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Which lower urinary tract symptom is most influential on life competence of older adults? A community-based cross-sectional survey in Japan

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Which lower urinary tract symptom is most influential on life competence of older adults? A community-based cross-sectional survey in Japan

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Abbreviations: LUTS, lower urinary tract symptoms; OAB, overactive bladder; QOL, quality of life; JST-IC, Japan Science and Technology Agency Index of Competence; AOR, adjusted odds ratio; CI, confidence interval

Word count: 1,491

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ABSTRACT

Objectives: Life competence, or the ability to live actively, is essential for healthy aging. However, which lower urinary tract symptoms (LUTS) affect older adults’ life competence is unknown. This study assessed association between the five types of LUTS and life competence among community-dwelling older adults (≥65 years old).

Design: Cross-sectional survey.

Setting: Community-dwelling older adults (≥65 years old) randomly selected from the basic resident register of Kashiwa City as part of the Kashiwa study.

Participants: The study included 916 community-dwelling older adults (481 males) in Japan.

Outcome measures: A self-administered questionnaire was used to collect data regarding LUTS, which included frequency, nocturia, urgency, urinary incontinence, and overactive bladder (OAB). Life competence was measured using the Japan Science and Technology Agency Index of Competence. Sex-stratified logistic regression analyses were adjusted for age, obesity, alcohol consumption, polypharmacy, and comorbidities. **Results:** Males experienced symptoms of frequency, nocturia, urgency, urinary incontinence, and OAB at rates of 68.0%, 89.0%, 16.0%, 3.7%, and 4.3%, respectively. Females experienced these symptoms at rates of 68.3%, 80.0%, 11.0%, 7.4%, and 8.5%, respectively. Among males, lower life competence was only associated with nocturia (≥3 times/night) (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower life competence among females was significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

Conclusion: The different associations between LUTS and life competence by sex might be related to differences in susceptibility to nocturnal awakening and musculoskeletal functions. To maintain life competence and promote healthy aging in older adults, LUTS should be prevented and treated well, especially nocturia among males, and frequency, urgency, and OAB among females.

Strengths and limitations of this study

- This study focused on life competence, an important ability for healthy aging, in the context of lower urinary tract symptoms.
- This study compared the different effects of five types of lower urinary tract symptoms on life competence of older males and females.
- We only used a self-administered questionnaire to measure lower urinary tract symptoms, so that recall bias is undeniable.

Keywords: lower urinary tract symptoms, competence, healthy aging, older adults

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INTRODUCTION

The concept of “healthy aging” provides a different perspective regarding the quality of life (QOL) of older adults [1] and was defined by the World Health Organization as “the process of developing and maintaining the functional ability that enables wellbeing in older age”.[2] Functional ability includes a person’s ability to fulfill their basic needs, learn, grow, make decisions, be mobile, build and maintain relationships, and contribute to society. This perspective re-frames older adults as individuals who can facilitate their healthy aging, rather than being passive receivers of support. Moreover, the maintenance of life competence to achieve healthy aging is becoming an important theme in countries with aging populations.[3]

Lower urinary tract symptoms (LUTS) include problems with storage, voiding, or post-micturition functions and are not limited to specific sexes, ages, or regions.[4] A study using the International Continence Society’s definitions estimated that 45.2% of the global population of individuals who are >20 years old have at least one LUTS.[5] Furthermore, LUTS is more prevalent among older adults, with one international population-based study estimating that 80.7% of older men and 79.3% of older women (>60 years old) have at least one type of LUTS, such as nocturia.[6] Moreover, global population aging might increase the proportion of individuals with LUTS, especially among older adults.[7, 8]

The presence of LUTS can negatively affect individuals’ QOL,[9, 10] and storage-related

symptoms (e.g., nocturia, urgency, or urinary incontinence) have negative and significant detrimental effects on people's QOL.[11, 12] For example, nocturia (≥ 2 times/night) can lead to decreased QOL due to interrupted sleep,[13] falls on the way to the toilet,[14] and fall-related fractures.[15] Urinary incontinence also affects QOL, which is related to the severity, type, and number of incontinent episodes.[16] Moreover, QOL tends to decrease with age, suggesting that older adults face a double burden of increased LUTS and decreased QOL. Although LUTS among older adults has been investigated in the context of QOL, it is unclear whether they affect life competence and which among them is most influential. Therefore, this study aimed to investigate the associations of various types of LUTS with life competence among older Japanese community-dwelling males and females.

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96 MATERIAL AND METHODS

97 We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) cross
98 sectional reporting guidelines.[17]

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100 Participants

101 The study participants were selected from a community-based study in Kashiwa City, Japan (the
102 Kashiwa study). The Kashiwa study evaluated 2,044 community-dwelling older adults (≥ 65 years

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103 old) who were randomly selected from the basic resident register of Kashiwa City in 2012. Surveys
104 were performed every 1–2 years, and the present study evaluated information on participants of the
105 2016 survey, when questions regarding LUTS were introduced. A total of 1,339 individuals who
106 were not in long-term care participated in the 2016 survey, although we excluded 423 individuals
107 with cognitive dysfunction (Mini-Mental State Examination score of ≤ 23), gait problems, or missing
108 data regarding the main variables. Finally, the present study evaluated data from 916 participants
109 (481 males and 435 females). The participants were not involved in the design, or conduct, or
110 reporting, or dissemination plans of our research.

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112 **Ethical considerations**

113 The study protocol was approved by the Ethics Committee of the University of Tokyo (approval
114 numbers: 12-8 and 18-166). All participants provided written informed consent before participating
115 in the Kashiwa study.

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117 **Life competence**

118 Life competence, an ability to live actively for healthy aging, was evaluated using the Japan Science
119 and Technology Agency Index of Competence (JST-IC).[18, 19] The JST-IC was developed to
120 comprehensively measure the competence of older adults based on 16 items regarding new device

use, information collection, life management, and social participation. The original Japanese version of the JST-IC was used in the research. The scores range from 0 to 16, with higher scores indicating greater competence.

Lower urinary tract symptoms

To collect data on the five types of LUTS (frequency, nocturia, urgency, urinary incontinence, and overactive bladder [OAB]), we used a self-administered questionnaire regarding the frequency of urination during the day and night, urgency, and urinary incontinence. Frequency was defined as ≥ 8 urinations during the day, while nocturia was defined as ≥ 1 urination during the night. Urgency was defined as “a compelling need to urinate, due to pain or an unpleasant sensation, that is difficult to defer”, [20] and the number of urinary incontinent episodes was recorded. We also considered the presence of OAB, which is clinically important and prevalent among older adults, which we defined as the occurrence of urgency with frequency or nocturia.

Other variables

Based on previous studies regarding LUTS, [21, 22] the following variables were selected as possible confounding factors: age, obesity (body mass index of ≥ 25 kg/m²), alcohol consumption (≥ 5 times/week), [23] polypharmacy (≥ 6 drugs/day), [24] and comorbidities (hypertension, heart disease,

diabetes, and dyslipidemia).[25-28]

Data analysis

The participants were stratified according to sex. Because the JST-IC data were not normally distributed (Shapiro-Wilk test p-value <0.05), we treated the JST-IC score as a categorical variable using the median (=12) for the multivariate analyses. To determine the association of each LUTS with life competence by sex, logistic regression analyses predicting JST-IC were run with the following independent variables: each LUTS (frequency, nocturia [1, 2, or ≥3 times per night], urgency, urinary incontinence, or OAB), age, obesity, alcohol intake, polypharmacy, and comorbidities (hypertension, heart disease, diabetes, and dyslipidemia). All statistical analyses were performed using SPSS Statistics for Windows, version 27.0 (IBM, Armonk, NY), and differences were considered statistically significant at p-values of <0.05.

RESULTS

Table 1 shows the participants’ characteristics stratified by sex. Males had significantly higher proportions of obesity, alcohol consumption, polypharmacy, comorbidities (hypertension, heart disease, and diabetes), and three types of LUTS (nocturia, urgency, and OAB). Females had significantly higher proportions of dyslipidemia and urinary incontinence.

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158 **Table 1.** Characteristics of participants

		Total		Males		Females		p
Characteristics		n=916		n=481		n=435		
		n	(%)	n	(%)	n	(%)	
Age	Mean, SD	76.3, 5.1		76.5, 5.2		76.1, 5.0		0.22
JST-IC ^a	≥12	488	(53.3)	258	(53.6)	230	(52.9)	0.82
	<12	428	(46.7)	223	(46.4)	205	(47.1)	
Obesity ^b	BMI≥25	199	(22.0)	121	(25.6)	78	(18.1)	0.01
	BMI<25	704	(78.0)	351	(74.4)	353	(81.9)	
Alcohol	≥5 times/week	250	(27.3)	213	(44.3)	37	(8.5)	<0.01
consumption ^b	<5 times/week	665	(72.7)	268	(55.7)	397	(91.5)	
Polypharmacy ^b	≥6 drugs/day	151	(16.6)	92	(19.2)	59	(13.7)	0.03
	<6 drugs/day	758	(83.4)	386	(80.8)	372	(86.3)	
Comorbidities								
Hypertension	Yes	407	(44.4)	238	(49.5)	169	(38.9)	<0.01
	No	509	(55.6)	243	(50.5)	266	(61.1)	
Heart disease	Yes	123	(13.4)	85	(17.7)	38	(8.7)	<0.01
	No	793	(86.6)	396	(82.3)	397	(91.3)	
Diabetes	Yes	101	(11.0)	68	(14.1)	33	(7.6)	<0.01
	No	815	(89.0)	413	(85.9)	402	(92.4)	
Dyslipidemia	Yes	307	(33.5)	123	(25.6)	184	(42.3)	<0.01
	No	609	(66.5)	358	(74.4)	251	(57.7)	
LUTS ^c								
Frequency	≥8 times/daytime	624	(68.1)	327	(68.0)	297	(68.3)	0.92

Nocturia	≥1 time/night	776 (84.7)	428 (89.0)	348 (80.0)	<0.01
	≥2 times/night	419 (45.7)	267 (55.5)	152 (34.9)	<0.01
	≥3 times/night	136 (14.8)	99 (20.6)	37 (8.5)	<0.01
Urgency	≥1 time/day	125 (13.6)	77 (16.0)	48 (11.0)	0.03
Urinary incontinence	≥1 time/day	50 (5.5)	18 (3.7)	32 (7.4)	0.02
OAB ^d		106 (11.6)	69 (14.3)	37 (8.5)	<0.01

^aJST-IC: Japan Science and Technology Agency Index of Competence.

