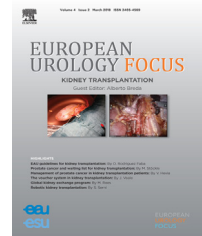


available at [www.sciencedirect.com](http://www.sciencedirect.com)

journal homepage: [www.europeanurology.com/eufocus](http://www.europeanurology.com/eufocus)



# Prostatic Urethral Lift Versus Medical Therapy: Examining the Impact on Sexual Function in Men with Benign Prostatic Hyperplasia

Claus G. Roehrborn<sup>a,\*</sup>, Daniel B. Rukstalis<sup>b</sup>

<sup>a</sup> UT Southwestern Medical Center, Dallas, TX, USA; <sup>b</sup> Prisma Health USC Medical Group, Division of Urology; 300 Palmetto Health Pkwy, Columbia, SC 29212

## Article info

### Article history:

Accepted December 17, 2020

Associate Editor: Christian Gratzke

### Keywords:

Benign prostatic hyperplasia  
Lower urinary tract symptoms  
Prostatic urethral lift  
 $\alpha$  blocker  
5 $\alpha$ -Reductase inhibitor  
Erectile function  
Ejaculatory function  
Sexual satisfaction

## Abstract

**Background:** Sexual dysfunction is a common side effect of medical therapy for benign prostatic hyperplasia (BPH), whereas prostatic urethral lift (PUL) offers safe and effective relief of lower urinary tract symptoms while preserving sexual function.

**Objective:** To compare the long-term impact on sexual health of PUL or daily medical therapy of doxazosin or finasteride alone or in combination in BPH patients.

**Design, setting, and participants:** This was a comparative analysis of sexual function outcomes from PUL studies (L.I.F.T. [ $n = 107$ ], Crossover [ $n = 42$ ], and MedLift [ $n = 39$ ]) and the Medical Therapy of Prostatic Symptoms (MTOPS) trial. The men included were sexually active with International Prostate Symptom Score  $\geq 13$ , Qmax  $\leq 12$  ml/s, and prostate volume 30–80 cm<sup>3</sup>. MTOPS subjects completed the Brief Male Sexual Function Inventory, while PUL subjects completed the International Index of Erectile Function and the Male Sexual Health Questionnaire for Ejaculatory Function.

**Outcome measurements and statistical analysis:** Mean percentage changes from baseline in erectile, ejaculatory, and sexual satisfaction domains were compared at 12, 24, 36, and 48 mo.

**Results and limitations:** PUL significantly improved erectile function through 24 mo, and ejaculatory function and sexual satisfaction across all time points. Medical therapy did not improve sexual function at any time point. Finasteride significantly decreased erectile function at 48 mo, and combined therapy significantly reduced ejaculatory function at 12 and 24 mo. Comparatively, PUL was superior to finasteride in preserving erectile function at 24 and 48 mo, and superior to doxazosin and combined therapy at 12 mo. PUL outperformed all three medical therapies at all time points in improving ejaculatory function and sexual satisfaction. Limitations include the use of distinct patient-reported questionnaires and narrowed data on comorbidities that influence male sexual function.

**Conclusions:** Indirect comparison reveals that PUL is superior to BPH medical therapy in preserving erectile and ejaculatory function and sexual satisfaction.

**Patient summary:** In our non-head-to-head study, only patients undergoing PUL for an enlarged prostate experienced improvements in sexual health. Conversely, patients on medical therapy experienced worsening of erectile and ejaculatory function.

© 2020 Published by Elsevier B.V. on behalf of European Association of Urology.

\* Corresponding author. UT Southwestern Medical Center, Dallas, TX, USA. Tel. +1 214-649-2941. E-mail address: [claus.roehrborn@utsouthwestern.edu](mailto:claus.roehrborn@utsouthwestern.edu) (C.G. Roehrborn).

## 1. Introduction

Sexual activity is highly prevalent among aging men and is an important aspect of their quality of life (QoL) [1]. Consequently, common age-related conditions that affect male sexual activity, including erectile dysfunction (ED), ejaculatory dysfunction (EjD), and benign prostatic hyperplasia (BPH), may have overlapping patient populations who are enduring repercussions such as anxiety and depression resulting from diminished QoL [2,3].

