
13 socioeconomic status and medical history. The statistical analysis results will not  
14 disseminate to study participants in short time.  
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21 Subjects were grouped into 3 strata according to age: 50-59, 60-69 and  $\geq 70$  years  
22 old. The marital status was divided into married and unmarried/separated/widowed.  
23 Education level was divided into 5 categories: no formal education, elementary  
24 school, middle school, high school and college degree or above. Geographic region  
25 was divided into rural and urban. The economic level were defined according to the  
26 tertile of GDP. We categorized their living localities into six regions, i.e., East (7  
27 provinces: Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Anhui, Jiangxi), North (2  
28 cities: Beijing and Tianjin and 3 provinces: Hebei, Shanxi and Inner Mongolia),  
29 North-East (3 provinces: Liaoning, Jilin and Heilongjiang), North-West (4 provinces:  
30 Shaanxi, Gansu, Qinghai and Xinjiang), South-Central (5 provinces: Henan, Hubei,  
31 Hunan, Guangdong and Guangxi) and South-West (1 city: Chongqing and 3 provinces:  
32 Sichuan, Guizhou and Yunnan). Individuals living in Hainan, Ningxia, Taiwan and Tibet  
33 were not selected in this survey.  
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#### 45 Statistical analyses 46 47

48 We used Stata to calculate the overall and age-specific prevalence of LUTS/BPH  
49 according to strata for each factor. The svy: logistic procedure in Stata version 14.2  
50 was used to examine the association between each risk factor and the prevalence of  
51 BPH, adjusting for other potential confounders including gender, age, area, education,  
52 GDP per capita, and region. Both procedures considered the complex survey design  
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3 and the non-response rate for the CHARLS survey when estimating the prevalence,  
4 prevalence odds ratio (OR), and corresponding standard errors.  
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## 8 RESULTS 9

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11 A total of 5,888 participants were involved in our study and the characteristics of the  
12 baseline population are given in Table 1. Five hundred and ninety-nine responded  
13 positively. Mean age was 62.78 (standard deviation: 8.56). Most of the participants  
14 were married. About a quarter of the participants did not receive formal education  
15 and half of the rest received elementary or middle school education. The majority of  
16 the respondent participants lived in rural areas. About one third of respondents were  
17 classified in three levels of GDP per capita.  
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27 The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval  
28 [CI]: 9.36, 12.12). The weighted results are listed in Table 2.  
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### 31 Age

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33 Aging men were more likely to be diagnosed with LUTS/BPH, and the weighted  
34 prevalence of LUTS/BPH increased with age. Compared with subjects age <60 years,  
35 the adjusted odds ratios (OR) for the prevalence of LUTS/BPH were 1.50 (95% CI: 1.20,  
36 1.87) for those age 60-69 years and 2.09 (95% CI: 1.58, 2.78) for those aged  $\geq 70$   
37 years (Table 3).  
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### 44 Marital status

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46 The prevalence of LUTS/BPH was slightly higher among married individuals, at 10.80%  
47 (95% CI: 9.61, 12.12) while the prevalence among unmarried/separated/widowed  
48 individuals was 9.87% (95% CI: 6.56, 14.60). The odds of LUTS/BPH in  
49 unmarried/separated/widowed individuals was approximately 0.91 times that of  
50 married individuals.  
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### Education and economic levels

There was variation in the prevalence of LUTS/BPH among various education and economic levels. Prevalence was much higher among individuals with more years of education and it was highest among individuals with college degrees or above ( $P < 0.05$ ). The prevalence of LUTS/BPH was lower among individuals with a low GDP per capita.

### Resident areas and regions

The prevalence of LUTS/BPH was higher among subjects residing in urban areas (rural: 8.38% [95% CI: 6.90, 10.15]; urban: 13.55% [95% CI: 10.95, 16.64]). The odds of LUTS/BPH in urban residents was 1.5 times that of rural residents. There was a significant difference in the prevalence of LUTS/BPH according to geographic location. The South-Central and South-West had the lowest prevalence of LUTS/BPH (9.76% and 9.53%, respectively), followed by the East (10.56%), North (12.18%) and North-East (12.24%) regions; prevalence was highest among respondents living in the North-West region (13.75%). Compared with the East region, the ORs for LUTS/BPH for the North, North-East, North-West, South-Central, South-West regions were 1.12 (95% CI: 0.75, 1.67), 1.03 (95% CI: 0.76, 1.39), 1.66 (95% CI: 1.12, 2.47), 0.90 (95% CI: 0.53, 1.55) and 1.01 (95% CI: 0.66, 1.53), respectively, after adjustment for age, marital status, rural/urban area, education and GDP per capita (Table 3). The prevalence of each region can be seen in Figure 1.

### DISCUSSION

The CHARLS set up a high quality, nationally representative, publicly available micro-database, providing a wide range of information regarding the households of the elderly as well as individual information on the elderly respondents and their spouses. Our research is based on data from the CHARLS. It was known from our study that LUTS/BPH was common among Chinese men age over 50 years. Age had great influence on prevalence of LUTS/BPH according to ours and other studies (15).

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5 Rapid population aging in China is increasing the prevalence of LUTS/BPH among  
6 older people and so does the economic burdens associated with it. In our study,  
7 adjusted prevalence of LUTS/BPH among men aged beyond 50 years reached 10.66%  
8 (95% CI: 9.36, 12.12), which could influence their life quality and impose economic  
9 burdens on both individuals and society. The cost of intervention and treatment of  
10 BPH is comprised of direct costs (drugs, procedures, imaging, office visits), indirect  
11 costs (lost earnings) and intangible costs (pain and suffering) (16). It is likely that the  
12 costs for LUTS/BPH will continuously increase in the future. Therefore, a prevalence  
13 study on LUTS/BPH can help guide public health policy.  
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23 As definition of BPH varies, the prevalence varies (17). When responding positively to  
24 a question regarding diagnosis of a benign prostate illness, an individual means that  
25 some symptoms of LUTS occurred in him, and that he sought for medical care and  
26 was diagnosed with a benign prostate illness. Benign prostate illness primarily refers  
27 to prostatitis and BPH, which shared many overlapping symptoms. Prostatitis without  
28 BPH is a diagnosis of young men, however, inflammation in the prostate is also  
29 observed in elderly men presenting with BPH. Gandaglia et al. (18) suggested that  
30 histological prostatitis affected the progression of BPH because of the inflammatory  
31 process. Inflammation is a modifiable risk factor in BPH pathogenesis (15). Patients  
32 presenting with BPH may have a component of category IV, asymptomatic prostatitis  
33 (19). Thus, in our study, individuals over age 50 who responded positively to the  
34 question regarding diagnosis with a benign prostate illness were counted as having  
35 LUTS/BPH.  
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49 BPH increases with age, as has been confirmed by numerous studies. Loeb et al. (20)  
50 enrolled 278 men from the Baltimore Longitudinal Study of Aging and reported that  
51 the median rate of volume change was 0.6 cc per year (range -9.9 to 62.1),  
52 corresponding to a median growth rate of 2.5% per year (range -29.2% to 176.4%).  
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56 The study was based on autopsy. Although prostate volume is not related to LUTS  
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3 severity directly, it is a risk factor. Roehrborn et al. (21) reported that larger prostate  
4 was associated with increased risks of urinary retention, increased future need for  
5 surgery and clinical progression of BPH. Another study, after follow-up for 16 years,  
6 reported significantly increased incidence and progression of LUTS in men with age  
7 (22). In our study, LUTS/BPH involved symptoms of LUTS and histological BPH.  
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9 Individuals aged 60-69 years and  $\geq 70$  years had a much higher prevalence of  
10 LUTS/BPH, and the adjusted ORs were 1.5 (95% CI: 1.20, 1.87) and 2.09 (95% CI: 1.58,  
11 2.78) respectively, compared with subjects age  $< 60$  years ( $p < 0.05$ ).  
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20 Studies of sex steroid hormones and BPH revealed that androstenediols play a role in  
21 BPH development (23). Unmarried/separated/widowed individuals accounted 13.20%  
22 in all the respondent participants, having a lower adjusted prevalence of LUTS/BPH at  
23 9.87% (95% CI: 6.56, 14.60). These people are usually thought have no or less sexual  
24 life compared with married men. Married men more often intended to visit doctor in  
25 case of their illness would have a negative impact on their spouse and family.  
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32 In several studies, socioeconomic status played an important role in progression of  
33 LUTS/BPH and might vary the results, particularly the prevalence and effects of  
34 LUTS/BPH (24). For example, some researchers found higher rates of BPH in upper  
35 income groups, but this may due to selection bias, because of higher utilization of  
36 medical care (25,26). Using data from the Korean Community Health Survey  
37 performed in 2011, Jo KJ et al. found that the severity of LUTS was associated with  
38 several socioeconomic factors, including education level, income level and living  
39 environment (27). Fowke et al. found that college education or higher levels was  
40 associated with a lower IPSS score (28). Education levels were obtained when people  
41 were young, and did not change with aging. Nevertheless, education influenced the  
42 understanding of disease and the decision-making progress. In our study, we  
43 analyzed socioeconomic factors including GDP per capita, education levels and  
44 geographic region. Individuals with education of college degree or above had a high  
45 adjusted OR of LUTS/BPH at 2.67 (95% CI: 1.57, 4.54) ( $P < 0.001$ ). Individuals residing  
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3 in urban areas were 1.5 times more likely to have the diagnosis than those in rural  
4 areas. We believe that there was inevitable selection bias, as residents living in urban  
5 areas may seek medical care more often than do those in rural areas. Some  
6 individuals lack the recognition of BPH and hospital visitation is often delayed.  
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12 We demonstrated an apparent geographic variation in the prevalence of LUTS/BPH in  
13 China. Residents in the South-West regions had a much lower prevalence of  
14 LUTS/BPH than did those living in the North-West regions of China. Individuals  
15 residing in the north regions, including North, North-East and North-West, had a  
16 relatively higher prevalence of LUTS/BPH than did those living in South-Central and  
17 South-West. Dietary differences may contribute to this discrepancy. Daily diet of  
18 individuals living in north regions contain much milk, dairy products and red meat,  
19 while individuals living in south regions consume more fruits and vegetables than do  
20 those in the north, which have both been confirmed to increase the risk of LUTS/BPH  
21 (29,30). Nevertheless, residents in East region did not show a high prevalence of  
22 LUTS/BPH. It was thought that socioeconomic development in the East region was, in  
23 general, higher than that of other regions, possibly contributing to the lower  
24 prevalence of LUTS/BPH. Furthermore, the genetic susceptibility of BPH was also a  
25 factor influencing the prevalence of LUTS/BPH in China. Several studies from China  
26 reported genetics associated with developing BPH (30), possibly one of the factors  
27 causing varying prevalence of LUTS/BPH in China.  
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43 Our research has several strengths. First, our data was based on the CHARLS, a  
44 national population survey. The interviewers were highly-trained and questionnaires  
45 were developed after a long and rigorous course. The participants were chosen via  
46 strict multistage probability sampling procedures. Hence, data from the CHARLS can  
47 represent the national condition. Second, the prevalence of LUTS/BPH in China is  
48 difficult to estimate, not only because of the large population but also because of the  
49 diagnostic criteria. Using data from the CHARLS, we avoided both questions.  
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3 There are some limitations as well. First, the CHARLS did not collect weight and  
4 height, so we could not analyze the relationship of BMI or obesity and prevalence of  
5 LUTS/BPH. Second, testicular androgens are required in the prostate for the  
6 development of BPH. Third, as China is a large country, and we all adhere to the  
7 principles of diagnosis from the China Urology Association (CUA), the diagnosis of  
8 LUTS/BPH may be slightly different among regions. We cannot detect these  
9 differences, since the data of CHARLS provides an established diagnosis.  
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18 In this study, we looked at the prevalence of LUTS/BPH via CHARLS data. We found  
19 that the LUTS/BPH is highly prevalent in older, urban-living men. The prevalence  
20 varied according to marital status, socioeconomic status and geographic regions.  
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#### 25 Funding statement

