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ORIGINAL RESEARCH

Treatment satisfaction among men with concurrent benign prostatic hyperplasia and erectile dysfunction treated with tadalafil or other phosphodiesterase type-5 inhibitor combinations

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Lulu K Lee[1]
Amir Goren[1]
Natalie N Boytsov[2]
Craig F Donatucci[2]
Kevin T McVary[3]

[1]Health Outcomes Practice, Kantar Health, New York, NY, [2]US Real World Outcomes Research, Eli Lily & Company, Indianapolis, IN, [3]Division of Urology, Southern Illinois University School of Medicine, Springfield, IL, USA

Correspondence: Lulu K Lee
Health Outcomes Practice, Kantar Health, 11 Madison Avenue, 12th Floor, New York, NY 10010, USA
Tel +1 650 720 2246
Fax +1 212 647 7659
Email lulu.lee@kantarhealth.com

Objective: Erectile dysfunction (ED) and benign prostatic hyperplasia (BPH) frequently co-occur in men aged ≥40, along with lower urinary tract symptoms (LUTS) secondary to BPH. Given little real-world evidence on treatment use or satisfaction with treatment for concurrent BPH/LUTS and/or ED, this study examined medication regimens and differences in satisfaction and health-related quality of life (HRQoL) across regimens among men with concurrent BPH and ED.

Methods: A cross-sectional study was conducted using an Internet survey of participants recruited through an online panel. Respondents (N=736) included men (aged ≥40) who self-reported a diagnosis of both ED and BPH with prescription treatment in the past 3 months for both conditions. Treatment satisfaction (eg, convenience and ease of planning) and HRQoL (eg, International Prostate Symptom Score, sleep quality) were self-reported. Generalized linear models examined the association of regimen with treatment satisfaction and HRQoL, adjusting for covariates (eg, age and comorbidities).

Results: Final analyses included participants (N=507) using: tadalafil once-daily monotherapy (22%), tadalafil for ED with an alternate BPH therapy (36%), or another phosphodiesterase type-5 inhibitor (PDE5-I) combination (41%). These groups represented the major categories of treatment regimens found in the sample, excluded participants with ambiguous regimens, and were aligned with current standard of care for BPH and ED. Overall, patients reported moderate levels of BPH and a moderate-to-severe degree of ED. Tadalafil monotherapy patients had higher treatment satisfaction scores and greater reported ease of treatment planning and convenience than PDE5-I combination patients. No significant intergroup differences were found on HRQoL.

Conclusion: A majority of patients (59%) took tadalafil alone or in combination for BPH/ED treatment. Tadalafil monotherapy patients reported greater treatment satisfaction than patients taking PDE5-I combination therapy. Higher satisfaction for both effectiveness and convenience of once-daily tadalafil may inform both patient and clinician decisions regarding pharmacotherapy regimens.

Keywords: once-daily tadalafil, alpha1-adrenergic blockers, 5-alpha-reductase inhibitors, International Prostate Symptom Score, treatment convenience, treatment satisfaction, Treatment Satisfaction Questionnaire for Medication

Introduction

Erectile dysfunction (ED) has been linked to benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS).[1–3] As LUTS become more severe, ED symptoms

also tend to increase in severity.[3,4] Among men aged 40–49, prevalence of concurrent LUTS and ED was 66%,[5] with higher prevalence (50%–70%) for men aged 50–80.[3] In aging men without neurologic disease, LUTS is presumed to be due to the development of prostatic disease.[6] Although the co-occurrence of BPH/LUTS and ED has long been recognized, ED as a comorbidity of BPH/LUTS has only been established recently.[2,7]

In the age of medical therapy, men with both BPH/LUTS and ED generally receive therapy directed at each condition. Systematic reviews such as the Cochrane Collaboration and specialty society clinical guidelines (American Urological Association, European Urology Association) provide evidence-based recommendations for drug therapy (alpha-blockers and 5-alpha-reductase inhibitors [5-ARIs]) and anticholinergic agents, alone or in combination, for the treatment of BPH/LUTS.[8] Similarly, evidence-based guidelines exist for the treatment of ED with phosphodiesterase type-5 inhibitors (PDE5-Is).[9] Early in the era of PDE5-I therapy for ED, Andersson et al observed that PDE5-Is might be effective in the reduction of LUTS associated with BPH,[10] while Mulhall et al first documented a reduction in International Prostate Symptom Score (I-PSS) in men with BPH/LUTS in response to the use of the PDE5-I sildenafil during the course of a randomized controlled trial (RCT) of ED.[11]

Among PDE5-Is, tadalafil is the only drug approved by regulatory agencies for single-agent treatment of comorbid BPH/LUTS and ED.[12] A systematic literature review, including RCTs on the efficacy of tadalafil, reported that BPH/LUTS and ED symptoms improved in a clinically meaningful way that reached statistical significance with an oral, once-daily dose of tadalafil, relative to placebo.[13] A recent study found significant improvements in BPH/LUTS, ED symptoms, and health-related quality of life (HRQoL) over baseline with tadalafil alone, tamsulosin alone, or a combination of the two.[14] Improvements were larger for the tadalafil–tamsulosin combination than for either of the monotherapy treatments. A meta-analysis of RCTs demonstrated that PDE5-I and alpha1-adrenergic blocker combination therapy produced statistically significant and clinically meaningful improvements in LUTS/BPH, compared with an alpha-blocker alone.[15] However, specialty society guidelines do not endorse the combination of PDE5-Is and alpha1-adrenergic blockers for the symptomatic relief of BPH/LUTS.[8]

While many studies examining the improvement in symptoms or quality of life associated with treatment exist, little is known about patient satisfaction with treatment for BPH/LUTS and/or ED. A recent RCT found that overall treatment and efficacy satisfaction was greater for tadalafil than for placebo, but no differences were found between tamsulosin and placebo.[16] Another RCT found that BPH-specific treatment satisfaction increased significantly with tadalafil, but not tamsulosin, relative to placebo.[17] As these results came from RCTs, there is a need for real-world evidence on treatment use and satisfaction among patients with concurrent BPH/LUTS and ED.