^bMissing cases: 13 in obesity, 1 in alcohol consumption, 7 in polypharmacy.

^cLUTS: lower urinary tract symptom.

^dOAB: overactive bladder (frequency & nocturia [≥1] & urgency).

Figures 1 and 2 show the results of the logistic regression analyses to determine the association of each LUTS type with life competence, after adjustment for age, obesity, alcohol consumption, polypharmacy, and comorbidities. Among males, lower life competence was significantly associated with nocturia (≥3 times/night) only (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower life competence among females was significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

DISCUSSION

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6 170 The results indicated that nocturia (≥ 3 times/night) was significantly associated with lower life
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15 173 First, nocturia was more prevalent in males than in females, as shown in Table 1. A possible
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18 174 explanation is the lifestyle difference between both sexes. For example, eating salty food and
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24 176 likely to have hypertension and to consume alcohol. It is likely that they prefer to eat salty food and
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27 177 drink water at night. Such lifestyles could increase the prevalence of nocturia in males. Regarding
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30 178 the different associations between nocturia and life competence among males and females,
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33 179 susceptibility to sleep disturbance could be a reason. Females generally experience more sleep
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36 180 difficulties, such as insomnia,[31] and males may not be used to nocturnal awakening. For example,
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48 184 Lower life competence was significantly associated with frequency, urgency, and OAB only
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51 185 among females. This could be explained by the physical differences between males and females, as
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54 186 older females have a greater risk of musculoskeletal problems, such as sarcopenia, osteoporosis, and
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57 187 osteoarthritis.[33] Toileting is a complex physical activity that involves several musculoskeletal
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functions,[34] and it is possible that physical fatigue due to frequent toileting and anxiety related to urgency, could lead to lower competence among such frail older females.[35]

The present study had several limitations. First, recall bias is undeniable because a self-administered questionnaire was used to measure the frequency of urination, urgency, and urinary incontinence. However, we aimed to minimize the possibility of underestimation or overestimation by double-checking the responses with the participants when the questionnaires were collected. Second, the cross-sectional design precludes a conclusion regarding the causality of the relationship between LUTS and competence. A well-designed prospective study is needed to evaluate the causality of this relationship and the related mechanism(s).

To the best of our knowledge, this is the first study to reveal that the life competence associated LUTS vary according to sex. Among males, lower life competence was associated with nocturia (≥ 3 times/night) only, while it was associated with frequency, urgency, and OAB among females. These sex-based differences may be due to the different susceptibility between the sexes to nocturnal awakening and musculoskeletal function. Therefore, to maintain life competence and promote healthy aging among older adults, LUTS should be prevented and treated well, especially nocturia among males, and frequency, urgency, and OAB among females.

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207

208 **Conflict of interest**

209 The authors declare they have no conflict of interest with respect to this research study and paper.

210

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213

214 **Author contributions**

215 KT conceptualized the study. KT, TT, YY, MFSS and KI collected the data. KT analyzed and

216 interpreted the data, and wrote the first draft of the manuscript. TT, YY, MFSS, BKS and KI have

217 given critical feedback. All authors contributed to review and edit the manuscript.

218

219 **Data availability**

220 Data are available upon reasonable request.

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FIGURE LEGENDS

Figure 1. Results of the logistic regression analyses to determine the association of each LUTS type with life competence, after adjustment for age, obesity, alcohol consumption, polypharmacy, and comorbidities among older males (n = 468).

Figure 2. Results of the logistic regression analyses to determine the association of each LUTS type with life competence, after adjustment for age, obesity, alcohol consumption, polypharmacy, and comorbidities among older females (n = 424).

Males

AOR (95%CI)

Frequency

Nocturia (>=1)

Nocturia (>=2)

Nocturia (>=3)

Urgency

Urinary incontinence

OAB

1.04

1.22

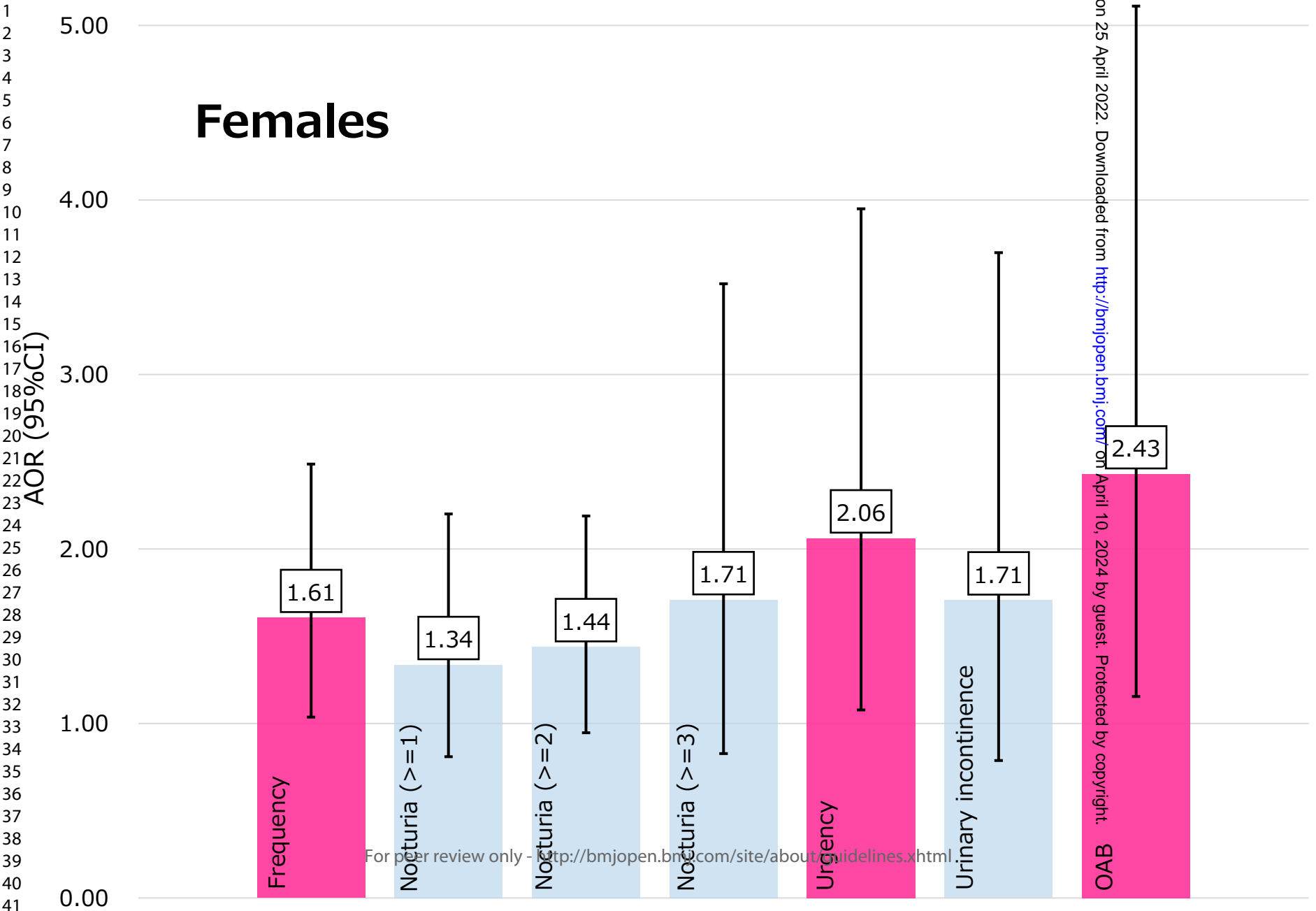
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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	6-7
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
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	7-8
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(e) Describe any sensitivity analyses	n/a
Results			

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	5-6
		(b) Give reasons for non-participation at each stage	5-6
		(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	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
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	10
		(b) Report category boundaries when continuous variables were categorized	7-8
		(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
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
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	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
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	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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.

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Which lower urinary tract symptom is most influential on functional ability of older adults? A community-based cross-sectional survey in Japan

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Which lower urinary tract symptom is most influential on functional ability of older adults? A community-based cross-sectional survey in Japan

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Abbreviations: LUTS, lower urinary tract symptoms; OAB, overactive bladder; QOL, quality of life; JST-IC, Japan Science and Technology Agency Index of Competence; AOR, adjusted odds ratio; CI, confidence interval

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ABSTRACT

Objectives: Functional ability, or the ability to live actively in older age, is essential for healthy aging. However, which lower urinary tract symptoms (LUTS) affect older adults' functional ability is unknown. This study assessed association between the five types of LUTS and functional ability among community-dwelling older adults (≥ 65 years old).

Design: Cross-sectional survey.

Setting: Community-dwelling older adults (≥ 65 years old) randomly selected from the basic resident register of Kashiwa City as part of the Kashiwa study.

Participants: The study included 916 community-dwelling older adults (481 males) in Japan.

Outcome measures: A self-administered questionnaire was used to collect data regarding LUTS, which included frequency, nocturia, urgency, urinary incontinence, and overactive bladder (OAB). Functional ability was measured using the Japan Science and Technology Agency Index of Competence. Sex-stratified logistic regression analyses were adjusted for age, obesity, alcohol consumption, polypharmacy, and comorbidities.

Results: Males experienced symptoms of frequency, nocturia, urgency, urinary incontinence, and OAB at rates of 68.0%, 89.0%, 16.0%, 3.7%, and 4.3%, respectively. Females experienced these symptoms at rates of 68.3%, 80.0%, 11.0%, 7.4%, and 8.5%, respectively. Among males, lower functional ability was only associated with nocturia (≥ 3 times/night) (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower functional ability among females was significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

Conclusion: The different associations between LUTS and functional ability by sex might be related to differences in comorbidities and musculoskeletal functions. To maintain functional ability and promote healthy aging in older adults, LUTS should be prevented and treated well, especially nocturia among males, and frequency, urgency, and OAB among females.