26 This research received no specific grant from any funding agency in the public,  
27 commercial or not-for-profit sectors.  
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#### 32 Competing interest statement

33 None declared.  
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#### 38 Author statement

39 Weiyu Zhang, Xiaopeng Zhang: Designed the study and drafted the article

40 Haibin Li, Feng Wu: Dealt with the statistics

41 Huanrui Wang, Meishan Zhao: help with data sorting, literature retrieve, language  
42 polish and other chores  
43  
44

45 Hao Hu, Kexin Xu: Constructive revision and grasp of the overall situation  
46  
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#### 50 Acknowledgements

51 The authors are full of gratitude to the office of CHARLS for sharing the data. The  
52 data can be accessed at the official website.  
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3 Data sharing statement

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5 No additional unpublished data are available.  
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Table 1 Baseline population characteristics

Characteristic	Men (n=5888)
Age, mean (SD)	62.78 (8.56)
Age group, No. (%)	
50-59	2356 (40.01)
60-69	2250 (38.21)
$\geq 70$	1282 (21.77)
Marital status, No. (%)	
Married	5111 (86.80)
Unmarried/Separated /Widowed	777 (13.20)
Education levels, No. (%) <sup>*</sup>	
No formal education	1918 (32.84)
Elementary school	1573 (26.93)
Middle school	1426 (24.42)
High school	556 (9.52)
College degree or above	367 (6.28)
Geographic region, No. (%)	
Rural	3742 (63.55)
Urban	2146 (36.45)
GDP per capita, No. (%)	
Low	2114 (35.90)
Middle	1960 (33.29)
High	1814 (30.81)
Region, No. (%)	
East	2506 (42.56)
North	779 (13.23)
North-East	404 (6.86)
North-West	224 (3.80)
South-Central	974 (16.54)
South-West	1001 (17.00)

<sup>\*</sup>, Education levels values of 48 cases was missed.

Table 2 Weighted prevalence

Characteristic	Case, No. (%)	Prevalence (%)	95% CI
Total	599 (10.17)	10.66	9.36-12.12
Age group, No. (%)			
50-59	182 (7.72)	8.39	7.01-9.98
60-69	236 (10.49)	10.61	8.67-12.91
≥70	181 (14.12)	14.67	11.80-18.09
Marital status, No. (%)			
Married	522 (10.21)	10.80	9.61-12.12
Unmarried/Separated /Widowed	77 (9.91)	9.87	6.56-14.60
Education levels, No. (%) <sup>*</sup>			
No formal education	162 (8.45)	8.20	6.54-10.23
Elementary school	166 (10.55)	10.69	8.20-13.83
Middle school	130 (9.12)	9.17	6.71-12.40
High school	55 (9.89)	13.99	7.62-24.29
College degree or above	84 (22.89)	21.26	13.55-31.73
Geographic region, No. (%)			
Rural	328 (8.77)	8.38	6.90-10.15
Urban	271 (12.63)	13.55	10.95-16.64
GDP per capita, No. (%)			
Low	203 (9.60)	10.69	8.20-13.83
Middle	232 (11.84)	11.54	10.09-13.16
High	164 (9.04)	9.83	7.44-12.88
Region, No. (%)			
East	244 (9.74)	10.56	8.68-12.81
North	98 (12.58)	12.18	8.63-16.92
North-East	42 (10.40)	12.24	9.11-16.25
North-West	29 (12.95)	13.75	9.92-18.75
South-Central	91 (9.34)	9.76	6.47-14.45
South-West	95 (9.49)	9.53	6.24-14.31

<sup>\*</sup>, Education levels values of 48 cases was missed.

Table 3 The adjusted odds ratio (OR) for the prevalence of LUTS/BPH

Characteristic	Crude OR (95 % CI)	Adjusted OR (95 % CI)	P value
Age group, No. (%)			<0.001
50-59	1.00 (reference)	1.00 (reference)	
60-69	1.29 (0.98-1.71)	1.50 (1.20-1.87)	0.001
≥70	1.87 (1.31-2.69)	2.09 (1.58-2.78)	<0.001
Marital status, No. (%)			
Married	1.00 (reference)	1.00 (reference)	
Unmarried/Separated /Widowed	0.90(0.59-1.38)	0.91 (0.63-1.30)	0.597
Education levels, No. (%)			0.001
No formal education	1.00 (reference)	1.00 (reference)	
Elementary school	1.34 (0.95-1.88)	1.36 (0.97-1.91)	0.074
Middle school	1.12 (0.79-1.61)	1.30 (0.93-1.82)	0.120
High school	1.82 (0.84-3.92)	2.27 (1.03-4.99)	0.043
College degree or above	3.02 (1.67-5.43)	2.67 (1.57-4.54)	0.000
Geographic region, No. (%)			
Rural	1.00 (reference)	1.00 (reference)	
Urban	1.71 (1.24-2.36)	1.50 (1.71-1.92)	0.002
GDP per capita, No. (%)			0.156
Low	1.00 (reference)	1.00 (reference)	
Middle	1.08(0.77-1.53)	1.23 (0.94-1.62)	0.130
High	0.91(0.58-1.42)	0.99 (0.69-1.42)	0.958
Region, No. (%)			0.200
East	1.00 (reference)	1.00 (reference)	
North	1.17 (0.74-1.84)	1.12 (0.75-1.67)	0.578
North-East	1.18 (0.77-1.79)	1.03 (0.76-1.39)	0.844
North-West	1.35 (0.86-2.11)	1.66 (1.12-2.47)	0.012
South-Central	0.91 (0.55-1.51)	0.90 (0.53-1.55)	0.696
South-West	0.89 (0.53-1.50)	1.01 (0.66-1.53)	0.970

# The prevalence of clinical BPH in China in 2011

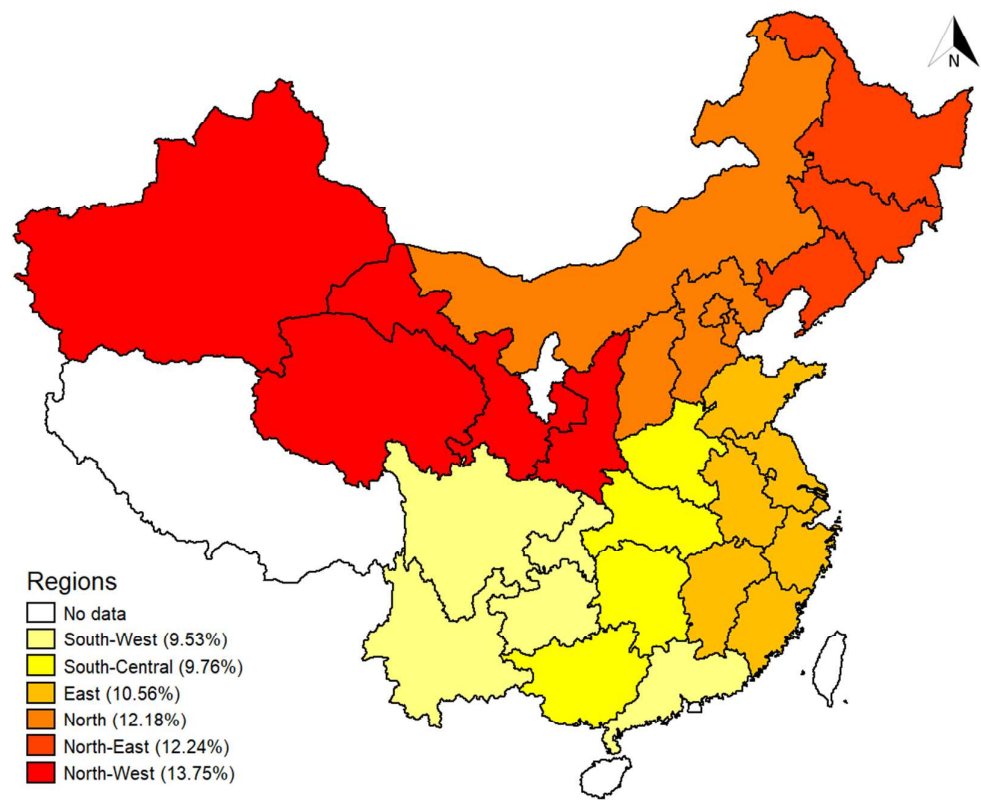


Figure 1 The prevalence of each region

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The prevalence of clinical BPH in China in 2011