Objectives

The current study examined real-world treatment (eg, which treatments were actually prescribed, including combination vs monotherapy regimens), as well as associated treatment satisfaction and HRQoL among men who experienced both BPH and ED, to help contribute to the limited real-world evidence in spite of the known links between these conditions.[18] Predictors of treatment satisfaction among men diagnosed with concurrent BPH and ED were examined: primarily, types of pharmacological treatments, and secondarily, patient demographics and characteristics. HRQoL differences by treatment group were also examined.

Methods

Study sample

This study used data from a cross-sectional, self-reported Internet survey (fielded in 2014) in the US. Participants were recruited through the online panel of Lightspeed Research (LSR) and its affiliates. This is an opt-in panel, in which panelists choose to participate in surveys. LSR panels are formed in such a way as to approximate the demographic characteristics of the adult population in the US (ie, respondents are recruited from diverse online sources such as partner panels, opt-in emails, etc). The panel is regularly maintained by LSR, with panelists' demographic information updated routinely to ensure appropriate sample selection.

The study was originally designed to have sufficient statistical power (80%) to detect modest effect size differences (Cohen's d=0.3) across any two groups (among three equally distributed treatment groups) with two-tailed statistical significance set at α=0.05. However, as one purpose of the study was to examine natural treatment distributions within the population, there were no quotas for specific treatment regimens, and therefore the sampling plan precluded anticipating the exact sample size per final treatment group.

Male patients (≥40 years old), who self-reported a physician's diagnosis of ED and BPH and were currently taking, or had taken in the past 3 months, medication for both conditions, were recruited. Participant consent was collected electronically by way of the online survey; participants read the consent agreement and clicked on I agree to participate and then were directed to the survey. If they selected not to agree, they

exited the session. Respondents completed screening items to determine eligibility to participate. The study was approved by Sterling Institutional Review Board (Atlanta, GA, USA).

Predictor variables

Patient characteristics

Respondents' ethnicity, educational attainment, exercise, body mass index (BMI), income, age, and ED and BPH baseline severity were examined. Respondents were asked, prior to starting treatment, how mild or severe their ED, bladder emptying, and bladder storage symptoms (1= mild to 5= severe) were, to obtain baselines measures of ED and BPH severity. The Quan et al updated version of the Charlson comorbidity index (CCI)[19,20] was used to assess mortality risk associated with preexisting comorbidities. The CCI weights the presence of the following conditions and then sums the scores: HIV/AIDS, metastatic tumor, any malignancy/lymphoma/leukemia, renal disease, hemiplegia/paraplegia, mild liver disease, moderate/severe liver disease, rheumatologic disease, chronic pulmonary disease, dementia, congestive heart failure, and diabetes with end-organ damage. A higher CCI total score signifies a greater comorbidity burden.

Treatment groups

The treatment groups included self-reported use of: 1) once-daily tadalafil only (tadalafil once-daily for both BPH and ED), 2) tadalafil combination (tadalafil for ED with alpha-blockers and/or 5-ARIs for BPH), or 3) PDE5-I combination (non-tadalafil PDE5-I for ED with alpha-blockers and/or 5-ARIs for BPH).

Main outcome measures

Treatment satisfaction and convenience

Treatment satisfaction was assessed separately for BPH and ED medications, using the Treatment Satisfaction Questionnaire for Medication (TSQM-9)[21] and the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS).[22] The TSQM-9, a nine-item scale that can be used across multiple treatment areas, consists of three subscales (effectiveness, convenience, and global satisfaction). Subscale scores range from 0 to 100, with higher scores indicating greater treatment satisfaction.[21] The EDITS is an eleven-item disease-specific measure of ED treatment satisfaction. Scores range from 0 (extremely low treatment satisfaction) to 100 (extremely high treatment satisfaction).[22] Treatment convenience was measured using one item assessing the ease of planning for (1= extremely difficult to 7= extremely easy) and one item examining the convenience of (1= extremely inconvenient to 7= extremely convenient) taking both BPH and ED medications.

Clinical measures

BPH and ED disease-specific measures included the Sexual Health Inventory for Men (SHIM)[23] and the I-PSS.[24] The SHIM, which is a five-item version of the International Index of Erectile Function,[25] assesses severity of ED in the prior month. The SHIM includes five items measuring erectile function and produces scores indicating no ED (22–25) or mild-to-severe ED (5–21). The I-PSS is an eight-item measure of BPH/LUTS severity in the past month. Seven items assess BPH/LUTS severity (incomplete emptying, frequent urination, intermittent urination, urgency, weak stream, straining, and nocturia). Response options are summed to yield a total score ranging from 0 to 35, with higher scores indicating more severe BPH/LUTS.

HRQoL

HRQoL measures included the Jenkins Sleep Scale (JSS),[26] and one item from I-PSS.[24] The JSS is a four-item measure of HRQoL as it relates to sleep quality (difficulty falling asleep, difficulty staying asleep, waking up multiple times at night, and feeling tired after one's typical amount of sleep). Response options range from 1 (never) to 6 (every night), with higher scores reflecting poorer sleep quality.[26] A separately scored eighth item on the I-PSS measured satisfaction with one's current urinary condition on a scale of 0 (delighted) to 6 (terrible).[24]

Statistical analyses

Unadjusted, two-sample comparisons using binomial proportion tests (*z*-tests) for categorical and *t*-tests for continuous variables were conducted across treatment groups. Descriptive analyses, including percentages and frequencies (categorical variables) or means and standard deviations (continuous variables), were tabulated. Due to the a priori nature of the comparisons (eg, tadalafil vs each of the other treatment groups), no corrections for multiple comparisons were conducted. Multivariable generalized linear models were tested with different outcome measures (ie, treatment satisfaction, HRQoL, and clinical characteristics) as a function of treatment group, controlling for patient characteristics (covariates). Post hoc analyses, using Pearson's correlations, explored the validity of TSQM-9 scores, relative to disease-specific measures (eg, EDITS), for assessing BPH and ED treatment satisfaction and convenience. *P*-values <0.05 (two-tailed) were considered statistically significant.