58 **Strengths and limitations of this study**

- 59 ● The study participants were selected from randomly recruited older adults in a city.
- 60 ● Functional ability, an essential concept for healthy aging, was measured using a comprehensive scale.
- 61 ● Recall bias is undeniable because a self-administered questionnaire was used to measure lower
62 urinary tract symptoms.
- 63 ● A cross-sectional design precludes a conclusion regarding the causality of the relationship.

64
65 **Keywords:** lower urinary tract symptoms, functional ability, healthy aging, older adults

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INTRODUCTION

The concept of “healthy aging” provides a different perspective regarding the quality of life (QOL) of older adults [1] and was defined by the World Health Organization as “the process of developing and maintaining the functional ability that enables wellbeing in older age”.[2] Functional ability includes a person’s ability to fulfill their basic needs, learn, grow, make decisions, be mobile, build and maintain relationships, and contribute to society. This perspective re-frames older adults as individuals who can facilitate their healthy aging, rather than being passive receivers of support. Moreover, the maintenance of functional ability to achieve healthy aging is becoming an important theme in countries with aging populations.[3]

Lower urinary tract symptoms (LUTS) include problems with storage, voiding, or post-micturition functions and are not limited to specific sexes, ages, or regions.[4] A study using the International Continence Society’s definitions estimated that 45.2% of the global population of individuals who are >20 years old have at least one LUTS.[5] Furthermore, LUTS is more prevalent among older adults, with one international population-based study estimating that 80.7% of older men and 79.3% of older women (>60 years old) have at least one type of LUTS, such as nocturia.[6] However, despite the high prevalence of LUTS, the consultation rate remains low. [7] As global population aging continues, the proportion of individuals suffering from LUTS might increase, especially among older adults.[8, 9]

The presence of LUTS can negatively affect individuals' QOL,[10, 11] and storage-related symptoms (e.g., nocturia, urgency, or urinary incontinence) have negative and significant detrimental effects on people's QOL.[12, 13] For example, nocturia (≥ 2 times/night) can lead to decreased QOL due to interrupted sleep,[14] falls on the way to the toilet,[15] and fall-related fractures.[16] Urinary incontinence also affects QOL, which is related to the severity, type, and number of incontinent episodes.[17] Moreover, QOL tends to decrease with age, suggesting that older adults face a double burden of increased LUTS and decreased QOL.

Thus, studies showing a relationship between LUTS and QOL have been well accumulated. On the other hand, studies regarding LUTS in the context of functional ability that are important for healthy aging are limited. To promote healthy aging, it is necessary to investigate the relationship between LUTS and functional ability in detail. Therefore, this study aimed to examine the associations of various types of LUTS with functional ability among older Japanese community-dwelling males and females.

MATERIAL AND METHODS

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) cross-sectional reporting guidelines.[18]

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103 **Participants**

104 The study participants were selected from a community-based study in Kashiwa City, Japan (the
105 Kashiwa study). The Kashiwa study evaluated 2,044 community-dwelling older adults (≥ 65 years
106 old) who were randomly selected from the basic resident register of Kashiwa City in 2012. Surveys
107 were performed every 1–2 years, and the present study evaluated information on participants of the
108 2016 survey, when questions regarding LUTS were introduced. A total of 1,339 individuals who
109 were not in long-term care participated in the 2016 survey. Among them, we excluded 423
110 individuals with cognitive dysfunction (Mini-Mental State Examination score of ≤ 23) to ensure the
111 reliability of the data collected by the self-administered questionnaire, gait problems (whether they
112 reported that they can walk without any help) to eliminate the effects of physical movement
113 restrictions on functional ability and LUTS, or missing data regarding the main variables. Finally,
114 the present study evaluated data from 916 participants (481 males and 435 females).

115

116 **Ethical considerations**

117 The study protocol was approved by the Ethics Committee of the University of Tokyo (approval
118 numbers: 12-8 and 18-166). All participants provided written informed consent before participating
119 in the Kashiwa study.

120

121 **Functional ability**

122 In this study, we evaluated functional ability using the Japan Science and Technology Agency Index
123 of Competence (JST-IC).[19, 20] The JST-IC is a validated scale to measure the level of overall
124 competence to live actively in older age with 16 items regarding new device use, information
125 collection, life management, and social participation. The original Japanese version of the JST-IC
126 was used in the research. The scores range from 0 to 16, with higher scores indicating greater
127 functional ability.

129 **Lower urinary tract symptoms**

130 To collect data on the five types of LUTS (frequency, nocturia, urgency, urinary incontinence, and
131 overactive bladder [OAB]), we used a self-administered questionnaire regarding the frequency of
132 urination during the day and night, urgency, and urinary incontinence. Frequency was defined as ≥ 8
133 urinations during the day, while nocturia was defined as ≥ 1 urination during the night. Urgency was
134 defined as “a compelling need to urinate, due to pain or an unpleasant sensation, that is difficult to
135 defer”,[21] and the number of urinary incontinent episodes was recorded. We also considered the
136 presence of OAB, which is clinically important and prevalent among older adults, which we defined
137 as the occurrence of urgency with frequency or nocturia.

Other variables

Based on previous studies regarding LUTS,[22, 23] the following variables were selected as possible confounding factors: age, obesity (body mass index of ≥ 25 kg/m²), alcohol consumption (≥ 5 times/week),[24] polypharmacy (≥ 6 drugs/day),[25] and comorbidities (hypertension, heart disease, diabetes, and dyslipidemia).[26-29]

Data analysis

Considering that the characteristics of LUTS differ depending on sex, the participants were stratified according to sex. The distribution of all variables, sex differences, and the crude associations between the five types of LUTS and JST-IC were examined by univariate analysis. Since no clear cutoff value has been set for JST-IC, we initially planned to treat it as a continuous variable. However, we changed to treat it as a categorical variable using the median (=12) for the multivariate analyses due to the collected data that was not normally distributed (Shapiro-Wilk test p-value < 0.05). To determine the association of each LUTS with functional ability by sex, logistic regression analyses predicting lower JST-IC were run with the following independent variables: each LUTS (frequency, nocturia [1, 2, or ≥ 3 times per night], urgency, urinary incontinence, or OAB), age, obesity, alcohol intake, polypharmacy, and comorbidities (hypertension, heart disease, diabetes, and dyslipidemia). As the dependent variable of the logistic regression analyses, the binary variable of

JST-IC in which the high and low scores were reversed was used. All statistical analyses were performed using SPSS Statistics for Windows, version 27.0 (IBM, Armonk, NY), and differences were considered statistically significant at p-values of <0.05 .

Patients and public involvement

The participants were not involved in the design, or conduct, or reporting, or dissemination plans of our research. The study results will be available to the participants and the public through the open-access journal article.

RESULTS

Table 1 shows the participants' characteristics stratified by sex. Males had significantly higher proportions of obesity, alcohol consumption, polypharmacy, comorbidities (hypertension, heart disease, and diabetes), and three types of LUTS (nocturia, urgency, and OAB). Females had significantly higher proportions of dyslipidemia and urinary incontinence. Crude associations between each LUTS and the total score of JST-IC or its four components (new device use, information collection, life management, and social participation) are shown in supplemental tables.

Table 1. Characteristics of participants

		Total		Males		Females		p
Characteristics		n=916		n=481		n=435		
		n	(%)	n	(%)	n	(%)	
Age	Mean, SD	76.3, 5.1		76.5, 5.2		76.1, 5.0		0.22
JST-IC ^a	≥12	488	(53.3)	258	(53.6)	230	(52.9)	0.82
	<12	428	(46.7)	223	(46.4)	205	(47.1)	
Obesity ^b	BMI≥25	199	(22.0)	121	(25.6)	78	(18.1)	0.01
	BMI<25	704	(78.0)	351	(74.4)	353	(81.9)	
Alcohol	≥5 times/week	250	(27.3)	213	(44.3)	37	(8.5)	<0.01
consumption ^b	<5 times/week	665	(72.7)	268	(55.7)	397	(91.5)	
Polypharmacy ^b	≥6 drugs/day	151	(16.6)	92	(19.2)	59	(13.7)	0.03
	<6 drugs/day	758	(83.4)	386	(80.8)	372	(86.3)	
Comorbidities								
Hypertension	Yes	407	(44.4)	238	(49.5)	169	(38.9)	<0.01
	No	509	(55.6)	243	(50.5)	266	(61.1)	
Heart disease	Yes	123	(13.4)	85	(17.7)	38	(8.7)	<0.01
	No	793	(86.6)	396	(82.3)	397	(91.3)	
Diabetes	Yes	101	(11.0)	68	(14.1)	33	(7.6)	<0.01
	No	815	(89.0)	413	(85.9)	402	(92.4)	
Dyslipidemia	Yes	307	(33.5)	123	(25.6)	184	(42.3)	<0.01
	No	609	(66.5)	358	(74.4)	251	(57.7)	
LUTS ^c								
Frequency	≥8 times/daytime	624	(68.1)	327	(68.0)	297	(68.3)	0.92
Nocturia	≥1 time/night	776	(84.7)	428	(89.0)	348	(80.0)	<0.01
	≥2 times/night	419	(45.7)	267	(55.5)	152	(34.9)	<0.01
	≥3 times/night	136	(14.8)	99	(20.6)	37	(8.5)	<0.01
Urgency	≥1 time/day	125	(13.6)	77	(16.0)	48	(11.0)	0.03

Urinary								
incontinence	≥1 time/day	50	(5.5)	18	(3.7)	32	(7.4)	0.02
OAB ^d		106	(11.6)	69	(14.3)	37	(8.5)	<0.01

^aJST-IC: Japan Science and Technology Agency Index of Competence.

^bMissing cases: 13 in obesity, 1 in alcohol consumption, 7 in polypharmacy.

^cLUTS: lower urinary tract symptom.

^dOAB: overactive bladder (frequency & nocturia [≥1] & urgency).