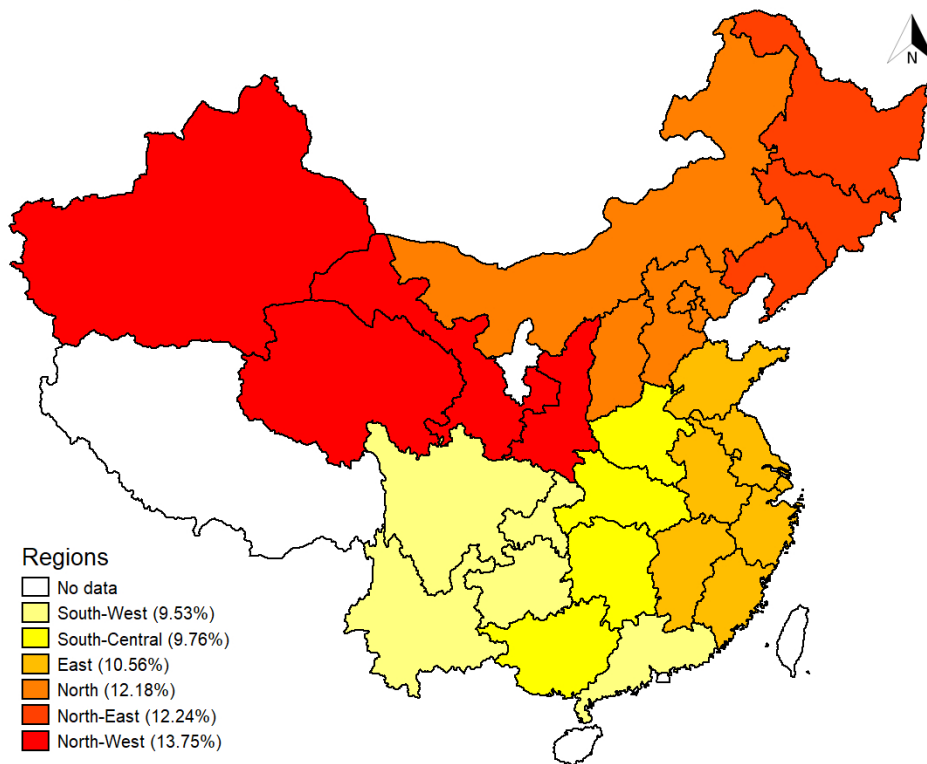


Figure 1. The prevalence of LUTS/BPH in each regions

403x331mm (72 x 72 DPI)



# BMJ Open

## The prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022792.R2
Article Type:	Research
Date Submitted by the Author:	27-Nov-2018
Complete List of Authors:	Zhang, Weiyu; Peking University People's Hospital Zhang, Xiaopeng; Peking University People's Hospital, Urology Li, Haibin; Capital Medical University, Epidemiology and Health Statistics Wu, Feng; Institute for Disease Control and Prevention, Chinese PLA Wang, Huanrui; Peking University People's Hospital Zhao, Meishan; Capital Medical University Affiliated Beijing Friendship Hospital Hu, Hao; Peking University People's Hospital, Urology Xu, Kexin; Peking University People's Hospital
<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health, Urology
Keywords:	LUTS/BPH, Epidemiology < TROPICAL MEDICINE, China

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Manuscripts

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4 **The prevalence of lower urinary tract symptoms suggestive of benign prostatic**  
5 **hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement**  
6 **Longitudinal Study**  
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11 **The prevalence of LUTS/BPH in China**  
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## ABSTRACT

**Objective.** Rapid population aging in China is increasing the prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) among older people. The associated economic burdens are increasing as well. Relevant data from China is currently insufficient.

**Design.** Secondary analysis of a cohort sample.

**Setting.** A nationally representative cross-sectional survey—the China Health and Retirement Longitudinal Study (CHARLS) was conducted in 2011 in mainland China.

**Participants.** Individuals in the community selected from the CHARLS by multistage probability sampling. A total of 5888 participants aged 50 years and above were included.

**Outcome measures.** Self-reported morbid state was derived from a structured questionnaire. The weighted-prevalence of LUTS/BPH was estimated and stratified by age group, marital status, education levels, economic levels, residential areas and geographic regions. Multivariable weighted logistic regression was used to examine the association of socioeconomic status with the odds of BPH.

**Results.** The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval [CI], 9.36-12.12). Among individuals age over 70 years, the prevalence was 14.67% (95% CI, 11.80-18.09), and it increased with aging ( $P < 0.05$ ). The prevalence of LUTS/BPH among subjects residing the urban areas was higher [13.55% (95% CI, 10.95-16.64)] than those living in rural areas [8.38% (95% CI, 6.90-10.15)]. The prevalence of LUTS/BPH was lowest in the South-Central and South-West and highest the North-West region.

**Conclusions.** We found an increasing trend of prevalence of LUTS/BPH with aging. It varied according to marital status, socioeconomic status and geographic region.

**Keywords** LUTS/BPH; epidemiology; China

### Strengths and limitations

- Our data is based on the CHARLS, a strict national population survey.
- Prevalence of LUTS/BPH in China is difficult to estimate, not only because of the large population but also because of the diagnostic criteria.
- The CHARLS did not collect weights and heights, so we could not analyze the relationship of BMI and obesity with prevalence of LUTS/BPH.

For peer review only

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4 Benign prostatic hyperplasia (BPH) is a common disease of men, representing a  
5 substantial disease burden. BPH is characterized by a proliferation of both stromal  
6 and epithelial cells of the prostate in the transitional zone surrounding the urethra  
7 (1). Approximately 50% of men >50 years of age have pathological evidence of BPH,  
8 increasing to >80% as men reach their eighth decade of life and older (2). When men  
9 reach 80 years, this number increases to 83% (3). As the world population aged, the  
10 incidence and prevalence of BPH have rapidly increased (4). Lower urinary tract  
11 symptoms (LUTS) have been specified by the standardization subcommittee of the  
12 International Continence Society (ICS) in February 2002: "LUTS are the subjective  
13 indicators of a disease or change in conditions as perceived by the patients, carer or  
14 partners and may lead him/her to seek help from health care professionals.  
15 Symptoms may either be volunteered or described during the patient interview.  
16 They are usually qualitative" (5). However, in 2006, Chapple and Roehrborn  
17 emphasized that the presence of LUTS does not need to be associated with prostatic  
18 pathology only (6). Therefore, LUTS/BPH in our study referred to symptomatic BPH.  
19 Although it is not life-threatening, LUTS/BPH is associated with serious morbidities  
20 and decreases quality of life (7,8). In America, LUTS/BPH affects more than 20% of  
21 American men aged 30 to 79 years, or roughly 15 million men (9,10). The prevalence  
22 of BPH in China is currently determined from autopsy data and a few studies based  
23 on the general population that cannot accurately reflect the current status of the  
24 disease (11). No study has been conducted for LUTS/BPH in China. Therefore, there  
25 is a paucity of data regarding prevalence of LUTS/BPH and its potential risk factors  
26 among the elderly in China.  
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50 China has a population of 1.3 billion, 25.3% aged 50 years or older and 13.26% aged  
51 more than 60 years (12). The aging of the general population means that elderly  
52 people now account for a much greater proportion of patients with BPH. Many  
53 modifiable risk factors play roles in pathogenesis of BPH, including sex steroid  
54 hormones, the metabolic syndrome cardiovascular disease, obesity, diabetes, diet,  
55 physical activity and inflammation. These risk factors cause a large variation of  
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4 prevalence of LUTS/BPH in various regions of China. Epidemiological studies  
5 comparing prevalence of LUTS/BPH according to age, socioeconomic status and  
6 geographic region by the same research method will provide reliable estimates on  
7 the understanding of potential risk factors of LUTS/BPH and help design health care  
8 plans.  
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13 Using data collected from the China Health and Retirement Longitudinal Study  
14 (CHARLS), a national random sample of the Chinese population (13), we estimated  
15 the prevalence of LUTS/BPH among residents aged 50 years or older in China  
16 according to age, marital status, education levels, geographic region and  
17 socioeconomic status.  
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23 The project team filed an ethics review application to Ethical Review Committee  
24 (IRB) at Peking University in June 2008 and obtained approval.  
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## 27 28 29 METHODS

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33 The CHARLS is a survey of the elderly in China, based on a sample of households with  
34 members middle-aged and elderly and their spouses. Individuals aged 50 years and  
35 above were included in this study. Data on social-economic and health status were  
36 collected using standardized questionnaire (13). The baseline survey was conducted  
37 in 2011–2012 covering 450 villages/urban communities in 28 provinces. Eligible  
38 individuals were selected through four-stage, stratified cluster sampling.  
39 Probabilities proportional to size (PPS) sampling were used in the determination of  
40 sample size. Detailed descriptions were provided in a previous publication (14).  
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### 50 51 Definitions of LUTS/BPH

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53 BPH is a term reserved for the typical histological pattern that defines the disease.  
54 However, many men with histological BPH never seek medical care, nor do they  
55 require treatment for it. The condition proceeds differently when it is associated  
56 with LUTS. Individuals with histologic BPH visit a doctor only when LUTS occurs.  
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59 Residents who participated in CHARLS were asked whether they have ever been  
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4 diagnosed with a prostate illness (excluding prostatic cancer). We defined him as a  
5 subject with LUTS/BPH if he responded positively to this question.  
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#### 8 9 Data collection and grouping