Results

Sample characteristics

Data were collected on a total of 736 participants; however, the final sample analyzed (N=507) included only those who

self-reported taking once-daily tadalafil only (n=113, 22%), tadalafil in combination (n=184, 36%), or another PDE5-I in combination (n=210, 41%) for treating BPH and ED. Participants were excluded (n=229) from analyses if the ambiguity of their treatment regimens (eg, patients who took tadalafil and another PDE5-I) did not allow sufficient confidence of the intended indication for use. The final treatment groups analyzed therefore represented the major categories of regimens aligning with current standard of care for BPH and ED.[8,9]

The sample mean age was 61.2 years old (median =62.0 years, standard deviation [SD] =10.1 years, 25th percentile =54.0 years, 75th percentile =68.0 years, range: 40–88 years), 84.2% of respondents were white, and the mean CCI score was 0.454 (SD =1.03). Once-daily tadalafil only patients were younger than tadalafil combination and PDE5-I combination patients (56.7 vs 60.5 and 64.3 years old, $P<0.05$, respectively) and had lower comorbidity burden than PDE5-I combination patients (CCI =0.240 vs 0.600, $P<0.05$) and were more frequently obese than PDE5-I combination patients (obese BMI =40.7% vs 29.5%, $P<0.05$). However, once-daily tadalafil only patients reported higher recalled baseline bladder emptying severity than tadalafil combination and PDE5-I combination patients (1.86 vs 1.70 and 1.71, $P<0.05$). There were no differences in recalled baseline bladder storage and ED severity between treatment groups (Table 1).

In terms of treatment duration, once-daily tadalafil only patients and tadalafil combination patients on average had

Table 1 Patient demographics and characteristics

	Once-daily tadalafil only (n=113)		Tadalafil combination (n=184)		PDE5-I combination (n=210)		Total (N=507)	
Age, years (mean, SD)	56.7*,#	9.00	60.5*	10.1	64.3	9.55	61.2	10.1
Ethnicity								
White (%, n)	81.4%	92	85.3%	157	84.8%	178	84.2%	427
Black (%, n)	1.8%	2	1.1%	2	1.4%	3	1.4%	7
African-American (%, n)	0.9%	1	1.1%	2	4.3%	9	2.4%	12
Asian or Pacific Islander (%, n)	5.3%*	6	2.2%	4	1.4%	3	2.6%	13
Native American or Alaskan native (%, n)	0.0%‡	0	1.6%	3	1.9%	4	1.4%	7
Mixed racial background (%, n)	0.0%‡	0	1.1%	2	1.0%	2	0.8%	4
Other (%, n)	0.0%‡	0	0.0%‡	0	1.0%	2	0.4%	2
Declined to answer (%, n)	10.6%*	12	7.6%	14	4.3%	9	6.9%	35
Education								
<4-year degree (%, n)	42.5%	48	37.5%	69	39.5%	83	39.4%	200
4-year college degree or higher (%, n)	57.5%	65	62.5%	115	60.5%	127	60.6%	307
Annual household income								
<US$25,000 (%, n)	3.5%	4	6.5%	12	7.6%	16	6.3%	32
US$25,000 to <50,000 (%, n)	17.7%	20	16.3%	30	13.8%	29	15.6%	79
US$50,000 to <75,000 (%, n)	19.5%	22	20.7%	38	25.2%	53	22.3%	113
≥US$75,000 (%, n)	57.5%	65	52.2%	96	51.9%	109	53.3%	270
Declined to answer (%, n)	1.8%	2	4.3%	8	1.4%	3	2.6%	13
CCI score (mean, SD)	0.240*	0.909	0.410	0.883	0.600	1.170	0.454	1.03
BMI category								
Underweight (%, n)	0.9%	1	0.0%‡	0	1.4%	3	0.8%	4
Normal weight (%, n)	21.2%	24	18.5%	34	26.2%	55	22.3%	113
Overweight (%, n)	37.2%	42	47.3%	87	42.9%	90	43.2%	219
Obese (%, n)	40.7%*	46	34.2%	63	29.5%	62	33.7%	171
Exercise 20+ minutes in past month								
Exercise: 0–11 times (%, n)	57.5%	65	47.3%	87	52.9%	111	51.9%	263
Exercise: 12+ times (%, n)	42.5%	48	52.7%	97	47.1%	99	48.1%	244
Baseline bladder emptying severity (mean, SD)	1.86*,#	0.35	1.70	0.46	1.71	0.45	1.74	0.44
Baseline bladder storage severity (mean, SD)	1.82	0.38	1.82	0.39	1.76	0.43	1.79	0.41
Baseline ED severity (mean, SD)	1.96	0.21	1.92	0.27	1.92	0.27	1.93	0.26

Notes: Presented in each column are results from two-sample comparisons using binomial proportion tests or *t*-tests for categorical and continuous variables, respectively. Treatment groups: once-daily tadalafil only (tadalafil for BPH and ED), tadalafil combination (tadalafil for ED with 5-ARIs and/or alpha blockers for BPH), PDE5-I combination (non-tadalafil PDE5-I for ED with 5-ARIs and/or alpha blockers for BPH). Variables of conceptual interest are included in the table, as are a subset of all variables collected in the study. *$P<0.05$ for differences between the value shown and the value in PDE5-I combination, within a given row. #$P<0.05$ for differences between the value shown and the value in tadalafil combination, within a given row. ‡This category was not analyzed in pair-wise comparisons because its value was equal to 0 or 1.

Abbreviations: SD, standard deviation; BMI, body mass index; BPH, benign prostatic hyperplasia; CCI, Charlson comorbidity index; ED, erectile dysfunction; PDE5-I, phosphodiesterase type-5 inhibitor.

Table 2 Treatment duration

	Once-daily tadalafil only (n=113)		Tadalafil combination (n=184)		PDE5-I combination (n=210)		Total (N=507)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Tadalafil for BPH	2.20	2.43	2.11	1.82	–	–	2.17	2.26
5-ARIs	–	–	0.58	0.36	0.68	0.40	0.64	0.38
Alpha blockers	–	–	4.25	4.17	5.91	5.97	5.10	5.23
PDE5-I	–	–	–	–	5.79	4.83	5.79	4.83
Tadalafil as needed for ED	–	–	5.07	5.75	–	–	5.07	5.75
Tadalafil daily for ED	2.11	1.76	2.33	1.76	–	–	2.21	1.76

Notes: Presented as mean years on treatment. "–" indicates there was no data.
Abbreviations: SD, standard deviation; PDE5-I, phosphodiesterase type-5 inhibitor; BPH, benign prostatic hyperplasia; 5-ARI, 5-alpha-reductase inhibitors; ED, erectile dysfunction.

been taking tadalafil for slightly longer than 2 years for the treatment of BPH and ED. Patients in the tadalafil combination or PDE5-I combination groups had been using 5-ARIs for less than a year and alpha blockers for approximately 4–6 years. Patients on PDE5-I combination had been using PDE5-Is for nearly 6 years (Table 2).