The prevalence of BPH among men amounts to 50% at age 50 yr and is as high as 90% at 80 yr of age [4]. Of this population, approximately 50% are at high risk of developing age-related sexual dysfunction [5]. The association between lower urinary tract symptoms (LUTS) and sexual dysfunction has been consistently demonstrated in multiple epidemiological and clinical studies, and it has been found that LUTS is one of the strongest predictors of male sexual dysfunction [1,6]. From a clinical perspective, the impact of BPH interventions on male sexual function has become increasingly relevant, with the American Urological Association and European Association of Urology now recommending that patients be assessed and counseled about their sexual health before and after treatment [7,8].

Within the treatment space for LUTS/BPH,  $\alpha$  blockers and 5 $\alpha$ -reductase inhibitors (5-ARIs), either alone or in combination, have gained a stronghold as first-line therapy. Although they have demonstrated clinical efficacy, their use has been associated with sexual side effects, which vary in rate among different drug classes and between members in the same class [9,10]. For example, 5-ARIs have been associated with sexual adverse events such as ED, EjD, change in libido, and gynecomastia. Alpha blockers have been linked to impaired ejaculation where the super-selective tamsulosin and silodosin have been associated with EjD, including lower ejaculate volume and anejaculation [9].

Conversely, the prostatic urethral lift (PUL) procedure using UroLift System implants is the only leading minimally invasive surgical therapy that offers rapid, significant, and durable symptom relief of LUTS without causing new,

sustained ED or EjD [11–15]. The safety profile, which consists of mild to moderate side effects that typically resolve by 2–4 wk, and effectiveness of PUL have been established in multiple clinical studies, as well as in the real-world setting in more than 1400 patients [11,12,14–16]. Non-head-to-head comparisons have demonstrated a mean International Prostate Symptom Score (IPSS) reduction of 10.6–11.4 points at 12 mo after PUL, versus 3.5–7.5 points with medication [11,12,17].

In this comparative analysis examining the impact of PUL or medical therapy on male sexual health, we challenge the idea that medical therapy is the most conservative, minimally invasive treatment option for BPH patients. Erectile, ejaculatory, and sexual satisfaction outcomes for sexually active men from three separate PUL clinical studies are combined and compared to results from the Medical Therapy of Prostatic Symptoms (MTOPS) trial, one of the largest and longest trials to assess the effects of medication on BPH progression [18].

## 2. Patients and methods

### 2.1. Patient cohorts

Extensive details of the three PUL studies used—L.I.F.T. [11], Crossover [14], and MedLift [15]—and the MTOPS [18] trial have previously been published and are summarized in Table 1. Only sexually active men in MTOPS who met the enrollment criteria of the L.I.F.T. study (IPSS  $\geq$  13, Qmax  $\leq$  12 ml/s, and prostate volume 30–80 cm<sup>3</sup>) were included in the comparative analysis.

### 2.2. Study assessments and statistics

The primary objective of this study was to examine treatment-related changes in sexual function as reported using validated patient questionnaires. PUL subjects completed the International Index of Erectile Function (IIEF) [19], and the Male Sexual Health Questionnaire for Ejaculatory Function (MSHQ-EjD) [20]. MTOPS subjects completed the Brief

**Table 1 – Design details of PUL clinical studies and the MTOPS trial and subjects used for the comparative analysis.**

Clinical study	BPH intervention	Design	Subjects used in the comparative analysis
L.I.F.T. <sup>a</sup>	PUL	RCT, sham-control FU: 5 yr	107 sexually active men aged $\geq$ 50 yr, IPSS $\geq$ 13, Qmax $\leq$ 12 ml/s, prostate volume 30–80 cm <sup>3</sup>
Crossover <sup>a</sup>	PUL	Sham-crossover FU: 5 yr	44 sexually active sham-treated men from the L.I.F.T. study who crossed over after unblinding
MedLift <sup>a</sup>	PUL	FDA IDE extension FU: 1 yr	39 sexually active men who met the inclusion criteria of the L.I.F.T. study and had an obstructive middle lobe
MTOPS	Doxazosin 4–8 mg Finasteride 5 mg Combination therapy Placebo	RCT, placebo-control FU: 5 yr	849 sexually active men with IPSS $\geq$ 13, Qmax $\leq$ 12 ml/s, prostate volume 30–80 cm <sup>3</sup>

BPH = benign prostatic hyperplasia; FU = follow-up; IPSS = International Prostate Symptom Score; PUL = prostatic urethral lift; RCT = randomized controlled trial.