10 The households were selected randomly and age-eligibly. All participants had a  
11 face-to-face household-interview using a structured questionnaire. Information  
12 collected during the household-interview included demographic factors,  
13 socioeconomic status and medical history. The statistical analysis results will not  
14 disseminate to study participants in short time.  
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23 Subjects were grouped into 3 strata according to age: 50-59, 60-69 and  $\geq 70$  years  
24 old. The marital status was divided into married and unmarried/separated/widowed.  
25 Education level was divided into 5 categories: no formal education, elementary  
26 school, middle school, high school and college degree or above. Geographic region  
27 was divided into rural and urban. The economic level were defined according to the  
28 tertile of GDP. We categorized their living localities into six regions, i.e., East (7  
29 provinces: Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Anhui, Jiangxi), North (2  
30 cities: Beijing and Tianjin and 3 provinces: Hebei, Shanxi and Inner Mongolia),  
31 North-East (3 provinces: Liaoning, Jilin and Heilongjiang), North-West (4 provinces:  
32 Shaanxi, Gansu, Qinghai and Xinjiang), South-Central (5 provinces: Henan, Hubei,  
33 Hunan, Guangdong and Guangxi) and South-West (1 city: Chongqing and 3  
34 provinces: Sichuan, Guizhou and Yunnan). Individuals living in Hainan, Ningxia,  
35 Taiwan and Tibet were not selected in this survey.  
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#### 50 Patient and Public Involvement

51 Patients and/or public were not involved in the design or conduct of this study.  
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#### 56 Statistical analyses

57 We used Stata to calculate the overall and age-specific prevalence of LUTS/BPH  
58 according to strata for each factor. The svy: logistic procedure in Stata version 14.2  
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4 was used to examine the association between each risk factor and the prevalence of  
5 BPH, adjusting for other potential confounders including gender, age, area,  
6 education, GDP per capita, and region. Both procedures considered the complex  
7 survey design and the non-response rate for the CHARLS survey when estimating the  
8 prevalence, prevalence odds ratio (OR), and corresponding standard errors.  
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## 13 14 15 RESULTS

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19 A total of 5,888 participants were involved in our study and the characteristics of the  
20 baseline population are given in Table 1. Five hundred and ninety-nine responded  
21 positively. Mean age was 62.78 (standard deviation: 8.56). Most of the participants  
22 were married. About a quarter of the participants did not receive formal education  
23 and half of the rest received elementary or middle school education. The majority of  
24 the respondent participants lived in rural areas. About one third of respondents  
25 were classified in three levels of GDP per capita.  
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35 The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval  
36 [CI]: 9.36, 12.12). The weighted results are listed in Table 2.  
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### 41 Age

42 Aging men were more likely to be diagnosed with LUTS/BPH, and the weighted  
43 prevalence of LUTS/BPH increased with age. Compared with subjects age <60 years,  
44 the adjusted odds ratios (OR) for the prevalence of LUTS/BPH were 1.50 (95% CI:  
45 1.20, 1.87) for those age 60-69 years and 2.09 (95% CI: 1.58, 2.78) for those aged  $\geq$   
46 70 years (Table 3).  
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### 54 Marital status

55 The prevalence of LUTS/BPH was slightly higher among married individuals, at  
56 10.80% (95% CI: 9.61, 12.12) while the prevalence among  
57 unmarried/separated/widowed individuals was 9.87% (95% CI: 6.56, 14.60). The  
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4 odds of LUTS/BPH in unmarried/separated/widowed individuals was approximately  
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6 0.91 times that of married individuals.  
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#### 9 10 Education and economic levels

11 There was variation in the prevalence of LUTS/BPH among various education and  
12  
13 economic levels. Prevalence was higher among individuals with more years of  
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15 education and it was highest among individuals with college degrees or above ( $P <$   
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17 0.05). The prevalence of LUTS/BPH was lower among individuals with a low GDP per  
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19 capita.  
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#### 22 23 Resident areas and regions

24 The prevalence of LUTS/BPH was higher among subjects residing in urban areas  
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26 (rural: 8.38% [95% CI: 6.90, 10.15]; urban: 13.55% [95% CI: 10.95, 16.64]). The odds  
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28 of LUTS/BPH in urban residents was 1.5 times that of rural residents. There was a  
29  
30 significant difference in the prevalence of LUTS/BPH according to geographic  
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32 location. The South-Central and South-West had the lowest prevalence of LUTS/BPH  
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34 (9.76% and 9.53%, respectively), followed by the East (10.56%), North (12.18%) and  
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36 North-East (12.24%) regions; prevalence was highest among respondents living in  
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38 the North-West region (13.75%). Compared with the East region, the ORs for  
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40 LUTS/BPH for the North, North-East, North-West, South-Central, South-West regions  
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42 were 1.12 (95% CI: 0.75, 1.67), 1.03 (95% CI: 0.76, 1.39), 1.66 (95% CI: 1.12, 2.47),  
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44 0.90 (95% CI: 0.53, 1.55) and 1.01 (95% CI: 0.66, 1.53), respectively, after adjustment  
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46 for age, marital status, rural/urban area, education and GDP per capita (Table 3). The  
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48 prevalence of each region can be seen in Figure 1.  
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#### 51 52 DISCUSSION

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56 The CHARLS set up a high quality, nationally representative, publicly available  
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58 micro-database, providing a wide range of information regarding the households of  
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60 the elderly as well as individual information on the elderly respondents and their

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4 spouses. Our research is based on data from the CHARLS. It was known from our  
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6 study that LUTS/BPH was common among Chinese men age over 50 years. Age had  
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8 great influence on prevalence of LUTS/BPH according to ours and other studies (15).  
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11 Rapid population aging in China is increasing the prevalence of LUTS/BPH among  
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13 older people and so does the economic burdens associated with it. In our study,  
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15 adjusted prevalence of LUTS/BPH among men aged beyond 50 years reached 10.66%  
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17 (95% CI: 9.36, 12.12), which could influence their life quality and impose economic  
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19 burdens on both individuals and society. The cost of intervention and treatment of  
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21 BPH is comprised of direct costs (drugs, procedures, imaging, office visits), indirect  
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23 costs (lost earnings) and intangible costs (pain and suffering) (16). It is likely that the  
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25 costs for LUTS/BPH will continuously increase in the future. Therefore, a prevalence  
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27 study on LUTS/BPH can help guide public health policy.  
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31 As definition of BPH varies, the prevalence varies (17). When responding positively  
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33 to a question regarding diagnosis of a benign prostate illness, an individual means  
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35 that some symptoms of LUTS occurred in him, and that he sought for medical care  
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37 and was diagnosed with a benign prostate illness. Benign prostate illness primarily  
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39 refers to prostatitis and BPH, which shared many overlapping symptoms. Prostatitis  
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41 without BPH is a diagnosis of young men, however, inflammation in the prostate is  
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43 also observed in elderly men presenting with BPH. Gandaglia et al. (18) suggested  
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45 that histological prostatitis affected the progression of BPH because of the  
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47 inflammatory process. Inflammation is a modifiable risk factor in BPH pathogenesis  
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49 (15). Patients presenting with BPH may have a component of category IV,  
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51 asymptomatic prostatitis (19). Thus, in our study, individuals over age 50 who  
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53 responded positively to the question regarding diagnosis with a benign prostate  
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55 illness were counted as having LUTS/BPH.  
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59 BPH increases with age, as has been confirmed by numerous studies. Loeb et al. (20)  
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enrolled 278 men from the Baltimore Longitudinal Study of Aging and reported that