Treatment satisfaction and convenience

Bivariate comparisons

For ED treatment satisfaction, once-daily tadalafil only patients scored higher than tadalafil combination and PDE5-I combination patients on TSQM-9 effectiveness (70.0 vs 60.8 and 56.5, respectively), convenience (83.1 vs 74.7 and 68.6), and global satisfaction subscales (71.1 vs 60.7 and 54.4), all $P<0.05$. Additionally, once-daily tadalafil only patients reported higher EDITS scores than tadalafil combination and PDE5-I combination patients (80.2 vs 70.0 and 66.3, $P<0.05$). For BPH treatment satisfaction, once-daily tadalafil only patients also scored higher than tadalafil combination and PDE5-I combination respondents on TSQM-9 effectiveness (69.0 vs 60.7 and 58.0, respectively), convenience (82.5 vs 78.1 and 76.7), and global satisfaction subscales (70.3 vs 61.8 and 57.6), all $P<0.05$. Once-daily tadalafil only patients, compared with tadalafil combination and PDE5-I combination patients, found it much easier to plan for the use of the medication (38.1% vs 23.9% and 14.8%, $P<0.05$) and more convenient to take it (38.9% vs 25.5% and 20.0%, $P<0.05$) (Table 3).

Multivariable comparisons

Covariates in the multivariable models included: age, CCI score, education (<4-year degree vs 4-year or greater degree), exercise (0–11 times a month vs 12 times or more a month), ethnicity (Hispanic vs non-Hispanic), ED baseline severity, income (<US$25,000, US$25,000 to <50,000, US$50,000 to <75,000, or declined to answer, vs ≥US$75,000), and BMI (underweight, overweight, or obese, vs normal weight).

While simultaneously controlling for other covariates, treatment group remained a significant predictor of treatment satisfaction. Once-daily tadalafil only patients scored higher on all measures of treatment satisfaction than PDE5-I combination patients. Relative to PDE5-I combination patients, once-daily tadalafil only patients scored 12.3 points higher on TSQM-9 global for BPH medications, 15.0 points higher on TSQM-9 global for ED medications, and 11.0 points higher on EDITS, all $P<0.001$. Once-daily tadalafil only patients reported greater ease of planning (adjusted means: 6.03 vs 5.04) and greater convenience (adjusted means: 6.04 vs 5.20) for both BPH and ED medications than PDE5-I combination patients, all $P<0.001$ (data not shown). Other significant predictors of BPH treatment satisfaction (TSQM-9: global) included younger age, lower ED baseline severity, having annual income <US$25,000, and lower BMI. Other significant predictors of ED treatment satisfaction (TSQM-9: global and EDITS) included younger age, lower ED baseline severity, and lower BMI (Table 4).

HRQoL and disease severity

Bivariate comparisons

The mean I-PSS score (16.0) and the mean SHIM score (13.4) for the entire sample indicated moderate levels of BPH and moderate to severe levels of ED, respectively. Relative to tadalafil combination patients, once-daily tadalafil only patients had less severe ED as measured by the SHIM (14.7 vs 12.6), $P<0.05$. There were no significant differences in BPH severity (I-PSS) between treatment groups. Additionally, scores on the single I-PSS HRQoL item and the JSS did not differ significantly between treatment groups (Table 5).

Multivariable comparisons

After controlling for patient characteristics, there were no significant differences in disease-specific symptom severity (ie, SHIM and I-PSS) and BPH or ED HRQoL outcomes (ie, I-PSS and JSS) between treatment groups (data not shown).

Table 3 Treatment satisfaction

	Once-daily tadalafil only (n=113)		Tadalafil combination (n=184)		PDE5-I combination (n=210)		Total (N=507)	
EDITS total score (mean, SD)	80.2*,#	16.8	70.0	23.3	66.3	22.5	70.8	22.3
TSQM-9 effectiveness: ED treatment (mean, SD)	70.0*,#	19.9	60.8	21.9	56.5	22.9	61.1	22.4
TSQM-9 convenience: ED treatment (mean, SD)	83.1*,#	16.8	74.7*	18.2	68.6	18.5	74.1	18.9
TSQM-9 global satisfaction: ED treatment (mean, SD)	71.1*,#	21.1	60.7*	23.0	54.4	25.5	60.4	24.5
TSQM-9 effectiveness: BPH treatment (mean, SD)	69.0*,#	19.2	60.7	19.7	58.0	22.1	61.5	21.0
TSQM-9 convenience: BPH treatment (mean, SD)	82.5*,#	16.8	78.1#	17.0	76.7	20.1	78.5	18.4
TSQM-9 global satisfaction: BPH treatment (mean, SD)	70.3*,#	21.2	61.8	22.3	57.6	25.5	61.9	23.9
How easy or difficult is it to plan when you will use the medication(s) (both BPH and ED) each time?								
Extremely difficult (%, n)	0.0%‡	0	0.5%	1	0.0%‡	0	0.2%	1
Very difficult (%, n)	0.0%‡	0	0.0%‡	0	1.9%	4	0.8%	4
Difficult (%, n)	0.9%*	1	3.3%	6	6.7%	14	4.1%	21
Somewhat easy (%, n)	11.5%*	13	19.6%	36	25.2%	53	20.1%	102
Easy (%, n)	15.9%*	18	23.9%	44	28.6%	60	24.1%	122
Very easy (%, n)	33.6%*	38	28.8%	53	22.9%	48	27.4%	139
Extremely easy (%, n)	38.1%*,#	43	23.9%*	44	14.8%	31	23.3%	118
Mean (mean, SD)	6.00*,#	1.00	5.00*	1.00	5.00	1.00	5.00	1.00
How convenient or inconvenient is it to take the medication(s) (both BPH and ED) as instructed?								
Extremely inconvenient (%, n)	0.0%‡	0	0.5%	1	0.5%	1	0.4%	2
Very inconvenient (%, n)	0.0%‡	0	0.0%‡	0	1.9%	4	0.8%	4
Inconvenient (%, n)	2.7%	3	1.6%	3	4.8%	10	3.2%	16
Somewhat convenient (%, n)	5.3%*,#	6	19.0%	35	22.4%	47	17.4%	88
Convenient (%, n)	22.1%	25	22.8%	42	27.1%	57	24.5%	124
Very convenient (%, n)	31.0%	35	30.4%	56	23.3%	49	27.6%	140
Extremely convenient (%, n)	38.9%*,#	44	25.5%	47	20.0%	42	26.2%	133
Mean (mean, SD)	6.00*,#	1.00	6.00*	1.00	5.00	1.00	6.00	1.00