Figures 1 and 2 show the results of the logistic regression analyses to determine the association of each LUTS type with the lower functional ability, after adjustment for age, obesity, alcohol consumption, polypharmacy, and comorbidities. Among males, the lower functional ability was significantly associated with nocturia (≥3 times/night) only (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower functional ability among females was significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

DISCUSSION

The results indicated that nocturia (≥3 times/night) was significantly associated with lower functional ability among males, it was significantly associated with frequency, urgency, and OAB among females. Thus, the association of LUTS with functional ability may vary according to sex.

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188 Nocturia was more prevalent and influential in males than in females. One of the reasons for
189 this may be the influence of comorbidities. Male participants were more likely to have hypertension,
190 heart disease, and diabetes which are known as risk factors of nocturia.[26-28] It is possible that
191 these comorbidities increase nighttime urination and at the same time have a negative impact on
192 various daytime activities. In addition, it is necessary to consider the effects of polypharmacy.[30]
193 As shown in Table 1, males were taking more drugs than females. In recent years, it is known that an
194 increase in the number of medications taken in older adults leads to adverse events.[31] Taking high
195 doses of drugs for the treatment of comorbidities may lead to polypharmacy and reduce functional
196 ability. Thus, the effect of nocturia may be judged to be more serious among males.

197 Lower functional ability was significantly associated with frequency, urgency, and OAB
198 only among females. This could be explained by the physical differences between males and
199 females, as older females have a greater risk of musculoskeletal problems, such as sarcopenia,
200 osteoporosis, and osteoarthritis.[32] Toileting is a complex physical activity that involves several
201 musculoskeletal functions,[33] and it is possible that physical fatigue due to frequent toileting and
202 anxiety related to urgency, could lead to lower competence among such frail older females.[34]

203 The present study had several limitations. First, recall bias is undeniable because a self-
204 administered questionnaire was used to measure the frequency of urination, urgency, and urinary
205 incontinence. However, we aimed to minimize the possibility of underestimation or overestimation

206 by double-checking the responses with the participants when the questionnaires were collected.

207 Second, the cross-sectional design precludes a conclusion regarding the causality of the relationship
208 between LUTS and competence. A well-designed prospective study is needed to evaluate the
209 causality of this relationship and the related mechanism(s).

210 To the best of our knowledge, this is the first study to reveal that the functional ability
211 associated with LUTS vary according to sex. Among males, the lower functional ability was
212 associated with nocturia (≥ 3 times/night) only, while it was associated with frequency, urgency, and
213 OAB among females. These sex-based differences may be due to the sex-related difference in
214 comorbidities and musculoskeletal function. Therefore, to maintain functional ability and promote
215 healthy aging among older adults, LUTS should be prevented and treated well, especially nocturia
216 among males, and frequency, urgency, and OAB among females.

217

218 **Acknowledgments**

219 The authors are deeply thankful to the participants in this study.

220

221 **Conflict of interest**

222 The authors declare they have no conflict of interest with respect to this research study and paper.

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226

227 **Author contributions**

228 KT conceptualized the study. KT, TT, YY, MFSS, and KI collected the data. KT analyzed and
229 interpreted the data, and wrote the first draft of the manuscript. TT, YY, MFSS, BKS, and KI have
230 given critical feedback. All authors contributed to review and edit the manuscript.

231

232 **Data availability**

233 Data are available upon reasonable request.

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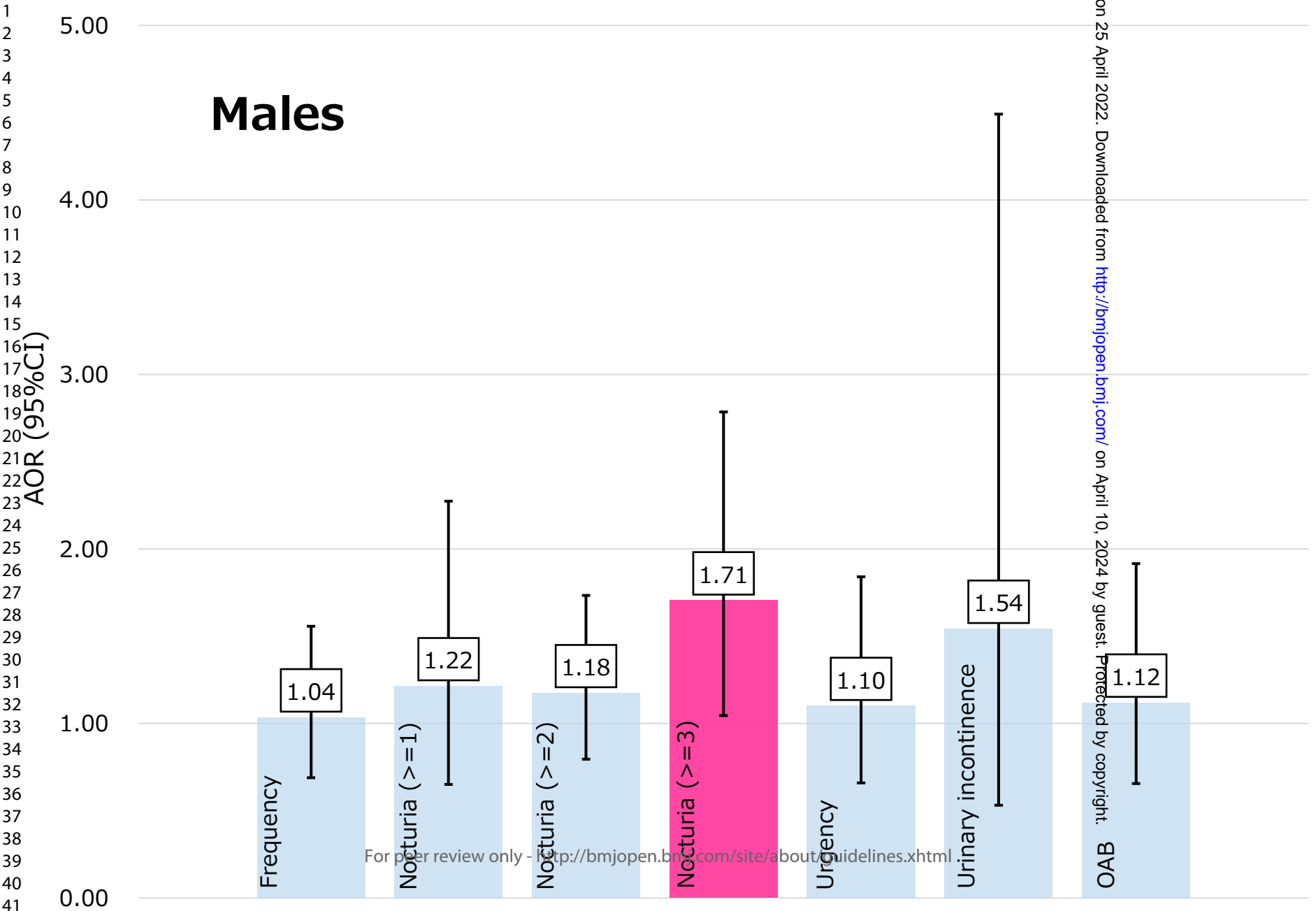
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313 FIGURE LEGENDS

314 **Figure 1.** Results of the logistic regression analyses predicting lower functional ability with various
315 types of LUTS in older males (n=468). The JST-IC was used as a binary dependent variable in which
316 the high and low scores were reversed. In each analysis, age, obesity, alcohol consumption,
317 polypharmacy, and comorbidities were adjusted.

319 **Figure 2.** Results of the logistic regression analyses predicting lower functional ability with various
320 types of LUTS in older females (n=424). The JST-IC was used as a binary dependent variable in which
321 the high and low scores were reversed. In each analysis, age, obesity, alcohol consumption,
322 polypharmacy, and comorbidities were adjusted.



Females

AOR (95%CI)

Frequency

1.61

Nocturia (>=1)

1.34

Nocturia (>=2)

1.44

Nocturia (>=3)

1.71

Urgency

2.06

Urinary incontinence

1.71

OAB

2.43

Supplemental Table 1: Crude associations between sub-types of LUTS and JST-IC

Sub-types of LUTS		JST-IC (total)					
		Total	p	Males	p	Females	p
Frequency	No	11.8±2.7	<0.01	11.8±2.7	0.23	11.8±2.6	<0.01
	Yes	11.3±2.9		11.5±2.9		11.0±2.9	
Nocturia (Once or more)	No	11.9±2.8	0.03	12.1±2.8	0.15	11.8±2.8	0.06
	Yes	11.4±2.9		11.5±2.9		11.2±2.9	
Nocturia (Twice or more)	No	11.8±2.7	<0.01	12.0±2.7	<0.01	11.6±2.7	<0.01
	Yes	11.1±3.0		11.3±3.0		10.7±3.0	
Nocturia (Three times or more)	No	11.6±2.8	<0.01	11.9±2.8	<0.01	11.4±2.8	<0.01
	Yes	10.5±2.9		10.6±2.8		10.0±2.9	
Urgency	No	11.6±2.8	<0.01	11.7±2.8	0.05	11.4±2.8	<0.01
	Yes	10.7±3.1		11.0±3.1		10.2±3.2	
Urinary incontinence	No	11.5±2.8	0.01	11.6±2.9	0.08	11.4±2.7	0.08
	Yes	10.2±3.5		10.4±2.7		10.1±3.9	
OAB	No	11.5±2.8	<0.01	11.7±2.9	0.19	11.4±2.8	<0.01
	Yes	10.8±3.1		11.2±2.9		10.0±3.2	

LUTS: lower urinary tract symptom.
JST-IC: Japan Science and Technology Agency Index of Competence.
Student's t-tests were performed.