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3 the median rate of volume change was 0.6 cc per year (range -9.9 to 62.1),  
4 corresponding to a median growth rate of 2.5% per year (range -29.2% to 176.4%).  
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6 The study was based on autopsy. Although prostate volume is not related to LUTS  
7 severity directly, it is a risk factor. Roehrborn et al. (21) reported that larger prostate  
8 was associated with increased risks of urinary retention, increased future need for  
9 surgery and clinical progression of BPH. Another study, after follow-up for 16 years,  
10 reported significantly increased incidence and progression of LUTS in men with age  
11 (22). In our study, LUTS/BPH involved symptoms of LUTS and histological BPH.  
12  
13 Individuals aged 60-69 years and  $\geq 70$  years had a higher prevalence of LUTS/BPH,  
14 and the adjusted ORs were 1.5 (95% CI: 1.20, 1.87) and 2.09 (95% CI: 1.58, 2.78)  
15 respectively, compared with subjects age <60 years ( $p < 0.05$ ).  
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27 Studies of sex steroid hormones and BPH revealed that androstane diols play a role in  
28 BPH development (23). Unmarried/separated/widowed individuals accounted  
29 13.20% in all the respondent participants, having a lower adjusted prevalence of  
30 LUTS/BPH at 9.87% (95% CI: 6.56, 14.60). These people are usually thought have no  
31 or less sexual life compared with married men. Married men more often intended to  
32 visit doctor in case of their illness would have a negative impact on their spouse and  
33 family.  
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43 In several studies, socioeconomic status played an important role in progression of  
44 LUTS/BPH and might vary the results, particularly the prevalence and effects of  
45 LUTS/BPH (24). For example, some researchers found higher rates of BPH in upper  
46 income groups, but this may due to selection bias, because of higher utilization of  
47 medical care (25,26). Using data from the Korean Community Health Survey  
48 performed in 2011, Jo KJ et al. found that the severity of LUTS was associated with  
49 several socioeconomic factors, including education level, income level and living  
50 environment (27). Fowke et al. found that college education or higher levels was  
51 associated with a lower IPSS score (28). Education levels were obtained when people  
52 were young, and did not change with aging. Nevertheless, education influenced the  
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4 understanding of disease and the decision-making progress. In our study, we  
5 analyzed socioeconomic factors including GDP per capita, education levels and  
6 geographic region. Individuals with education of college degree or above had a high  
7 adjusted OR of LUTS/BPH at 2.67 (95% CI: 1.57, 4.54) ( $P<0.001$ ), compared to  
8 individuals with no formal education. Individuals residing in urban areas were 1.5  
9 times more likely to have the diagnosis than those in rural areas. We believe that  
10 there was inevitable selection bias, as residents living in urban areas may seek  
11 medical care more often than do those in rural areas. Some individuals lack the  
12 recognition of BPH and hospital visitation is often delayed.  
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23 We demonstrated an apparent geographic variation in the prevalence of LUTS/BPH  
24 in China. Residents in the South-West regions had a much lower prevalence of  
25 LUTS/BPH than did those living in the North-West regions of China. Individuals  
26 residing in the north regions, including North, North-East and North-West, had a  
27 relatively higher prevalence of LUTS/BPH than did those living in South-Central and  
28 South-West. Dietary differences may contribute to this discrepancy. Daily diet of  
29 individuals living in north regions contain much milk, dairy products and red meat,  
30 while individuals living in south regions consume more fruits and vegetables than do  
31 those in the north, which have both been confirmed to increase the risk of LUTS/BPH  
32 (29,30). Nevertheless, residents in East region did not show a high prevalence of  
33 LUTS/BPH. It was thought that socioeconomic development in the East region was, in  
34 general, higher than that of other regions, possibly contributing to the lower  
35 prevalence of LUTS/BPH. Furthermore, the genetic susceptibility of BPH was also a  
36 factor influencing the prevalence of LUTS/BPH in China. Several studies from China  
37 reported genetics associated with developing BPH (30), possibly one of the factors  
38 causing varying prevalence of LUTS/BPH in China.  
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56 Our research has several strengths. First, our data was based on the CHARLS, a  
57 national population survey. The interviewers were highly-trained and questionnaires  
58 were developed after a long and rigorous course. The participants were chosen via  
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4 strict multistage probability sampling procedures. Hence, data from the CHARLS can  
5 represent the national condition. Second, the prevalence of LUTS/BPH in China is  
6 difficult to estimate, not only because of the large population but also because of the  
7 diagnostic criteria. Using data from the CHARLS, we avoided both questions.  
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13 There are some limitations as well. First, the CHARLS did not collect weight and  
14 height, so we could not analyze the relationship of BMI or obesity and prevalence of  
15 LUTS/BPH. Second, testicular androgens are required in the prostate for the  
16 development of BPH. Third, as China is a large country, and we all adhere to the  
17 principles of diagnosis from the China Urology Association (CUA), the diagnosis of  
18 LUTS/BPH may be slightly different among regions. We cannot detect these  
19 differences, since the data of CHARLS provides an established diagnosis.  
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29 In this study, we looked at the prevalence of LUTS/BPH via CHARLS data. We found  
30 that the LUTS/BPH is highly prevalent in older, urban-living men. The prevalence  
31 varied according to marital status, socioeconomic status and geographic regions.  
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#### 37 Funding statement

38 This research received no specific grant from any funding agency in the public,  
39 commercial or not-for-profit sectors.  
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#### 44 Competing interest statement

45 None declared.  
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#### 50 Author statement

51 Weiyu Zhang, Xiaopeng Zhang: Designed the study and drafted the article  
52  
53

54 Haibin Li, Feng Wu: Dealt with the statistics  
55

56 Huanrui Wang, Meishan Zhao: Help with data sorting, literature retrieve, language  
57 polish and other chores  
58  
59

60 Hao Hu, Kexin Xu: Constructive revision and grasp of the overall situation

## Acknowledgements

The authors are full of gratitude to the office of CHARLS for sharing the data. The data can be accessed at the official website.

## Data sharing statement

No additional unpublished data are available.

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Table 1 The baseline of population

Characteristic	Men (n=5888)
Age, mean (SD)	62.78 (8.56)
Age group, No. (%)	
50-59	2356 (40.01)
60-69	2250 (38.21)
≥70	1282 (21.77)
Marital status, No. (%)	
Married	5111 (86.80)
Unmarried/Separated /Widowed	777 (13.20)
Education levels, No. (%)	
No formal education	1918 (32.84)
Elementary school	1573 (26.93)
Middle school	1426 (24.42)
High school	556 (9.52)
College degree or above	367 (6.28)
Geographic region, No. (%)	
Rural	3742 (63.55)
Urban	2146 (36.45)
GDP per capita, No. (%)	
Low	2114 (35.90)
Middle	1960 (33.29)
High	1814 (30.81)
Region, No. (%)	
East	2506 (42.56)
North	779 (13.23)
North-East	404 (6.86)
North-West	224 (3.80)
South-Central	974 (16.54)
South-West	1001 (17.00)

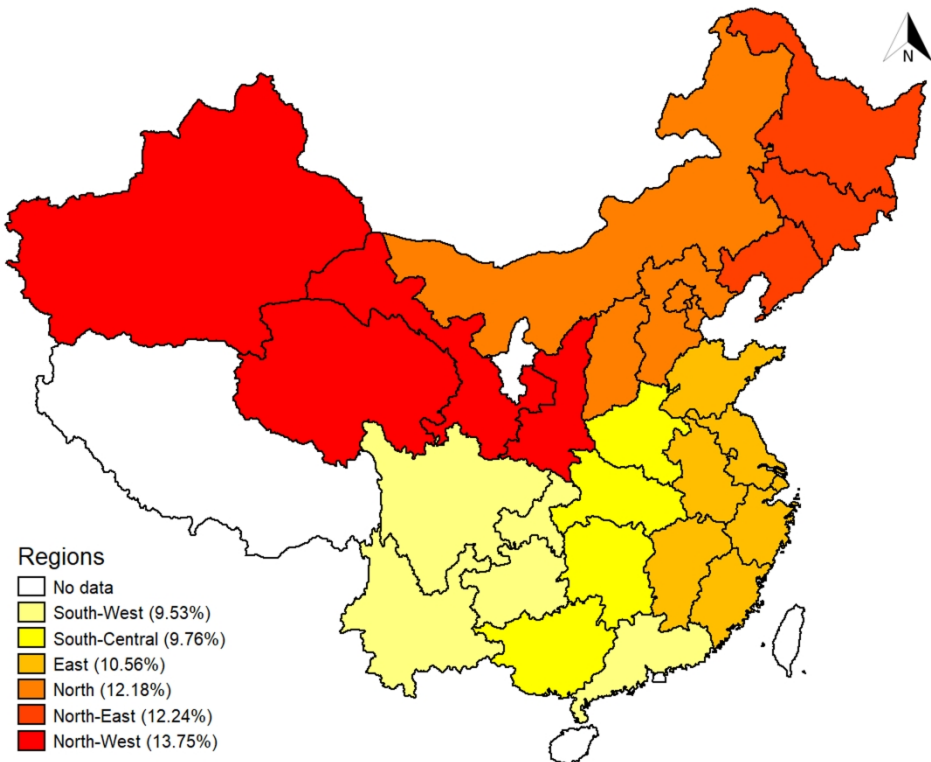
Table 2 The weighted prevalence

Characteristic	Case, No. (%)	Prevalence (%)	95% CI
Total	599 (10.17)	10.66	9.36-12.12
Age group, No. (%)			
50-59	182 (7.72)	8.39	7.01-9.98
60-69	236 (10.49)	10.61	8.67-12.91
≥70	181 (14.12)	14.67	11.80-18.09
Marital status, No. (%)			
Married	522 (10.21)	10.80	9.61-12.12
Unmarried/Separated /Widowed	77 (9.91)	9.87	6.56-14.60
Education levels, No. (%)			
No formal education	162 (8.45)	8.20	6.54-10.23
Elementary school	166 (10.55)	10.69	8.20-13.83
Middle school	130 (9.12)	9.17	6.71-12.40
High school	55 (9.89)	13.99	7.62-24.29
College degree or above	84 (22.89)	21.26	13.55-31.73
Geographic region, No. (%)			
Rural	328 (8.77)	8.38	6.90-10.15
Urban	271 (12.63)	13.55	10.95-16.64
GDP per capita, No. (%)			
Low	203 (9.60)	10.69	8.20-13.83
Middle	232 (11.84)	11.54	10.09-13.16
High	164 (9.04)	9.83	7.44-12.88
Region, No. (%)			
East	244 (9.74)	10.56	8.68-12.81
North	98 (12.58)	12.18	8.63-16.92
North-East	42 (10.40)	12.24	9.11-16.25
North-West	29 (12.95)	13.75	9.92-18.75
South-Central	91 (9.34)	9.76	6.47-14.45
South-West	95 (9.49)	9.53	6.24-14.31

Table 3 The adjusted odds ratio (OR) for the prevalence of LUTS/BPH

Characteristic	Crude OR (95 % CI)	Adjusted OR (95 % CI)	P value
Age group, No. (%)			
50-59	1.00 (reference)	1.00 (reference)	
60-69	1.29 (0.98-1.71)	1.50 (1.20-1.87)	0.001
≥70	1.87 (1.31-2.69)	2.09 (1.58-2.78)	0.000
Marital status, No. (%)			
Married	1.00 (reference)	1.00 (reference)	
Unmarried/Separated /Widowed	0.90(0.59-1.38)	0.91 (0.63-1.30)	0.597
Education levels, No. (%)			
No formal education	1.00 (reference)	1.00 (reference)	
Elementary school	1.34 (0.95-1.88)	1.36 (0.97-1.91)	0.074
Middle school	1.12 (0.79-1.61)	1.30 (0.93-1.82)	0.120
High school	1.82 (0.84-3.92)	2.27 (1.03-4.99)	0.043
College degree or above	3.02 (1.67-5.43)	2.67 (1.57-4.54)	0.000
Geographic region, No. (%)			
Rural	1.00 (reference)	1.00 (reference)	
Urban	1.71 (1.24-2.36)	1.50 (1.71-1.92)	0.002
GDP per capita, No. (%)			
Low	1.00 (reference)	1.00 (reference)	
Middle	1.08(0.77-1.53)	1.23 (0.94-1.62)	0.130
High	0.91(0.58-1.42)	0.99 (0.69-1.42)	0.958
Region, No. (%)			
East	1.00 (reference)	1.00 (reference)	
North	1.17 (0.74-1.84)	1.12 (0.75-1.67)	0.578
North-East	1.18 (0.77-1.79)	1.03 (0.76-1.39)	0.844
North-West	1.35 (0.86-2.11)	1.66 (1.12-2.47)	0.012
South-Central	0.91 (0.55-1.51)	0.90 (0.53-1.55)	0.696
South-West	0.89 (0.53-1.50)	1.01 (0.66-1.53)	0.970