Notes: Presented in each column are results from two-sample comparisons using binomial proportion tests or *t*-tests for categorical and continuous variables, respectively. Treatment groups: once-daily tadalafil only (tadalafil for BPH and ED), tadalafil combination (tadalafil for ED with 5-ARIs and/or alpha blockers for BPH), PDE5-I combination (non-tadalafil PDE5-I for ED with 5-ARIs and/or alpha blockers for BPH). *$P<0.05$ for differences between the value shown and the value in PDE5-I combination, within a given row. #$P<0.05$ for differences between the value shown and the value in tadalafil combination, within a given row. ‡This category was not analyzed in pair-wise comparisons because its value was equal to zero or one.

Abbreviations: SD, standard deviation; BPH, benign prostatic hyperplasia; ED, erectile dysfunction; EDITS, Erectile Dysfunction Inventory of Treatment Satisfaction; PDE5-I, phosphodiesterase type-5 inhibitor; TSQM-9, Treatment Satisfaction Questionnaire for Medication; 5-ARI, 5-alpha-reductase inhibitors.

Post hoc analyses

Correlations between TSQM-9 global and EDITS scores ranged from moderate to high (r=0.318 to 0.828, $P<0.001$); results were similar for correlations between TSQM-9 effectiveness and EDITS scores (r=0.344 to 0.846, $P<0.001$). Yet, the correlations between TSQM-9 convenience and EDITS scores were smaller (r=0.080, P=0.07, to r=0.602, $P<0.001$). TSQM-9 global and SHIM scores were moderately to highly correlated (r=0.289 to 0.506, $P<0.001$). TSQM-9 effectiveness and SHIM scores were strongly related (r=0.401 to 0.534, $P<0.001$), but TSQM-9 convenience and SHIM scores were less strongly associated (r=0.112 to 0.289, $P<0.05$). Full intercorrelation results are not shown.

Discussion

Although the link between BPH/LUTS and ED is well-established,[18] this current study sought to add to the limited real-world data on treatment patterns, treatment satisfaction, and HRQoL of men who experience both BPH and ED concurrently, including examining these variables as a function of medication regimen and patient characteristics.

Among the 507 respondents analyzed, 59% used tadalafil (22% of those as once-daily monotherapy and 36% in combination with 5-ARIs or alpha blockers), while an additional 41% used other PDE5-Is in combination with 5-ARIs or alpha blockers. These findings demonstrate the real-world treatment patterns of men who experienced both BPH and ED, which have not been examined in US patients (eg, Kimura et al[27] examined PDE5-Is in Japan).

After controlling for covariates, once-daily tadalafil only patients scored significantly higher on all measures of treatment satisfaction than PDE5-I combination patients. Furthermore, once-daily tadalafil only patients reported significantly greater ease of planning and convenience regarding

Table 4 BPH and ED treatment satisfaction as a function of potential predictors

Predictors	TSQM-9 global: BPH b (95% LCI, UCI)	TSQM-9 global: ED b (95% LCI, UCI)	EDITS: ED b (95% LCI, UCI)	Ease of planning: BPH and ED b (95% LCI, UCI)	Convenience: BPH and ED b (95% LCI, UCI)
Once-daily tadalafil only	12.3* (6.88, 17.8)	15.0* (9.43, 20.5)	11.0* (6.10, 15.9)	0.991* (0.709, 1.27)	0.837* (0.552, 1.12)
Tadalafil combination	3.78 (−0.793, 8.35)	5.46* (0.835, 10.1)	2.25 (−1.88, 6.38)	0.457* (0.221, 0.694)	0.385* (0.146, 0.624)
Age	−0.353* (−0.580, −0.127)	−0.390* (−0.620, −0.161)	−0.544* (−0.748, −0.339)	0.010 (−0.002, 0.021)	0.008 (−0.004, 0.019)
CCI score	0.89 (−1.10, 2.87)	−0.432 (−2.44, 1.58)	−0.242 (−2.03, 1.55)	0.022 (−0.081, 0.125)	0.030 (−0.073, 0.134)
Education: <4-year degree	1.05 (−3.48, 5.59)	−2.87 (−7.46, 1.72)	−1.66 (−5.75, 2.44)	0.092 (−0.143, 0.327)	0.141 (−0.096, 0.378)
Exercise: 0–11 times a month	0.091 (−4.03, 4.21)	2.12 (−2.05, 6.29)	0.284 (−3.43, 4.00)	0.122 (−0.091, 0.335)	0.042 (−0.173, 0.257)
Ethnicity: Hispanic	−8.70 (−18.0, 0.631)	−6.91 (−16.4, 2.54)	−0.581 (−9.01, 7.85)	0.008 (−0.475, 0.492)	0.147 (−0.340, 0.635)
ED baseline severity	−4.46* (−6.91, −2.01)	−3.48* (−5.96, −0.992)	−4.61* (−6.82, −2.39)	−0.059 (−0.186, 0.068)	−0.065 (−0.193, 0.063)
BPH baseline severity	1.26 (−0.930, 3.45)	1.66 (−0.559, 3.88)	1.16 (−0.817, 3.14)	0.034 (−0.079, 0.148)	0.010 (−0.105, 0.124)
Income: <US$25,000	9.18* (0.555, 17.8)	5.90 (−2.83, 14.6)	5.23 (−2.55, 13.0)	0.345 (−0.101, 0.792)	0.084 (−0.366, 0.534)
Income: US$25,000 to <50,000	−2.85 (−8.94, 3.25)	0.333 (−5.84, 6.51)	0.411 (−5.09, 5.92)	−0.062 (−0.378, 0.254)	−0.217 (−0.536, 0.101)
Income: US$50,000 to <75,000	−1.42 (−6.51, 3.67)	−1.19 (−6.34, 3.97)	−0.730 (−5.33, 3.87)	−0.110 (−0.374, 0.153)	−0.157 (−0.423, 0.108)
Income: declined to answer	0.092 (−12.6, 12.7)	0.478 (−12.3, 13.3)	−5.34 (−16.8, 6.08)	0.091 (−0.564, 0.746)	−0.245 (−0.906, 0.415)
BMI: underweight	−20.4 (−43.1, 2.38)	−18.3 (−41.4, 4.68)	−8.95 (−29.5, 11.6)	−0.571 (1.75, 0.606)	−0.635 (−1.82, 0.552)
BMI: overweight	−6.00* (−11.2, −0.836)	−7.59* (−12.8, −2.36)	−5.30* (−9.97, −0.634)	−0.113 (−0.381, 0.154)	−0.093 (−0.363, 0.177)
BMI: obese	−9.98* (−15.5, −4.42)	−10.8* (−16.4, −5.14)	−9.74* (−14.8, −4.73)	−0.309* (−0.597, −0.021)	−0.358* (−0.648, −0.068)