Supplemental Table 2: Crude associations between sub-types of LUTS and the new device use component of JST-IC

Sub-types of LUTS		JST-IC (new device use)					
		Total	p	Males	p	Females	p
Frequency	No	3.4±1.0	<0.01	3.5±0.9	0.05	3.2±0.9	0.01
	Yes	3.1±1.1		3.3±1.0		2.9±1.1	
Nocturia (Once or more)	No	3.3±1.0	0.11	3.6±0.7	<0.01	3.2±1.1	0.20
	Yes	3.2±1.1		3.4±1.0		3.0±1.1	
Nocturia (Twice or more)	No	3.3±1.0	0.07	3.5±0.9	0.02	3.1±1.1	0.07
	Yes	3.1±1.1		3.3±1.1		2.9±1.1	
Nocturia (Three times or more)	No	3.3±1.0	0.03	3.5±0.9	<0.01	3.0±1.1	0.44
	Yes	3.0±1.2		3.1±1.2		2.9±1.2	
Urgency	No	3.2±1.0	0.06	3.4±1.0	0.03	3.1±1.1	0.35
	Yes	3.0±1.3		3.1±1.2		2.9±1.4	
Urinary incontinence	No	3.2±1.0	0.06	3.4±1.0	0.25	3.1±1.1	0.22
	Yes	2.9±1.3		3.1±1.2		2.8±1.3	
OAB	No	3.2±1.0	0.08	3.4±1.0	0.09	3.1±1.1	0.16
	Yes	3.0±1.2		3.2±1.1		2.7±1.5	

LUTS: lower urinary tract symptom.

JST-IC: Japan Science and Technology Agency Index of Competence.

Student's t-tests were performed.

Supplemental Table 3: Crude associations between sub-types of LUTS and the information collection component of JST-IC

Sub-types of LUTS		JST-IC (information collection)					
		Total	p	Males	p	Females	p
Frequency	No	3.4±0.9	0.21	3.4±0.8	0.74	3.5±0.9	0.15
	Yes	3.3±0.9		3.3±1.0		3.3±1.0	
Nocturia (Once or more)	No	3.5±0.8	0.18	3.4±0.8	0.57	3.5±0.8	0.22
	Yes	3.3±0.9		3.3±0.9		3.3±1.0	
Nocturia (Twice or more)	No	3.5±0.8	<0.01	3.5±0.8	<0.01	3.5±0.8	<0.01
	Yes	3.2±1.0		3.3±0.9		3.2±1.1	
Nocturia (Three times or more)	No	3.4±0.8	<0.01	3.4±0.8	<0.01	3.4±0.9	<0.01
	Yes	3.0±1.1		3.1±1.1		2.8±1.3	
Urgency	No	3.4±0.9	0.02	3.4±0.8	0.15	3.4±0.9	0.02
	Yes	3.1±1.1		3.2±1.1		3.1±1.1	
Urinary incontinence	No	3.4±0.9	<0.01	3.4±0.9	0.14	3.4±0.9	0.02
	Yes	2.9±1.2		3.1±1.1		2.8±1.2	
OAB	No	3.4±0.9	0.02	3.4±0.8	0.13	3.4±0.9	0.02
	Yes	3.1±1.1		3.2±1.1		3.0±1.1	

LUTS: lower urinary tract symptom.
JST-IC: Japan Science and Technology Agency Index of Competence.
Student's t-tests were performed.

Supplemental Table 4: Crude associations between sub-types of LUTS and the life management component of JST-IC

Sub-types of LUTS		JST-IC (life management)					
		Total	p	Males	p	Females	p
Frequency	No	3.2±1.0	0.05	3.0±1.1	0.66	3.4±0.8	<0.01
	Yes	3.1±1.0		3.0±1.0		3.2±1.0	
Nocturia (Once or more)	No	3.2±1.0	0.40	3.1±1.1	0.72	3.3±0.9	0.79
	Yes	3.1±1.0		3.0±1.0		3.2±1.0	
Nocturia (Twice or more)	No	3.2±0.9	<0.01	3.1±1.0	0.25	3.3±0.9	0.03
	Yes	3.0±1.1		3.0±1.1		3.1±1.1	
Nocturia (Three times or more)	No	3.1±1.0	0.14	3.0±1.1	0.84	3.3±1.0	0.13
	Yes	3.0±1.0		3.0±1.0		3.0±0.9	
Urgency	No	3.1±1.0	0.05	3.0±1.0	0.75	3.3±0.9	0.01
	Yes	2.9±1.1		3.0±1.0		2.9±1.1	
Urinary incontinence	No	3.1±1.0	0.12	3.0±1.0	0.79	3.3±0.9	0.05
	Yes	2.9±1.2		2.9±1.1		2.8±1.2	
OAB	No	3.1±1.0	0.22	3.0±1.1	0.86	3.3±0.9	0.06
	Yes	3.0±1.0		3.0±1.0		3.0±1.1	

LUTS: lower urinary tract symptom.

JST-IC: Japan Science and Technology Agency Index of Competence.

Student's t-tests were performed.

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Supplemental Table 5: Crude associations between sub-types of LUTS and the social participation component of JST-IC

Sub-types of LUTS		JST-IC (social participation)					
		Total	p	Males	p	Females	p
Frequency	No	1.9±1.5	0.27	1.9±1.5	0.58	1.8±1.4	0.29
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Once or more)	No	2.0±1.5	0.10	2.0±1.6	0.40	1.9±1.4	0.07
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Twice or more)	No	1.8±1.4	0.29	1.9±1.5	0.29	1.7±1.4	0.29
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Three times or more)	No	1.8±1.4	<0.01	2.0±1.5	<0.01	1.7±1.4	0.14
	Yes	1.5±1.4		1.5±1.4		1.4±1.3	
Urgency	No	1.8±1.4	0.12	1.9±1.5	0.40	1.7±1.4	0.11
	Yes	1.6±1.5		1.7±1.6		1.4±1.4	
Urinary incontinence	No	1.8±1.4	0.29	1.9±1.5	0.13	1.7±1.4	0.95
	Yes	1.6±1.5		1.3±1.3		1.7±1.5	
OAB	No	1.8±1.4	0.24	1.9±1.5	0.69	1.7±1.4	0.06
	Yes	1.6±1.5		1.8±1.6		1.3±1.4	

LUTS: lower urinary tract symptom.
JST-IC: Japan Science and Technology Agency Index of Competence.
Student's t-tests were performed.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	6-7
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
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	7-8
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(e) Describe any sensitivity analyses	n/a
Results			

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	5-6
		(b) Give reasons for non-participation at each stage	5-6
		(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	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
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	10
		(b) Report category boundaries when continuous variables were categorized	7-8
		(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
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
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	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
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	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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.

BMJ Open

Lower urinary tract symptoms and functional ability in older adults: A community-based cross-sectional study

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Lower urinary tract symptoms and functional ability in older adults: A community-based cross-sectional study

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Abbreviations: LUTS, lower urinary tract symptoms; OAB, overactive bladder; QOL, quality of life; ADL, activities of daily living; JST-IC, Japan Science and Technology Agency Index of Competence; AOR, adjusted odds ratio; CI, confidence interval

Word count: 1,838

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ABSTRACT

Objectives: Functional ability, or the ability to live actively in older age, is essential for healthy aging. This study assessed the association between the five types of LUTS and functional ability among community-dwelling older adults (≥ 65 years old).

Design: Cross-sectional study.

Setting: Community-dwelling older adults (≥ 65 years old) randomly selected from the basic resident register of Kashiwa City as part of the Kashiwa study.

Participants: The study included 916 community-dwelling older adults (481 males) in Japan.

Outcome measures: A self-administered questionnaire was used to collect data regarding LUTS, which included frequency, nocturia, urgency, urinary incontinence, and overactive bladder (OAB). Functional ability was measured using the Japan Science and Technology Agency Index of Competence. Sex-stratified logistic regression analyses were conducted, adjusting age, obesity, alcohol consumption, polypharmacy, and comorbidities.

Results: Males experienced symptoms of frequency, nocturia, urgency, urinary incontinence, and OAB at rates of 68.0%, 89.0%, 16.0%, 3.7%, and 4.3%, respectively. Females experienced these symptoms at rates of 68.3%, 80.0%, 11.0%, 7.4%, and 8.5%, respectively. Among males, lower functional ability was only associated with nocturia (≥ 3 times/night) (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower functional ability among females was significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

Conclusion: The different associations between LUTS and functional ability by sex might be related to differences in the effect of comorbidities and physical fatigue. Our results help clarify the multifaceted effects of LUTS in old age, the need for early detection and treatment of LUTS, and the importance of maintaining functional ability.

58 **Strengths and limitations of this study**

- 59 ● The study participants were selected from randomly recruited older adults in a city.
- 60 ● Functional ability, an essential concept for healthy aging, was measured using a comprehensive scale.
- 61 ● Recall bias is undeniable because a self-administered questionnaire was used to measure lower
62 urinary tract symptoms.
- 63 ● A cross-sectional design precludes a conclusion regarding the causality of the relationship.

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65 **Keywords:** lower urinary tract symptoms, functional ability, healthy aging, older adults

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INTRODUCTION

The concept of “healthy aging” provides a different perspective regarding the quality of life (QOL) of older adults [1] and was defined by the World Health Organization as “the process of developing and maintaining the functional ability that enables wellbeing in older age”.[2] Functional ability includes a person’s ability to fulfill their basic needs, learn, grow, make decisions, be mobile, build and maintain relationships, and contribute to society. This perspective re-frames older adults as individuals who can facilitate their healthy aging rather than being passive receivers of support. Moreover, the maintenance of functional ability to achieve healthy aging is becoming an important theme in countries with aging populations.[3]

Lower urinary tract symptoms (LUTS) include problems with storage, voiding, or post-micturition functions and are not limited to specific sexes, ages, or regions.[4] A study using the International Continence Society’s definitions estimated that 45.2% of the global population of individuals who are >20 years old have at least one LUTS.[5] Furthermore, LUTS is more prevalent among older adults, with one international population-based study estimating that 80.7% of older men and 79.3% of older women (>60 years old) have at least one type of LUTS, such as nocturia.[6] However, despite the high prevalence of LUTS, the consultation rate remains low. [7] As global population aging continues, the proportion of individuals suffering from LUTS might increase, especially among older adults.[8, 9]

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7 85 The presence of LUTS can negatively affect individuals' QOL,[10, 11] and storage-related
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10 86 symptoms (e.g., nocturia, urgency, or urinary incontinence) have negative and significant
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13 87 detrimental effects on people's QOL.[12, 13] For example, nocturia (≥ 2 times/night) can lead to
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16 88 decreased QOL due to interrupted sleep,[14] falls on the way to the toilet,[15] and fall-related
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19 89 fractures.[16] Urinary incontinence also affects QOL, which is related to the severity, type, and
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22 90 number of incontinent episodes.[17] Moreover, QOL tends to decrease with age, suggesting that
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25 91 older adults face a double burden of increased LUTS and decreased QOL.