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The prevalence of LUTS/BPH in each regions

# BMJ Open

## The prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022792.R3
Article Type:	Research
Date Submitted by the Author:	07-Mar-2019
Complete List of Authors:	Zhang, Weiyu; Peking University People's Hospital Zhang, Xiaopeng; Peking University People's Hospital, Urology Li, Haibin; Capital Medical University, Epidemiology and Health Statistics Wu, Feng; Institute for Disease Control and Prevention PLA Wang, Huanrui; Peking University People's Hospital Zhao, Meishan; Capital Medical University Affiliated Beijing Friendship Hospital Hu, Hao; Peking University People's Hospital, Urology Xu, Kexin; Peking University People's Hospital
<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health, Urology
Keywords:	LUTS/BPH, Epidemiology < TROPICAL MEDICINE, China

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**The prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) in China: results from the China Health and Retirement Longitudinal Study**

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## ABSTRACT

**Objective.** Rapid population aging in China is increasing the prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) among older people. The associated economic burdens are increasing as well. Relevant data from China is currently insufficient.

**Design.** Secondary analysis of a cohort sample.

**Setting.** A nationally representative cross-sectional survey—the China Health and Retirement Longitudinal Study (CHARLS) was conducted in 2011 in mainland China.

**Participants.** Individuals in the community selected from the CHARLS by multistage probability sampling. A total of 5888 participants aged 50 years and above were included.

**Outcome measures.** Self-reported morbid state was derived from a structured questionnaire. The weighted-prevalence of LUTS/BPH was estimated and stratified by age group, marital status, education levels, economic levels, residential areas and geographic regions. Multivariable weighted logistic regression was used to examine the association of socioeconomic status with the odds of BPH.

**Results.** The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval [CI], 9.36-12.12). Among individuals age over 70 years, the prevalence was 14.67% (95% CI, 11.80-18.09), and it increased with aging ( $P < 0.05$ ). The prevalence of LUTS/BPH among subjects residing the urban areas was higher [13.55% (95% CI, 10.95-16.64)] than those living in rural areas [8.38% (95% CI, 6.90-10.15)]. The prevalence of LUTS/BPH was lowest in the South-Central and South-West and highest the North-West region.

**Conclusions.** We found an increasing trend of prevalence of LUTS/BPH with aging. It varied according to marital status, socioeconomic status and geographic region.

**Keywords** LUTS/BPH; epidemiology; China

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### Strengths and limitations

- Our data is based on the CHARLS, a strict national population survey.
- Prevalence of LUTS/BPH in China is difficult to estimate, not only because of the large population but also because of the diagnostic criteria.
- The CHARLS did not collect weights and heights, so we could not analyze the relationship of BMI and obesity with prevalence of LUTS/BPH.

For peer review only



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4 Benign prostatic hyperplasia (BPH) is a common disease of men, representing a  
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6 substantial disease burden. BPH is characterized by a proliferation of both stromal  
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8 and epithelial cells of the prostate in the transitional zone surrounding the urethra  
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10 (1). Approximately 50% of men >50 years of age have pathological evidence of BPH,  
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12 increasing to >80% as men reach their eighth decade of life and older (2). When men  
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14 reach 80 years, this number increases to 83% (3). As the world population aged, the  
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16 incidence and prevalence of BPH have rapidly increased (4). Lower urinary tract  
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18 symptoms (LUTS) have been specified by the standardization subcommittee of the  
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20 International Continence Society (ICS) in February 2002: "LUTS are the subjective  
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22 indicators of a disease or change in conditions as perceived by the patients, carer or  
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24 partners and may lead him/her to seek help from health care professionals.  
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26 Symptoms may either be volunteered or described during the patient interview.  
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28 They are usually qualitative" (5). However, in 2006, Chapple and Roehrborn  
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30 emphasized that the presence of LUTS does not need to be associated with prostatic  
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32 pathology only (6). Therefore, LUTS/BPH in our study referred to symptomatic BPH.  
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34 Although it is not life-threatening, LUTS/BPH is associated with serious morbidities  
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36 and decreases quality of life (7,8). In America, LUTS/BPH affects more than 20% of  
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38 American men aged 30 to 79 years, or roughly 15 million men (9,10). The prevalence  
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40 of BPH in China is currently determined from autopsy data and a few studies based  
41  
42 on the general population that cannot accurately reflect the current status of the  
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44 disease (11). No study has been conducted for LUTS/BPH in China. Therefore, there  
45  
46 is a paucity of data regarding prevalence of LUTS/BPH and its potential risk factors  
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48 among the elderly in China.

49  
50 China has a population of 1.3 billion, 25.3% aged 50 years or older and 13.26% aged  
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52 more than 60 years (12). The aging of the general population means that elderly  
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54 people now account for a much greater proportion of patients with BPH. Many  
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56 modifiable risk factors play roles in pathogenesis of BPH, including sex steroid  
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58 hormones, the metabolic syndrome cardiovascular disease, obesity, diabetes, diet,  
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60 physical activity and inflammation. These risk factors cause a large variation of

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4 prevalence of LUTS/BPH in various regions of China. Epidemiological studies  
5 comparing prevalence of LUTS/BPH according to age, socioeconomic status and  
6 geographic region by the same research method will provide reliable estimates on  
7 the understanding of potential risk factors of LUTS/BPH and help design health care  
8 plans.  
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13 Using data collected from the China Health and Retirement Longitudinal Study  
14 (CHARLS), a national random sample of the Chinese population (13), we estimated  
15 the prevalence of LUTS/BPH among residents aged 50 years or older in China  
16 according to age, marital status, education levels, geographic region and  
17 socioeconomic status.  
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23 The project team filed an ethics review application to Ethical Review Committee (IRB)  
24 at Peking University in June 2008 and obtained approval.  
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## 28 29 METHODS

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33 The CHARLS is a survey of the elderly in China, based on a sample of households with  
34 members middle-aged and elderly and their spouses. Individuals aged 50 years and  
35 above were included in this study. Data on social-economic and health status were  
36 collected using standardized questionnaire (13). The baseline survey was conducted  
37 in 2011–2012 covering 450 villages/urban communities in 28 provinces. Eligible  
38 individuals were selected through four-stage, stratified cluster sampling.  
39 Probabilities proportional to size (PPS) sampling were used in the determination of  
40 sample size. Detailed descriptions were provided in a previous publication (14).  
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### 50 51 Definitions of LUTS/BPH

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53 BPH is a term reserved for the typical histological pattern that defines the disease.  
54 However, many men with histological BPH never seek medical care, nor do they  
55 require treatment for it. The condition proceeds differently when it is associated  
56 with LUTS. Individuals with histologic BPH visit a doctor only when LUTS occurs.  
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60 Residents who participated in CHARLS were asked whether they have ever been

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4 diagnosed with a prostate illness (excluding prostatic cancer). We defined him as a  
5 subject with LUTS/BPH if he responded positively to this question.  
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#### 8 9 Data collection and grouping

10 The households were selected randomly and age-eligibly. All participants had a  
11 face-to-face household-interview using a structured questionnaire. Information  
12 collected during the household-interview included demographic factors,  
13 socioeconomic status and medical history. The statistical analysis results will not  
14 disseminate to study participants in short time.  
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23 Subjects were grouped into 3 strata according to age: 50-59, 60-69 and  $\geq 70$  years  
24 old. The marital status was divided into married and unmarried/separated/widowed.  
25 Education level was divided into 5 categories: no formal education, elementary  
26 school, middle school, high school and college degree or above. Geographic region  
27 was divided into rural and urban. The economic level were defined according to the  
28 tertile of GDP. We categorized their living localities into six regions, i.e., East (7  
29 provinces: Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Anhui, Jiangxi), North (2  
30 cities: Beijing and Tianjin and 3 provinces: Hebei, Shanxi and Inner Mongolia),  
31 North-East (3 provinces: Liaoning, Jilin and Heilongjiang), North-West (4 provinces:  
32 Shaanxi, Gansu, Qinghai and Xinjiang), South-Central (5 provinces: Henan, Hubei,  
33 Hunan, Guangdong and Guangxi) and South-West (1 city: Chongqing and 3 provinces:  
34 Sichuan, Guizhou and Yunnan). Individuals living in Hainan, Ningxia, Taiwan and Tibet  
35 were not selected in this survey.  
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#### 50 Patient and Public Involvement

51 Patients and/or public were not involved in the design or conduct of this study.  
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#### 56 Statistical analyses

57 We used Stata to calculate the overall and age-specific prevalence of LUTS/BPH  
58 according to strata for each factor. The svy: logistic procedure in Stata version 14.2  
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4 was used to examine the association between each risk factor and the prevalence of  
5 BPH, adjusting for other potential confounders including gender, age, area,  
6 education, GDP per capita, and region. Both procedures considered the complex  
7 survey design and the non-response rate for the CHARLS survey when estimating the  
8 prevalence, prevalence odds ratio (OR), and corresponding standard errors.  
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## 15 RESULTS

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19 A total of 5,888 participants were involved in our study and the characteristics of the  
20 baseline population are given in Table 1. Five hundred and ninety-nine responded  
21 positively. Mean age was 62.78 (standard deviation: 8.56). Most of the participants  
22 were married. About a quarter of the participants did not receive formal education  
23 and half of the rest received elementary or middle school education. The majority of  
24 the respondent participants lived in rural areas. About one third of respondents  
25 were classified in three levels of GDP per capita.  
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35 The weighted overall prevalence of LUTS/BPH was 10.66% (95% confidence interval  
36 [CI]: 9.36, 12.12). The weighted results are listed in Table 2.  
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### 41 Age