Notes: Presented in each column are the results of a single regression model predicting the outcome as a function of all predictors listed in the rows. Treatment groups: once-daily tadalafil only (tadalafil for BPH and ED), tadalafil combination (tadalafil for ED with 5-ARIs and/or alpha blockers for BPH), PDE5-I combination (non-tadalafil PDE5-I for ED with 5-ARIs and/or alpha blockers for BPH). Treatment reference group: PDE5-I combination. Patient characteristics reference groups: ethnicity, non-Hispanic; education, 4-year or more degree; exercise, 12+ times a month; BMI, normal weight; income, ≥US$75,000. *$P<0.05$, two-tailed.

Abbreviations: b, unstandardized beta coefficient; LCI, lower confidence interval; UCI, upper confidence interval; BMI, body mass index; CCI, Charlson comorbidity index; BPH, benign prostatic hyperplasia; ED, erectile dysfunction; EDITS, Erectile Dysfunction Inventory of Treatment Satisfaction; TSQM-9, Treatment Satisfaction Questionnaire for Medication; 5-ARI, 5-alpha-reductase inhibitors.

Table 5 Health-related quality of life by treatment group (as assessed at time of survey)

	Once-daily tadalafil only (n=113)		Tadalafil combination (n=184)		PDE5-I combination (n=210)		Total (N=507)	
I-PSS total (higher scores, greater severity) (mean, SD)	16.0	8.59	16.8	8.18	15.3	7.98	16.0	8.20
SHIM total (lower scores, greater severity) (mean, SD)	14.7*	5.70	12.6	6.20	13.5	6.00	13.4	6.05
I-PSS QoL: If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?								
Delighted (%, n)	3.5%	4	0.5%	1	1.0%	2	1.4%	7
Pleased (%, n)	4.4%	5	4.9%	9	5.2%	11	4.9%	25
Mostly satisfied (%, n)	14.2%	16	13.6%	25	20.0%	42	16.4%	83
Mixed (%, n)	23.9%	27	26.6%	49	29.5%	62	27.2%	138
Mostly dissatisfied (%, n)	22.1%	25	20.7%	38	21.0%	44	21.1%	107
Unhappy (%, n)	19.5%	22	20.1%	37	15.7%	33	18.1%	92
Terrible (%, n)	12.4%	14	13.6%	25	7.6%	16	10.8%	55
Jenkins sleep questionnaire total (mean, SD)	13.6	5.41	13.7	4.93	13.2	5.00	13.5	5.06

Notes: Presented in each column are results from two-sample comparisons using binomial proportion tests or *t*-tests for categorical and continuous variables, respectively. Treatment groups: once-daily tadalafil only (tadalafil for BPH and ED), tadalafil combination (tadalafil for ED with 5-ARIs and/or alpha blockers for BPH), PDE5-I combination (non-tadalafil PDE5-I for ED with 5-ARIs and/or alpha blockers for BPH). *$P<0.05$ for differences between the value shown and the value in tadalafil combination, within a given row.

Abbreviations: SD, standard deviation; PDE5-I, phosphodiesterase type-5 inhibitor; SHIM, Sexual Health Inventory for Men; BPH, benign prostatic hyperplasia; ED, erectile dysfunction; I-PSS, International Prostate Symptom Score; QoL, quality of life; 5-ARI, 5-alpha-reductase inhibitors.

their BPH and ED medications than PDE5-I combination patients. A common side-effect of alpha blockers is sexual dysfunction related to changes in ejaculation (retrograde or diminished ejaculation).[28] Thus, it is possible that the lower treatment satisfaction reported by the tadalafil combination or PDE5-I combination groups (both of which include the use of alpha blockers) compared with the once-daily tadalafil only group may be related to ejaculatory dysfunction related to alpha blockers. Aligned with this possibility, in unadjusted comparisons, SHIM scores were significantly lower, indicating higher severity among the tadalafil combination and PDE5-I combination groups compared with the once-daily tadalafil only group. However, after controlling for other confounding factors (ie, patient demographics and health characteristics), SHIM scores were no longer significantly different between treatment groups; suggesting that (to the extent that SHIM reflects ejaculatory issues) there is no evidence of residual differences in ejaculatory issues across groups. Further research utilizing a specific validated instrument measuring patient-reported ejaculatory issues is needed in order to better understand the relationship between alpha blockers, ejaculatory issues, and ED satisfaction.

No differences were detected between treatment groups on HRQoL. Although a previous meta-analysis of PDE5-I and alpha blocker combination therapy suggested a mild synergistic effect of these treatments on HRQoL,[29] for the current study, it may be that once-daily tadalafil achieved significant symptom relief, but did not accrue additional perceived benefit to the patient as measured by the HRQoL indicators (ie, a type of ceiling effect). Thus, the findings suggest that medication regimen may substantially affect patients' perceptions of both treatment satisfaction and expediency, while not differentially influencing perceived BPH- or ED-related HRQoL.