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27 92 In recent years, studies have been conducted to clarify the association between LUTS and
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30 93 more complex abilities than activities of daily living (ADL). An American study analyzed data from
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33 94 the National Health and Nutrition Examination Surveys and found a significant association between
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36 95 urinary incontinence and functional limitations, such as difficulty stooping, crouching, or kneeling,
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39 96 in women in the community.[18] In a longitudinal study of community-dwelling older men, the risk
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42 97 of onset of functional limitations (mobility, ADL, and cognitive dysfunctions) two years later was
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45 98 examined in relation to the severity of LUTS. The results showed that the more severe the LUTS, the
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48 99 worse the mobility and ADL, but not cognitive dysfunction.[19] In order to promote healthy aging, it
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51 100 will be important to add the research considering the association between various types of LUTS and
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54 101 more complex abilities. Therefore, this study aimed to compare five types of LUTS with a
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57 102 comprehensively assessed functional ability in community-dwelling older adults.
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104 **MATERIAL AND METHODS**

105 We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) cross-

106 sectional reporting guidelines.[20]

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108 **Participants**

109 The study participants were selected from a community-based study in Kashiwa City, Japan (the

110 Kashiwa study). The Kashiwa study evaluated 2,044 community-dwelling older adults (≥ 65 years

111 old) who were randomly selected from the basic resident register of Kashiwa City in 2012. Surveys

112 were performed every 1–2 years, and the present study evaluated information on participants of the

113 2016 survey when questions regarding LUTS were introduced. A total of 1,339 individuals who

114 were not in long-term care participated in the 2016 survey. Among them, we excluded 423

115 individuals with cognitive dysfunction (Mini-Mental State Examination score of ≤ 23) to ensure the

116 reliability of the data collected by the self-administered questionnaire, gait problems (whether they

117 reported that they could walk without any help) to eliminate the effects of physical movement

118 restrictions on functional ability and LUTS, or missing data regarding the main variables. Finally,

119 the present study evaluated data from 916 participants (481 males and 435 females).

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121 **Ethical considerations**

122 The study protocol was approved by the Ethics Committee of the University of Tokyo (approval
123 numbers: 12-8 and 18-166). All participants provided written informed consent before participating
124 in the Kashiwa study.

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126 **Functional ability**

127 In this study, we evaluated functional ability using the Japan Science and Technology Agency Index
128 of Competence (JST-IC).[21, 22] The JST-IC is a validated scale to measure the level of overall
129 competence to live actively in older age with 16 items regarding new device use, information
130 collection, life management, and social participation (Figure 1). The original Japanese version of the
131 JST-IC was used in the research. The scores range from 0 to 16, with higher scores indicating greater
132 functional ability.

133

134 **Lower urinary tract symptoms**

135 To collect data on the five types of LUTS (frequency, nocturia, urgency, urinary incontinence, and
136 overactive bladder [OAB]), we used a self-administered questionnaire regarding the frequency of
137 urination during the day and night, urgency, and urinary incontinence. Frequency was defined as ≥ 8
138 urinations during the day, while nocturia was defined as ≥ 1 urination during the night. Urgency was

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139 defined as “a compelling need to urinate, due to pain or an unpleasant sensation, that is difficult to
140 defer”,[23] and the number of urinary incontinent episodes was recorded. We also considered the
141 presence of OAB, which is clinically important and prevalent among older adults, which we defined
142 as the occurrence of urgency with frequency or nocturia.

143

144 **Other variables**

145 Based on previous studies regarding LUTS,[24, 25] the following variables were selected as possible
146 confounding factors: age, obesity (body mass index of ≥ 25 kg/m²), alcohol consumption (≥ 5
147 times/week),[26] polypharmacy (≥ 6 drugs/day),[27] and comorbidities (hypertension, heart disease,
148 diabetes, and dyslipidemia).[28-31]

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150 **Data analysis**

151 Considering that the characteristics of LUTS differ depending on sex, the participants were stratified
152 according to sex. The distribution of all variables, sex differences, and the crude associations
153 between the five types of LUTS and JST-IC were examined by univariate analysis. Since no clear
154 cutoff value has been set for JST-IC, we initially planned to treat it as a continuous variable.
155 However, we changed to treat it as a categorical variable using the median (=12) for the multivariate
156 analyses due to the collected data that was not normally distributed (Shapiro-Wilk test p-value

<0.05). To determine the association of each LUTS with functional ability by sex, logistic regression analyses predicting lower JST-IC were run with the following independent variables: each LUTS (frequency, nocturia [1, 2, or ≥ 3 times per night], urgency, urinary incontinence, or OAB), age, obesity, alcohol intake, polypharmacy, and comorbidities (hypertension, heart disease, diabetes, and dyslipidemia). As the dependent variable of the logistic regression analyses, the binary variable of JST-IC in which the high and low scores were reversed was used. All statistical analyses were performed using SPSS Statistics for Windows, version 27.0 (IBM, Armonk, NY), and differences were considered statistically significant at p-values of <0.05.

Patients and public involvement

The participants were not involved in the design, conduct, reporting, or dissemination plans of our research. However, the study results will be available to the participants and the public through the open-access journal article.

RESULTS

Table 1 shows the participants' characteristics stratified by sex. Males had significantly higher proportions of obesity, alcohol consumption, polypharmacy, comorbidities (hypertension, heart disease, and diabetes), and three types of LUTS (nocturia, urgency, and OAB). On the other hand,

females had significantly higher proportions of dyslipidemia and urinary incontinence. Crude associations between each LUTS and the total score of JST-IC or its four components (new device use, information collection, life management, and social participation) are shown in supplemental tables.

Table 1. Characteristics of participants

Characteristics		Total		Males		Females		p
		n=916		n=481		n=435		
		n	(%)	n	(%)	n	(%)	
Age	Mean, SD	76.3, 5.1		76.5, 5.2		76.1, 5.0		0.22
JST-IC ^a	≥12	488	(53.3)	258	(53.6)	230	(52.9)	0.82
	<12	428	(46.7)	223	(46.4)	205	(47.1)	
Obesity ^{b,c}	BMI≥25	199	(22.0)	121	(25.6)	78	(18.1)	0.01
	BMI<25	704	(78.0)	351	(74.4)	353	(81.9)	
Alcohol	≥5 times/week	250	(27.3)	213	(44.3)	37	(8.5)	<0.01
consumption ^c	<5 times/week	665	(72.7)	268	(55.7)	397	(91.5)	
Polypharmacy ^c	≥6 drugs/day	151	(16.6)	92	(19.2)	59	(13.7)	0.03
	<6 drugs/day	758	(83.4)	386	(80.8)	372	(86.3)	
Comorbidities								
Hypertension	Yes	407	(44.4)	238	(49.5)	169	(38.9)	<0.01
	No	509	(55.6)	243	(50.5)	266	(61.1)	
Heart disease	Yes	123	(13.4)	85	(17.7)	38	(8.7)	<0.01
	No	793	(86.6)	396	(82.3)	397	(91.3)	

Diabetes	Yes	101	(11.0)	68	(14.1)	33	(7.6)	<0.01
	No	815	(89.0)	413	(85.9)	402	(92.4)	
Dyslipidemia	Yes	307	(33.5)	123	(25.6)	184	(42.3)	<0.01
	No	609	(66.5)	358	(74.4)	251	(57.7)	
LUTS ^d								
Frequency	≥8 times/daytime	624	(68.1)	327	(68.0)	297	(68.3)	0.92
Nocturia	≥1 time/night	776	(84.7)	428	(89.0)	348	(80.0)	<0.01
	≥2 times/night	419	(45.7)	267	(55.5)	152	(34.9)	<0.01
	≥3 times/night	136	(14.8)	99	(20.6)	37	(8.5)	<0.01
Urgency	≥1 time/day	125	(13.6)	77	(16.0)	48	(11.0)	0.03
Urinary incontinence	≥1 time/day	50	(5.5)	18	(3.7)	32	(7.4)	0.02
OAB ^e		106	(11.6)	69	(14.3)	37	(8.5)	<0.01

^aJST-IC: Japan Science and Technology Agency Index of Competence.

^bObesity was defined according to the Japanese guideline.[32]

^cMissing cases: 13 in obesity, 1 in alcohol consumption, 7 in polypharmacy.

^dLUTS: lower urinary tract symptom.

^eOAB: overactive bladder (frequency & nocturia [≥1] & urgency).

Figures 2 and 3 show the results of the logistic regression analyses to determine the association of each LUTS type with lower functional ability after adjustment for age, obesity, alcohol consumption, polypharmacy, and comorbidities. Among males, lower functional ability was significantly associated with nocturia (≥3 times/night) only (adjusted odds ratio [AOR]: 1.71, 95% confidence interval [CI]: 1.05–2.79). Contrarily, lower functional ability among females was

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significantly associated with frequency (AOR: 1.61, 95% CI: 1.04–2.49), urgency (AOR: 2.06, 95% CI: 1.08–3.95), and OAB (AOR: 2.43, 95% CI: 1.15–5.11).

DISCUSSION

The results indicated that nocturia (≥ 3 times/night) was significantly associated with lower functional ability among males; it was significantly associated with frequency, urgency, and OAB among females. Thus, the association of LUTS with functional ability may vary according to sex.

Nocturia was more prevalent and influential in males than in females. One of the reasons for this may be the influence of comorbidities. Male participants were more likely to have hypertension, heart disease, and diabetes which are known as risk factors for nocturia.[28-30] It is possible that these comorbidities increase nighttime urination and, at the same time, have a negative impact on various daytime activities. In addition, it is necessary to consider the effects of polypharmacy.[33] As shown in Table 1, males were taking more drugs than females. In recent years, it is known that an increase in the number of medications taken by older adults leads to adverse events.[34] Taking high doses of drugs for the treatment of comorbidities may lead to polypharmacy and reduce functional ability. Another possibility is that alcohol intake has an effect. It is known that even a small amount of alcohol has an adverse effect on health.[35] In this study, male participants consumed more alcohol, which may have a negative impact on the health that underpins functional ability. Thus, the

205 effect of nocturia may be judged to be more serious among males.