42 Aging men were more likely to be diagnosed with LUTS/BPH, and the weighted  
43 prevalence of LUTS/BPH increased with age. Compared with subjects age <60 years,  
44 the adjusted odds ratios (OR) for the prevalence of LUTS/BPH were 1.50 (95% CI:  
45 1.20, 1.87) for those age 60-69 years and 2.09 (95% CI: 1.58, 2.78) for those aged  $\geq$   
46 70 years (Table 3).  
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### 54 Marital status

55 The prevalence of LUTS/BPH was slightly higher among married individuals, at 10.80%  
56 (95% CI: 9.61, 12.12) while the prevalence among unmarried/separated/widowed  
57 individuals was 9.87% (95% CI: 6.56, 14.60). The odds of LUTS/BPH in  
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4 unmarried/separated/widowed individuals was approximately 0.91 times that of  
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6 married individuals.  
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#### 8 9 Education and economic levels

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11 There was variation in the prevalence of LUTS/BPH among various education and  
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13 economic levels. Prevalence was higher among individuals with more years of  
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15 education and it was highest among individuals with college degrees or above ( $P <$   
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17 0.05). The prevalence of LUTS/BPH was lower among individuals with a low GDP per  
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19 capita.  
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#### 22 23 Resident areas and regions

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25 The prevalence of LUTS/BPH was higher among subjects residing in urban areas  
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27 (rural: 8.38% [95% CI: 6.90, 10.15]; urban: 13.55% [95% CI: 10.95, 16.64]). The odds  
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29 of LUTS/BPH in urban residents was 1.5 times that of rural residents. There was a  
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31 significant difference in the prevalence of LUTS/BPH according to geographic  
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33 location. The South-Central and South-West had the lowest prevalence of LUTS/BPH  
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35 (9.76% and 9.53%, respectively), followed by the East (10.56%), North (12.18%) and  
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37 North-East (12.24%) regions; prevalence was highest among respondents living in  
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39 the North-West region (13.75%). Compared with the East region, the ORs for  
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41 LUTS/BPH for the North, North-East, North-West, South-Central, South-West regions  
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43 were 1.12 (95% CI: 0.75, 1.67), 1.03 (95% CI: 0.76, 1.39), 1.66 (95% CI: 1.12, 2.47),  
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45 0.90 (95% CI: 0.53, 1.55) and 1.01 (95% CI: 0.66, 1.53), respectively, after adjustment  
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47 for age, marital status, rural/urban area, education and GDP per capita (Table 3). The  
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49 prevalence of each region can be seen in Figure 1.  
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#### 51 52 DISCUSSION

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56 The CHARLS set up a high quality, nationally representative, publicly available  
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58 micro-database, providing a wide range of information regarding the households of  
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60 the elderly as well as individual information on the elderly respondents and their

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4 spouses. Our research is based on data from the CHARLS. It was known from our  
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6 study that LUTS/BPH was common among Chinese men age over 50 years. Age had  
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8 great influence on prevalence of LUTS/BPH according to ours and other studies (15).  
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11 Rapid population aging in China is increasing the prevalence of LUTS/BPH among  
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13 older people and so does the economic burdens associated with it. In our study,  
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15 adjusted prevalence of LUTS/BPH among men aged beyond 50 years reached 10.66%  
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17 (95% CI: 9.36, 12.12), which could influence their life quality and impose economic  
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19 burdens on both individuals and society. The cost of intervention and treatment of  
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21 BPH is comprised of direct costs (drugs, procedures, imaging, office visits), indirect  
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23 costs (lost earnings) and intangible costs (pain and suffering) (16). It is likely that the  
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25 costs for LUTS/BPH will continuously increase in the future. Therefore, a prevalence  
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27 study on LUTS/BPH can help guide public health policy.  
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31 As definition of BPH varies, the prevalence varies (17). When responding positively  
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33 to a question regarding diagnosis of a benign prostate illness, an individual means  
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35 that some symptoms of LUTS occurred in him, and that he sought for medical care  
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37 and was diagnosed with a benign prostate illness. Benign prostate illness primarily  
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39 refers to prostatitis and BPH, which shared many overlapping symptoms. Prostatitis  
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41 without BPH is a diagnosis of young men, however, inflammation in the prostate is  
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43 also observed in elderly men presenting with BPH. Gandaglia et al. (18) suggested  
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45 that histological prostatitis affected the progression of BPH because of the  
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47 inflammatory process. Inflammation is a modifiable risk factor in BPH pathogenesis  
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49 (15). Patients presenting with BPH may have a component of category IV,  
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51 asymptomatic prostatitis (19). Thus, in our study, individuals over age 50 who  
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53 responded positively to the question regarding diagnosis with a benign prostate  
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55 illness were counted as having LUTS/BPH.  
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59 BPH increases with age, as has been confirmed by numerous studies. Loeb et al. (20)  
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enrolled 278 men from the Baltimore Longitudinal Study of Aging and reported that

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3 the median rate of volume change was 0.6 cc per year (range -9.9 to 62.1),  
4 corresponding to a median growth rate of 2.5% per year (range -29.2% to 176.4%).  
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6 The study was based on autopsy. Although prostate volume is not related to LUTS  
7 severity directly, it is a risk factor. Roehrborn et al. (21) reported that larger prostate  
8 was associated with increased risks of urinary retention, increased future need for  
9 surgery and clinical progression of BPH. Another study, after follow-up for 16 years,  
10 reported significantly increased incidence and progression of LUTS in men with age  
11 (22). In our study, LUTS/BPH involved symptoms of LUTS and histological BPH.  
12  
13 Individuals aged 60-69 years and  $\geq 70$  years had a higher prevalence of LUTS/BPH,  
14 and the adjusted ORs were 1.5 (95% CI: 1.20, 1.87) and 2.09 (95% CI: 1.58, 2.78)  
15 respectively, compared with subjects age <60 years ( $p < 0.05$ ).  
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27 Studies of sex steroid hormones and BPH revealed that androstane diols play a role in  
28 BPH development (23). Unmarried/separated/widowed individuals accounted 13.20%  
29 in all the respondent participants, having a lower adjusted prevalence of LUTS/BPH  
30 at 9.87% (95% CI: 6.56, 14.60). These people are usually thought have no or less  
31 sexual life compared with married men. Married men more often intended to visit  
32 doctor in case of their illness would have a negative impact on their spouse and  
33 family.  
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43 In several studies, socioeconomic status played an important role in progression of  
44 LUTS/BPH and might vary the results, particularly the prevalence and effects of  
45 LUTS/BPH (24). For example, some researchers found higher rates of BPH in upper  
46 income groups, but this may due to selection bias, because of higher utilization of  
47 medical care (25,26). Using data from the Korean Community Health Survey  
48 performed in 2011, Jo KJ et al. found that the severity of LUTS was associated with  
49 several socioeconomic factors, including education level, income level and living  
50 environment (27). Fowke et al. found that college education or higher levels was  
51 associated with a lower IPSS score (28). Education levels were obtained when people  
52 were young, and did not change with aging. Nevertheless, education influenced the  
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4 understanding of disease and the decision-making progress. In our study, we  
5 analyzed socioeconomic factors including GDP per capita, education levels and  
6 geographic region. Individuals with education of college degree or above had a high  
7 adjusted OR of LUTS/BPH at 2.67 (95% CI: 1.57, 4.54) ( $P<0.001$ ), compared to  
8 individuals with no formal education. Individuals residing in urban areas were 1.5  
9 times more likely to have the diagnosis than those in rural areas. We believe that  
10 there was inevitable selection bias, as residents living in urban areas may seek  
11 medical care more often than do those in rural areas. Some individuals lack the  
12 recognition of BPH and hospital visitation is often delayed.  
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23 We demonstrated an apparent geographic variation in the prevalence of LUTS/BPH  
24 in China. Residents in the South-West regions had a much lower prevalence of  
25 LUTS/BPH than did those living in the North-West regions of China. Individuals  
26 residing in the north regions, including North, North-East and North-West, had a  
27 relatively higher prevalence of LUTS/BPH than did those living in South-Central and  
28 South-West. Dietary differences may contribute to this discrepancy. Daily diet of  
29 individuals living in north regions contain much milk, dairy products and red meat,  
30 while individuals living in south regions consume more fruits and vegetables than do  
31 those in the north, which have both been confirmed to increase the risk of LUTS/BPH  
32 (29,30). Nevertheless, residents in East region did not show a high prevalence of  
33 LUTS/BPH. It was thought that socioeconomic development in the East region was, in  
34 general, higher than that of other regions, possibly contributing to the lower  
35 prevalence of LUTS/BPH. Furthermore, the genetic susceptibility of BPH was also a  
36 factor influencing the prevalence of LUTS/BPH in China. Several studies from China  
37 reported genetics associated with developing BPH (30), possibly one of the factors  
38 causing varying prevalence of LUTS/BPH in China.  
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56 Our research has several strengths. First, our data was based on the CHARLS, a  
57 national population survey. The interviewers were highly-trained and questionnaires  
58 were developed after a long and rigorous course. The participants were chosen via  
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4 strict multistage probability sampling procedures. Hence, data from the CHARLS can  
5 represent the national condition. Second, the prevalence of LUTS/BPH in China is  
6 difficult to estimate, not only because of the large population but also because of the  
7 diagnostic criteria. Using data from the CHARLS, we avoided both questions.  
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13 There are some limitations as well. First, the CHARLS did not collect weight and  
14 height, so we could not analyze the relationship of BMI or obesity and prevalence of  
15 LUTS/BPH. Second, testicular androgens are required in the prostate for the  
16 development of BPH. Third, as China is a large country, and we all adhere to the  
17 principles of diagnosis from the China Urology Association (CUA), the diagnosis of  
18 LUTS/BPH may be slightly different among regions. We cannot detect these  
19 differences, since the data of CHARLS provides an established diagnosis.  
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29 In this study, we looked at the prevalence of LUTS/BPH via CHARLS data. We found  
30 that the LUTS/BPH is highly prevalent in older, urban-living men. The prevalence  
31 varied according to marital status, socioeconomic status and geographic regions.  
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#### 37 Funding statement

38 This research received no specific grant from any funding agency in the public,  
39 commercial or not-for-profit sectors.  
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#### 44 Competing interest statement

45 None declared.  
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#### 50 Author statement

51 Weiyu Zhang, Xiaopeng Zhang: Designed the study and drafted the article

52 Haibin Li, Feng Wu: Dealt with the statistics

53 Huanrui Wang, Meishan Zhao: Help with data sorting, literature retrieve, language  
54 polish and other chores  
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56  
57  
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59 Hao Hu, Kexin Xu: Constructive revision and grasp of the overall situation  
60

## Acknowledgements

The authors are full of gratitude to the office of CHARLS for sharing the data. The data can be accessed at the official website.