Findings appear inconsistent with prior research showing greater improvements in BPH/LUTS, ED symptoms, and HRQoL for patients taking combination therapy (tadalafil and tamsulosin) than for those using monotherapy.[14] However, a comparison between the study of Singh et al[14] and the current one is difficult due to differences in study design (prospective randomized study vs real-world, cross-sectional study, respectively) and the divergent medication regimens being compared with tadalafil.

The present findings are aligned with previous research evaluating BPH/LUTS and/or ED treatment satisfaction. The limited evidence has demonstrated that men taking tadalafil have higher overall treatment satisfaction and satisfaction with treatment effectiveness than men taking tamsulosin or a placebo.[16] Additionally, the greater ease of planning and convenience findings were consistent with prior research on patient preferences showing that a majority of patients preferred tadalafil over either sildenafil or vardenafil; patients perceived that tadalafil allowed them greater sexual spontaneity.[30] Moreover, while BPH/LUTS improved significantly with either tadalafil or tamsulosin monotherapy, relative to a placebo, only tadalafil significantly improved ED symptoms.[17] Therefore, the collective evidence suggests that men may not only be more satisfied with the efficacy of

tadalafil treatment for BPH with (or without) ED but they may also perceive this treatment to be more convenient than some alternative pharmacotherapies.

The current study adds a number of important findings to the literature. We examined men who have, and are taking medications to treat, both BPH and ED. Comparisons across treatments contribute to the limited research examining the treatment of both conditions, despite the well-established frequent concurrent manifestation of BPH/LUTS and ED in patients.[1–3] Additionally, we examined treatment satisfaction and HRQoL using a breadth of measures, such as the TSQM-9 and the JSS, which have not been previously applied to evaluate the current treatment group comparisons among men with BPH/LUTS and ED symptoms. Most studies on treatment satisfaction of BPH/LUTS or ED tend to focus on disease-specific measures. We examined post hoc how well a global measure of treatment satisfaction, the TSQM-9, correlated with disease-specific measures. Specifically, we compared the TSQM-9 with the EDITS, a commonly used measure of ED treatment satisfaction, and the SHIM, an indicator of ED severity. These findings demonstrated the value of using the TSQM-9 for measuring treatment satisfaction, as it consists of components, such as convenience, not captured by the disease-specific measures. Although symptom improvement is an informative indicator for treatment satisfaction, convenience is equally important, as it may have implications for adherence. Patients may be more likely to adhere to more convenient treatment regimens, and greater adherence may lead to better disease management.

A systematic review of prior research has shown a negative association between number of daily doses required in a medication regimen and patients' treatment compliance.[31] Additionally, treatment satisfaction has been found to be positively related to patients' intentions to continue with their current treatments.[32] In light of this evidence, it is possible that tadalafil alone, which only requires a once-daily dose and was associated with higher treatment satisfaction in the current study, may elicit better medication adherence than multiple medication regimens, among men with BPH/LUTS and ED. As very few studies have assessed treatment satisfaction for BPH/LUTS and ED, the current study provided clarification regarding this key patient-reported outcome. Lastly, we utilized a patient-reported, Internet-based survey, which helped to assess the real-world experiences of patients who may not visit a physician regularly and/or who may be reluctant to reveal sensitive, personal information via other methods.

Limitations

As a cross-sectional survey was used to collect data, causal inferences cannot be made regarding the relationships examined. Although results were consistent with BPH and ED treatment types having an impact on treatment satisfaction, it is possible that other relationships were reflected in the data (eg, unmeasured variables may have affected both choice of treatment and satisfaction). Recall bias may have introduced measurement error, given that variables were assessed via self-report. Diagnosis and prescription medication use were self-reported and not confirmed with patient medical records or prescription claims data. To overcome any inaccuracies in recollection, a prospective study should incorporate medical charts or other, more objective data on diagnosis and treatment to independently confirm patient-reported responses. Additionally, certain variables may have been less reliable than others; for example, some evidence suggests that recalled baseline severity for voiding dysfunction and ED is unreliable.[33,34] In the current study, our baseline measure of severity was based on respondent recall and thus, may not accurately reflect true severity prior to treatment. Moreover, these baseline measures were items customized for the current study and were not based on a validated instrument assessing BPH or ED severity (such as I-PSS or SHIM). A related question worth noting is how one might interpret the I-PSS and SHIM scores found in the study in the absence of corresponding pretreatment baseline scores. The mean I-PSS of the entire sample was 16.0, indicating a moderate level of BPH severity.[35] The mean SHIM score for the sample was 13.4, and scores of 21 or less indicate ED symptoms serious enough to warrant consultation with a doctor.[23] Given the relatively high treatment satisfaction found using multiple satisfaction instruments across treatment groups, a likely interpretation is that these respondents had relatively severe baseline disease status and experienced notable improvement with subsequent treatment; and as a consequence, they were satisfied with their current treatment. However, this is speculative, and a randomized, controlled experiment that measures baseline severity with a validated instrument prior to start of treatment would be needed to better control for effects of baseline severity on treatment satisfaction.

While the survey was designed to be representative of the general US adult population, it is possible that the BPH and ED subpopulation may have been selectively underrepresented, due to age- and/or technology-related limitations. For example, very frail elderly patients are less likely to complete or have access to an Internet study. Thus, the

sample may have consisted of younger, healthier men than a truly population-based methodology may have produced, resulting in the underestimation of the effects of treatment type on treatment satisfaction or HRQoL. However, study participants had moderate levels of BPH and moderate-to-severe ED. Future research will be needed to replicate and validate the ad hoc treatment convenience measures used in the present study.

Conclusion

A majority of patients (59%) in the current study were taking tadalafil alone (once-daily) or in combination for the treatment of BPH and ED, with the remaining taking a PDE5-I in combination. Patients taking once-daily tadalafil alone reported significantly greater treatment satisfaction, ease, and convenience than patients taking a non-tadalafil PDE5-I combination therapy. However, there were no significant differences between treatment groups in HRQoL. Patient characteristics such as younger age, lower baseline symptom severity, and lower BMI also predicted higher BPH or ED treatment satisfaction. Higher satisfaction for both effectiveness and convenience for once-daily tadalafil may be informative for both patients and clinicians when deciding on pharmacotherapy regimens for the treatment of concurrent BPH and ED, and these preferences may also partly be reflected in current treatment patterns.