206 Lower functional ability was significantly associated with frequency, urgency, and OAB
207 only among females. This could be explained by the physical differences between males and
208 females. As shown in Table 1, female participants had a lower BMI. Weight loss and fatigue in old
209 age are strongly associated with each other and even cause frailty.[36] Toileting is a complex
210 physical activity,[37] and frequent toileting requires more physical strength and endurance. Older
211 females with lower weight could be more likely to have physical fatigue due to frequent toileting,
212 and it could lead to lower functional ability.[38]

213 The present study had several limitations. First, recall bias is undeniable because a self-
214 administered questionnaire was used to measure the frequency of urination, urgency, and urinary
215 incontinence. However, we aimed to minimize the possibility of underestimation or overestimation
216 by double-checking the responses with the participants when the questionnaires were collected.
217 Second, the relatively small sample size could have affected the results, and the cross-sectional
218 design precludes a conclusion regarding the causality of the relationship between LUTS and
219 competence. A well-designed prospective study with a larger sample size is needed to deeply
220 evaluate the causality of this relationship and the related mechanism(s).

221 This study examined the association between five types of LUTS and functional ability for
222 healthy aging. Among males, lower functional ability was associated with nocturia (≥ 3 times/night)

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223 only, while it was associated with frequency, urgency, and OAB among females. These sex-based
224 differences may be due to the sex-related difference in the effect of comorbidities and physical
225 fatigue. Our results help clarify the multifaceted effects of LUTS in old age, the need for early
226 detection and treatment of LUTS, and the importance of maintaining functional ability.

227

228 **Acknowledgments**

229 The authors are deeply thankful to the participants in this study. Also, we thank Editage
230 (www.editage.com) for English language editing.

231

232 **Conflict of interest**

233 The authors declare they have no conflict of interest with respect to this research study and paper.

234

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237

238 **Author contributions**

239 KT conceptualized the study. KT, TT, YY, MFSS, and KI collected the data. KT analyzed and
240 interpreted the data and wrote the first draft of the manuscript. TT, YY, MFSS, BKS, and KI have

241 given critical feedback. All authors contributed to reviewing and editing the manuscript.

242

243 **Data availability**

244 Data are available upon reasonable request.

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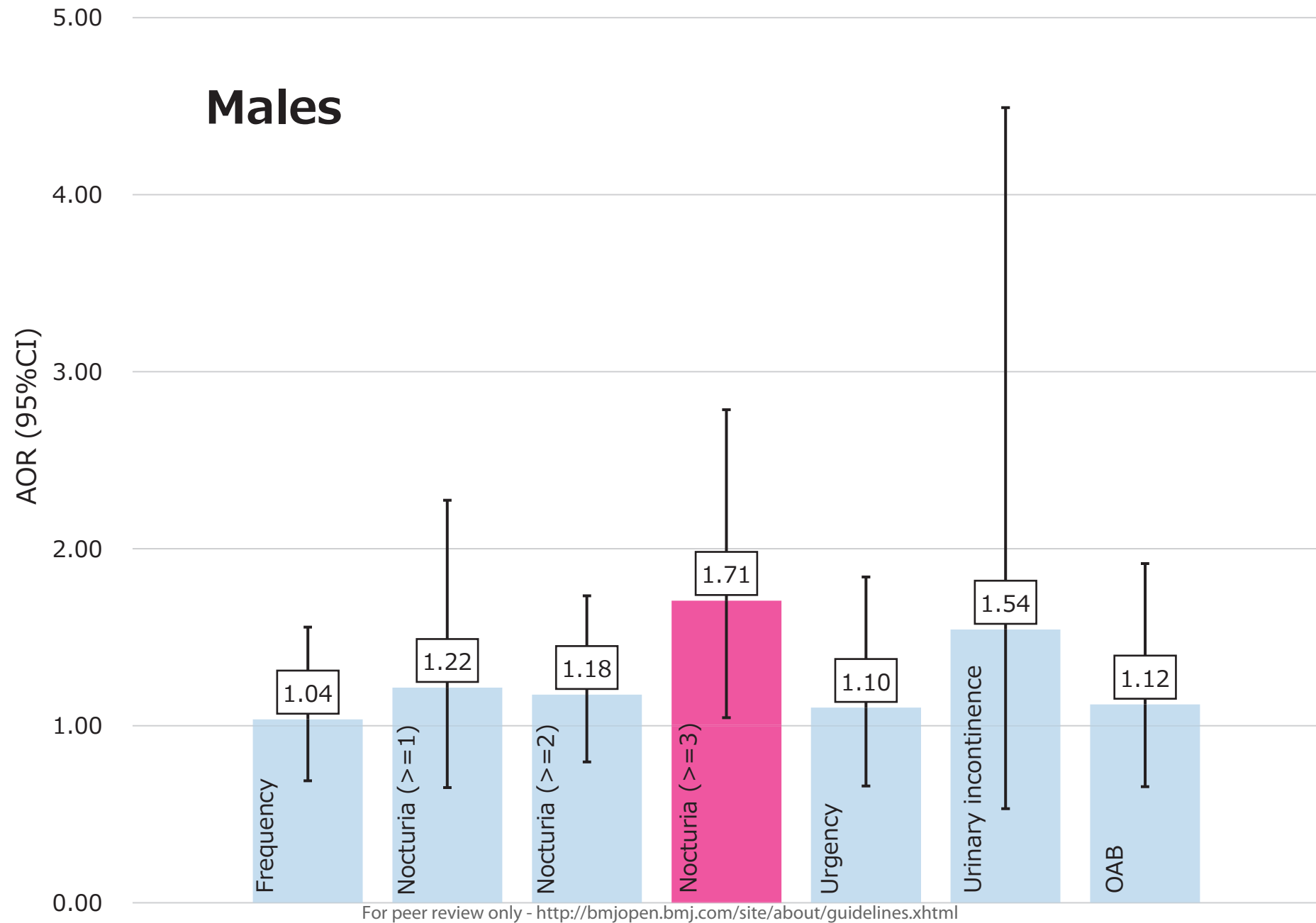
FIGURE LEGENDS

Figure 1. The English version of the Japan Science and Technology Agency Index of Competence. Scale developers translated the items from Japanese to English. The English version has not been validated.

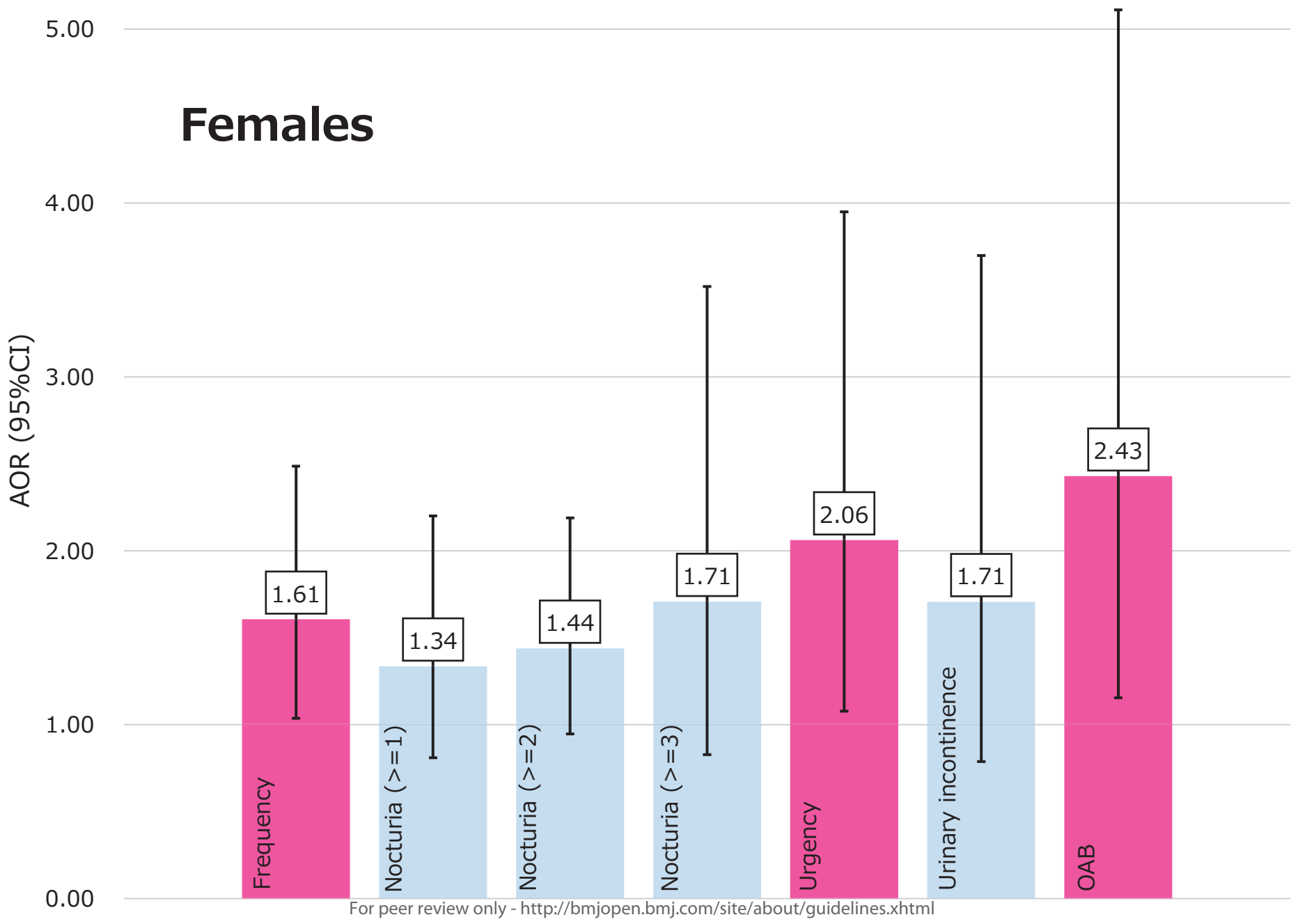
Figure 2. Results of the logistic regression analyses predicted lower functional ability with various types of LUTS in older males (n=468). The JST-IC was used as a binary dependent variable in which the high and low scores were reversed. In each analysis, age, obesity, alcohol consumption, polypharmacy, and comorbidities were adjusted.