## Data sharing statement

CHARLS is based on the Health and Retirement Study (HRS) and related aging surveys such as the English Longitudinal Study of Aging (ELSA) and the Survey of Health, Aging and Retirement in Europe (SHARE). All of the data was obtained from CHARLS database (<http://charls.pku.edu.cn/zh-CN>) with open access.

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Table 1 Baseline population characteristics

Characteristic	Men (n=5888)
Age, mean (SD)	62.78 (8.56)
Age group, No. (%)	
50-59	2356 (40.01)
60-69	2250 (38.21)
$\geq 70$	1282 (21.77)
Marital status, No. (%)	
Married	5111 (86.80)
Unmarried/Separated /Widowed	777 (13.20)
Education levels, No. (%)*	
No formal education	1918 (32.84)
Elementary school	1573 (26.93)
Middle school	1426 (24.42)
High school	556 (9.52)
College degree or above	367 (6.28)
Geographic region, No. (%)	
Rural	3742 (63.55)
Urban	2146 (36.45)
GDP per capita, No. (%)	
Low	2114 (35.90)
Middle	1960 (33.29)
High	1814 (30.81)
Region, No. (%)	
East	2506 (42.56)
North	779 (13.23)
North-East	404 (6.86)
North-West	224 (3.80)
South-Central	974 (16.54)
South-West	1001 (17.00)

\*, Education levels values of 48 cases was missed.

Table 2 Weighted prevalence

Characteristic	Case, No. (%)	Prevalence (%)	95% CI
Total	599 (10.17)	10.66	9.36-12.12
Age group, No. (%)			
50-59	182 (7.72)	8.39	7.01-9.98
60-69	236 (10.49)	10.61	8.67-12.91
≥70	181 (14.12)	14.67	11.80-18.09
Marital status, No. (%)			
Married	522 (10.21)	10.80	9.61-12.12
Unmarried/Separated /Widowed	77 (9.91)	9.87	6.56-14.60
Education levels, No. (%)*			
No formal education	162 (8.45)	8.20	6.54-10.23
Elementary school	166 (10.55)	10.69	8.20-13.83
Middle school	130 (9.12)	9.17	6.71-12.40
High school	55 (9.89)	13.99	7.62-24.29
College degree or above	84 (22.89)	21.26	13.55-31.73
Geographic region, No. (%)			
Rural	328 (8.77)	8.38	6.90-10.15
Urban	271 (12.63)	13.55	10.95-16.64
GDP per capita, No. (%)			
Low	203 (9.60)	10.69	8.20-13.83
Middle	232 (11.84)	11.54	10.09-13.16
High	164 (9.04)	9.83	7.44-12.88
Region, No. (%)			
East	244 (9.74)	10.56	8.68-12.81
North	98 (12.58)	12.18	8.63-16.92
North-East	42 (10.40)	12.24	9.11-16.25
North-West	29 (12.95)	13.75	9.92-18.75
South-Central	91 (9.34)	9.76	6.47-14.45
South-West	95 (9.49)	9.53	6.24-14.31

\*, Education levels values of 48 cases was missed.

Table 3 The adjusted odds ratio (OR) for the prevalence of LUTS/BPH

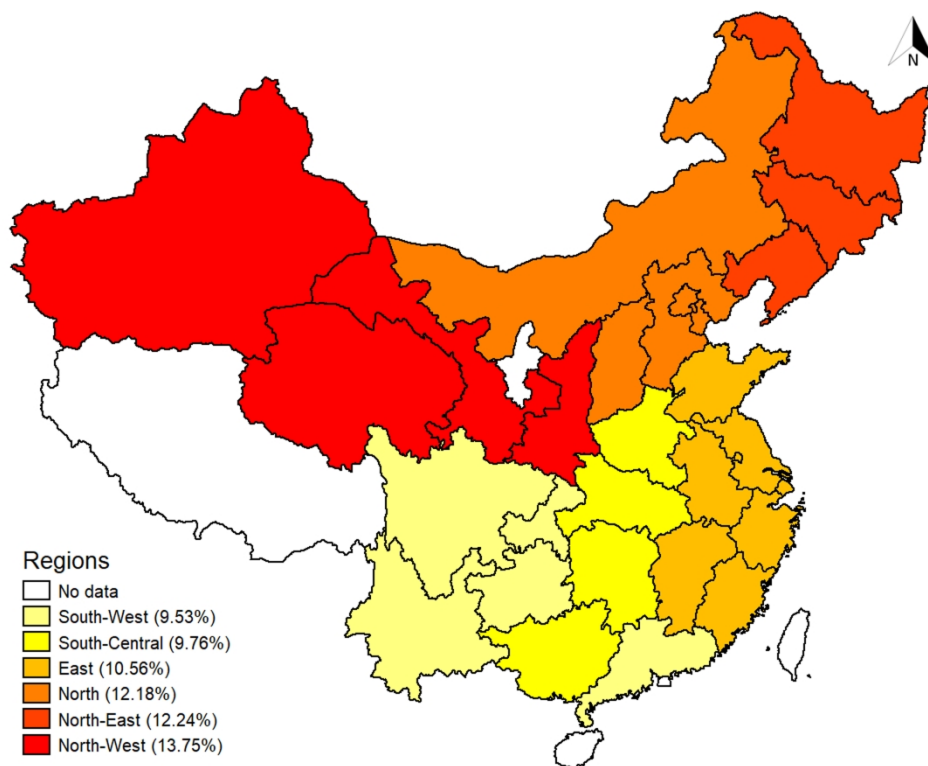
Characteristic	Crude OR (95 % CI)	Adjusted OR (95 % CI)	P value
Age group, No. (%)			<0.001
50-59	1.00 (reference)	1.00 (reference)	
60-69	1.29 (0.98-1.71)	1.50 (1.20-1.87)	0.001
≥70	1.87 (1.31-2.69)	2.09 (1.58-2.78)	<0.001
Marital status, No. (%)			
Married	1.00 (reference)	1.00 (reference)	
Unmarried/Separated /Widowed	0.90(0.59-1.38)	0.91 (0.63-1.30)	0.597
Education levels, No. (%)			0.001
No formal education	1.00 (reference)	1.00 (reference)	
Elementary school	1.34 (0.95-1.88)	1.36 (0.97-1.91)	0.074
Middle school	1.12 (0.79-1.61)	1.30 (0.93-1.82)	0.120
High school	1.82 (0.84-3.92)	2.27 (1.03-4.99)	0.043
College degree or above	3.02 (1.67-5.43)	2.67 (1.57-4.54)	0.000
Geographic region, No. (%)			
Rural	1.00 (reference)	1.00 (reference)	
Urban	1.71 (1.24-2.36)	1.50 (1.71-1.92)	0.002
GDP per capita, No. (%)			0.156
Low	1.00 (reference)	1.00 (reference)	
Middle	1.08(0.77-1.53)	1.23 (0.94-1.62)	0.130
High	0.91(0.58-1.42)	0.99 (0.69-1.42)	0.958
Region, No. (%)			0.200
East	1.00 (reference)	1.00 (reference)	
North	1.17 (0.74-1.84)	1.12 (0.75-1.67)	0.578
North-East	1.18 (0.77-1.79)	1.03 (0.76-1.39)	0.844
North-West	1.35 (0.86-2.11)	1.66 (1.12-2.47)	0.012
South-Central	0.91 (0.55-1.51)	0.90 (0.53-1.55)	0.696
South-West	0.89 (0.53-1.50)	1.01 (0.66-1.53)	0.970

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Figure 1 The prevalence of each region

For peer review only





The prevalence of LUTS/BPH in each regions

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract [2] (b) Provide in the abstract an informative and balanced summary of what was done and what was found [3]
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported [5]
Objectives	3	State specific objectives, including any prespecified hypotheses [5]
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper [6]
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [6-7]
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants [7]
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group [7]
Bias	9	Describe any efforts to address potential sources of bias [N/A]
Study size	10	Explain how the study size was arrived at [7]
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why [7]
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding [7-8] (b) Describe any methods used to examine subgroups and interactions [N/A] (c) Explain how missing data were addressed [N/A] (d) If applicable, describe analytical methods taking account of sampling strategy [N/A] (e) Describe any sensitivity analyses [N/A]
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed [8] (b) Give reasons for non-participation at each stage [N/A] (c) Consider use of a flow diagram [N/A]
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders [8-9] (b) Indicate number of participants with missing data for each variable of interest [N/A]
Outcome data	15*	Report numbers of outcome events or summary measures [8-9]
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included [18]

		(b) Report category boundaries when continuous variables were categorized [N/A]
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period [N/A]
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [N/A]
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives [13]
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [13]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence [9-12]
Generalisability	21	Discuss the generalisability (external validity) of the study results [N/A]
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based [N/A]

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).