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References

1. Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfuncion Erectil Masculina Study. *J Urol*. 2001;166:569–575.
2. McVary K. Lower urinary tract symptoms and sexual dysfunction: epidemiology and pathophysiology. *BJU Int*. 2006;97:23–28.
3. Rosen R, Altwein J, Boyle P, et al. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). *Eur Urol*. 2003;44:637–649.
4. Rosen RC, Wei JT, Althof SE, Seftel AD, Perelman MA. Association of sexual dysfunction with lower urinary tract symptoms of BPH and BPH medical therapies: results from the BPH registry. *Urology*. 2009;73:562–566.
5. McVary K, Foley KA, Long SR, Sander S, Curtice TG, Shah H. Identifying patients with benign prostatic hyperplasia through a diagnosis of, or treatment for, erectile dysfunction. *Curr Med Res Opin*. 2008;24:775–784.
6. Andersson KE, de Groat WC, McVary KT, et al. Tadalafil for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: pathophysiology and mechanism(s) of action. *Neurourol Urodyn*. 2011;30(3):292–301.
7. Cameron A, Sun P, Lage M. Comorbid conditions in men with ED before and after ED diagnosis: a retrospective database study. *Int J Impot Res*. 2006;18:375–381.
8. McVary KT, Roehrborn CG, Avins AL, et al. American Urological Association guideline: management of benign prostatic hyperplasia (BPH). Revised 2010. Available from: http://www.auanet.org/education/guidelines/benign-prostatic-hyperplasia.cfm. Accessed October 20, 2013.
9. Montague DK, Jarrow JP, Broderick GA, et al. American Urological Association guideline: the management of erectile dysfunction (2005). Available from: https://www.auanet.org/education/guidelines/erectile-dysfunction.cfm. Accessed December 8, 2015.
10. Andersson KE, Chapple CR, Höfner K. Future drugs for the treatment of benign prostatic hyperplasia. *World J Urol*. 2002;19:436–442.
11. Mulhall JP, Guhring P, Parker M, Hopps C. Assessment of the impact of sildenafil citrate on lower urinary tract symptoms in men with erectile dysfunction. *J Sex Med*. 2006;3:662–667.
12. Gravas S, Bach T, Bachmann A, et al. Guidelines on the management of non-neurogenic male lower urinary tract symptoms (LUTS), incl. benign prostatic obstruction (BPO). European Association of Urology-Update March 2015. Available from: http://www.uroweb.org/guidelines/. Accessed May 15, 2015.
13. Gacci M, Salvi M, Sebastianelli A, et al. The use of a single daily dose of tadalafil to treat the signs and symptoms of benign prostatic hyperplasia and erectile dysfunction. *Res Rep Urol*. 2013;5:99–111.
14. Singh DV, Mete UK, Mandal AK, Singh SK. A comparative randomized prospective study to evaluate efficacy and safety of combination of tamsulosin and tadalafil vs tamsulosin or tadalafil alone in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. *J Sex Med*. 2014;11:187–196.
15. Gacci M, Corona G, Salvi M, et al. A systematic review and meta-analysis of the use of phosphodiesterase 5 inhibitors alone or in combination with α-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia. *Eur Urol*. 2012;61:994–1003.
16. Oelke M, Giuliano F, Baygani SK, Melby T, Sontag A. Treatment satisfaction with tadalafil or tamsulosin vs placebo in men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH): results from a randomized, placebo-controlled study. *BJU Int*. 2014;114:568–575.
17. Oelke M, Giuliano F, Mirone V, Xu L, Cox D, Viktrup L. Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomized, parallel, placebo-controlled clinical trial. *Eur Urol*. 2012;61:917–925.
18. Seftel AD, de la Rosette J, Birt J, Porter V, Zarotsky V, Viktrup L. Coexisting lower urinary tract symptoms and erectile dysfunction: a systematic review of epidemiological data. *Int J Clin Pract*. 2012;67:32–45.
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.
20. Quan H, Li B, Couris CM, Fushimi K. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2011;173:676–682.

21. Bharmal M, Payne K, Atkinson MJ, Desrosiers MP, Morisky DE, Gemmen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. *Health Qual Life Outcomes*. 2009;7:36.
22. Althof SE, Corty EW, Levine SB, et al. EDITS: development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. *Urology*. 1999;53:793–799.
23. Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. *Int J Impot Res*. 2005; 17:307–319.
24. Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Measuring disease-specific health status in men with benign prostatic hyperplasia. *Med Care*. 1995;33:AS145–AS155.
25. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology*. 1997;49: 822–830.
26. Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol*. 1988;41: 313–321.
27. Kimura M, Shimura S, Kobayashi H, et al. Profiling characteristics of men who use phosphodiesterase type 5 inhibitors based on obtaining patterns: data from the nationwide Japanese population. *J Sex Med*. 2012; 9(6);1649–1658.
28. Kaplan SA. Side effects of α-blocker use: retrograde ejaculation. *Rev Urol*. 2009;11(Suppl 1):S14–S18.
29. Yan H, Zong H, Cui Y, Li N, Zhang Y. The efficacy of PDE5 inhibitors alone or in combination with alpha-blockers for the treatment of erectile dysfunction and lower urinary tract symptoms due to benign prostatic hyperplasia: a systematic review and meta-analysis. *J Sex Med*. 2014; 11:1539–1545.
30. Morales AM, Casillas M, Turbi C. Patients' preference in the treatment of erectile dysfunction: a critical review of the literature. *Int J Impot Res*. 2011;23:1–8.
31. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther*. 2001;23: 1296–1210.
32. Atkinson MJ, Sinha A, Hass SL, et al. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. *Health Qual Life Outcomes*. 2004;2:12.
33. Helfand BT, Fought A, Manvar AM, McVary KT. Determining the utility of recalled lower urinary tract symptoms. *Urology*. 2010;76: 442–447.
34. Salonia A, Gallina A, Briganti A, et al. Remembered International Index of Erectile Function domain scores are not accurate in assessing preoperative potency in candidates for bilateral nerve-sparing radical retropubic prostatectomy. *J Sex Med*. 2008;5:677–683.
35. Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol*. 1992;148:1549–1557.