Figure 3. Results of the logistic regression analyses predicted lower functional ability with various types of LUTS in older females (n=424). The JST-IC was used as a binary dependent variable in which the high and low scores were reversed. In each analysis, age, obesity, alcohol consumption, polypharmacy, and comorbidities were adjusted.

1. Can you use a mobile phone?
2. Can you use the ATM?
3. Can you operate a video recorder such as a Blu-ray recorder or DVD player?
4. Can you send an e-mail using a mobile phone or computer?
5. Are you interested in news and events from overseas?
6. Can you determine the credibility of health-related information?
7. Do you enjoy art, films, or music?
8. Do you watch educational/cultural programs?
9. Do you follow any measures to prevent yourself from becoming a victim of crimes.
10. Do you try to be creative while doing daily tasks (i.e., cleaning, cooking)?
11. Can you take care of an ill person?
12. Do you take care of your grandchildren, family members, or acquaintances?
13. Do you participate in regional festivals or events?
14. Do you participate in a neighborhood association or a residents' association?
15. Would you be able to assume a managerial position such as an organizer in a residents' association or group activities?
16. Do you engage in charity or volunteer activities?



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Supplemental Table 1: Crude associations between sub-types of LUTS and JST-IC

Sub-types of LUTS		JST-IC (total)					
		Total	p	Males	p	Females	p
Frequency	No	11.8±2.7	<0.01	11.8±2.7	0.23	11.8±2.6	<0.01
	Yes	11.3±2.9		11.5±2.9		11.0±2.9	
Nocturia (Once or more)	No	11.9±2.8	0.03	12.1±2.8	0.15	11.8±2.8	0.06
	Yes	11.4±2.9		11.5±2.9		11.2±2.9	
Nocturia (Twice or more)	No	11.8±2.7	<0.01	12.0±2.7	<0.01	11.6±2.7	<0.01
	Yes	11.1±3.0		11.3±3.0		10.7±3.0	
Nocturia (Three times or more)	No	11.6±2.8	<0.01	11.9±2.8	<0.01	11.4±2.8	<0.01
	Yes	10.5±2.9		10.6±2.8		10.0±2.9	
Urgency	No	11.6±2.8	<0.01	11.7±2.8	0.05	11.4±2.8	<0.01
	Yes	10.7±3.1		11.0±3.1		10.2±3.2	
Urinary incontinence	No	11.5±2.8	0.01	11.6±2.9	0.08	11.4±2.7	0.08
	Yes	10.2±3.5		10.4±2.7		10.1±3.9	
OAB	No	11.5±2.8	<0.01	11.7±2.9	0.19	11.4±2.8	<0.01
	Yes	10.8±3.1		11.2±2.9		10.0±3.2	

LUTS: lower urinary tract symptom.

JST-IC: Japan Science and Technology Agency Index of Competence.

Student's t-tests were performed.

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Supplemental Table 2: Crude associations between sub-types of LUTS and the new device use component of JST-IC

Sub-types of LUTS		JST-IC (new device use)					
		Total	p	Males	p	Females	p
Frequency	No	3.4±1.0	<0.01	3.5±0.9	0.05	3.2±0.9	0.01
	Yes	3.1±1.1		3.3±1.0		2.9±1.1	
Nocturia (Once or more)	No	3.3±1.0	0.11	3.6±0.7	<0.01	3.2±1.1	0.20
	Yes	3.2±1.1		3.4±1.0		3.0±1.1	
Nocturia (Twice or more)	No	3.3±1.0	0.07	3.5±0.9	0.02	3.1±1.1	0.07
	Yes	3.1±1.1		3.3±1.1		2.9±1.1	
Nocturia (Three times or more)	No	3.3±1.0	0.03	3.5±0.9	<0.01	3.0±1.1	0.44
	Yes	3.0±1.2		3.1±1.2		2.9±1.2	
Urgency	No	3.2±1.0	0.06	3.4±1.0	0.03	3.1±1.1	0.35
	Yes	3.0±1.3		3.1±1.2		2.9±1.4	
Urinary incontinence	No	3.2±1.0	0.06	3.4±1.0	0.25	3.1±1.1	0.22
	Yes	2.9±1.3		3.1±1.2		2.8±1.3	
OAB	No	3.2±1.0	0.08	3.4±1.0	0.09	3.1±1.1	0.16
	Yes	3.0±1.2		3.2±1.1		2.7±1.5	

LUTS: lower urinary tract symptom.
JST-IC: Japan Science and Technology Agency Index of Competence.
Student's t-tests were performed.

Supplemental Table 3: Crude associations between sub-types of LUTS and the information collection component of JST-IC

Sub-types of LUTS		JST-IC (information collection)					
		Total	p	Males	p	Females	p
Frequency	No	3.4±0.9	0.21	3.4±0.8	0.74	3.5±0.9	0.15
	Yes	3.3±0.9		3.3±1.0		3.3±1.0	
Nocturia (Once or more)	No	3.5±0.8	0.18	3.4±0.8	0.57	3.5±0.8	0.22
	Yes	3.3±0.9		3.3±0.9		3.3±1.0	
Nocturia (Twice or more)	No	3.5±0.8	<0.01	3.5±0.8	<0.01	3.5±0.8	<0.01
	Yes	3.2±1.0		3.3±0.9		3.2±1.1	
Nocturia (Three times or more)	No	3.4±0.8	<0.01	3.4±0.8	<0.01	3.4±0.9	<0.01
	Yes	3.0±1.1		3.1±1.1		2.8±1.3	
Urgency	No	3.4±0.9	0.02	3.4±0.8	0.15	3.4±0.9	0.02
	Yes	3.1±1.1		3.2±1.1		3.1±1.1	
Urinary incontinence	No	3.4±0.9	<0.01	3.4±0.9	0.14	3.4±0.9	0.02
	Yes	2.9±1.2		3.1±1.1		2.8±1.2	
OAB	No	3.4±0.9	0.02	3.4±0.8	0.13	3.4±0.9	0.02
	Yes	3.1±1.1		3.2±1.1		3.0±1.1	

LUTS: lower urinary tract symptom.

JST-IC: Japan Science and Technology Agency Index of Competence.

Student's t-tests were performed.

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Supplemental Table 4: Crude associations between sub-types of LUTS and the life management component of JST-IC

Sub-types of LUTS		JST-IC (life management)					
		Total	p	Males	p	Females	p
Frequency	No	3.2±1.0	0.05	3.0±1.1	0.66	3.4±0.8	<0.01
	Yes	3.1±1.0		3.0±1.0		3.2±1.0	
Nocturia (Once or more)	No	3.2±1.0	0.40	3.1±1.1	0.72	3.3±0.9	0.79
	Yes	3.1±1.0		3.0±1.0		3.2±1.0	
Nocturia (Twice or more)	No	3.2±0.9	<0.01	3.1±1.0	0.25	3.3±0.9	0.03
	Yes	3.0±1.1		3.0±1.1		3.1±1.1	
Nocturia (Three times or more)	No	3.1±1.0	0.14	3.0±1.1	0.84	3.3±1.0	0.13
	Yes	3.0±1.0		3.0±1.0		3.0±0.9	
Urgency	No	3.1±1.0	0.05	3.0±1.0	0.75	3.3±0.9	0.01
	Yes	2.9±1.1		3.0±1.0		2.9±1.1	
Urinary incontinence	No	3.1±1.0	0.12	3.0±1.0	0.79	3.3±0.9	0.05
	Yes	2.9±1.2		2.9±1.1		2.8±1.2	
OAB	No	3.1±1.0	0.22	3.0±1.1	0.86	3.3±0.9	0.06
	Yes	3.0±1.0		3.0±1.0		3.0±1.1	

LUTS: lower urinary tract symptom.
JST-IC: Japan Science and Technology Agency Index of Competence.
Student's t-tests were performed.

Supplemental Table 5: Crude associations between sub-types of LUTS and the social participation component of JST-IC

Sub-types of LUTS		JST-IC (social participation)					
		Total	p	Males	p	Females	p
Frequency	No	1.9±1.5	0.27	1.9±1.5	0.58	1.8±1.4	0.29
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Once or more)	No	2.0±1.5	0.10	2.0±1.6	0.40	1.9±1.4	0.07
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Twice or more)	No	1.8±1.4	0.29	1.9±1.5	0.29	1.7±1.4	0.29
	Yes	1.7±1.4		1.8±1.5		1.6±1.4	
Nocturia (Three times or more)	No	1.8±1.4	<0.01	2.0±1.5	<0.01	1.7±1.4	0.14
	Yes	1.5±1.4		1.5±1.4		1.4±1.3	
Urgency	No	1.8±1.4	0.12	1.9±1.5	0.40	1.7±1.4	0.11
	Yes	1.6±1.5		1.7±1.6		1.4±1.4	
Urinary incontinence	No	1.8±1.4	0.29	1.9±1.5	0.13	1.7±1.4	0.95
	Yes	1.6±1.5		1.3±1.3		1.7±1.5	
OAB	No	1.8±1.4	0.24	1.9±1.5	0.69	1.7±1.4	0.06
	Yes	1.6±1.5		1.8±1.6		1.3±1.4	

LUTS: lower urinary tract symptom.

JST-IC: Japan Science and Technology Agency Index of Competence.

Student's t-tests were performed.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	6-7
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
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	7-8
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(e) Describe any sensitivity analyses	n/a
Results			

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	5-6
		(b) Give reasons for non-participation at each stage	5-6
		(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	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	8-10
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	10
		(b) Report category boundaries when continuous variables were categorized	7-8
		(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
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
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	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
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	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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.