<sup>a</sup> In all the PUL studies, participants were required to undergo 2 wk of washout for  $\alpha$  blockers and 3 mo for 5 $\alpha$ -reductase inhibitors before undergoing the PUL or sham procedure. Full details of the PUL procedure are published in the literature [11,15].

**Table 2 – Comparison of validated patient-reported questionnaires completed by PUL and MTOPS subjects and specific questions that encompass domains on the BMSFI, IIEF, and MSHQ-EjD instruments.**

Domain	Study	Questionnaire	Questions	Total score range
Erectile function	PUL	IIEF	1–5	0–25
	MTOPS	BMSFI	3–5	0–12
Ejaculatory function	PUL	MSHQ-EjD	1–3	0–15
	MTOPS	BMSFI	6, 7	0–8
Sexual satisfaction	PUL	IIEF	13, 14	0–10
	MTOPS	BMSFI	11	0–4
	<b>IIEF or MSHQ</b>		<b>BMSFI</b>	
Erectile function	Q1: How often were you able to get an erection during sexual activity?		Q3: How often have you had partial or full sexual erections when you were sexually stimulated in any way?	
	Q2: When you had erections with sexual stimulation, how often were your erections hard enough for penetration?		Q4: When you had erections, how often were they firm enough to have sexual intercourse?	
	Q3: When you attempted intercourse, how often were you able to penetrate (enter) your partner?		Q5: How much difficulty did you have getting an erection during the past 30 days?	
	Q4: During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?		–	
	Q5: During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse		–	
	Commonalities: frequency of erections (Q1 & Q3); firmness of erection (Q2 & Q4)			
Sexual satisfaction	Q13: How satisfied have you been with your overall sex life?		Q11: Overall, how satisfied have you been with your sex life?	
	Q14: How satisfied have you been with your sexual relationship with your partner?		–	
	Commonalities: satisfaction with sex life (Q13 & Q11)			
Ejaculatory function	MSHQ-Q1: How often have you been able to ejaculate when having sexual activity?		Q6: How much difficulty have you had ejaculating when you have been sexually stimulated?	
	MSHQ-Q2: How would you rate the strength of force of your ejaculation?		Q7: How much did you consider the amount of semen you ejaculate to be a problem for you?	
	MSHQ-Q3: How would you rate the amount of volume of semen or fluid when you ejaculate?		–	
	Commonalities: ability to ejaculate (Q1 & Q6); amount of semen (Q3 & Q7)			
BMSFI = Brief Male Sexual Function Inventory; IIEF = International Index of Erectile Function; MSHQ-EjD = Male Sexual Health Questionnaire for Ejaculatory Function; PUL = prostatic urethral lift.				

Male Sexual Function Inventory (BMSFI) [21] questionnaire. All questionnaires have specific questions that map to erectile, ejaculatory, and sexual satisfaction domains, as presented in Table 2.

Baseline characteristics including age, body mass index, prostate volume, IPSS, QoL, Benign Prostatic Hyperplasia Impact Index, and Qmax were compared between MTOPS and PUL subjects and among PUL subjects across the three studies using one-way analysis of variance. The average percentage for the maximum score was also calculated at baseline for erectile, ejaculatory, and sexual satisfaction domains. The mean percentage change per sexual function domain was then assessed at each follow-up time point. Significant differences from baseline between specific MTOPS cohorts (ie, subjects on doxazosin, finasteride, or combination therapy) and the combined PUL group were analyzed using unpaired *t* tests and 95% confidence intervals (CI). Statistical significance was set at  $p < 0.05$ . SAS 9.4 was used for all statistical analyses.

### 3. Results

#### 3.1. Baseline demographics

Among a total of 238 participants in the PUL studies, 79.6% (188/236) were sexually active (Tables 1 and 3). No significant baseline differences in erectile function ( $p = 0.5$ ), ejaculatory function ( $p = 0.5$ ), or sexual satisfaction ( $p = 0.5$ ) were observed among PUL studies. The MTOPS trial had a total of 3047 participants, of whom 34% (1038/3047) had baseline IPSS  $\geq 13$ , Qmax  $\leq 12$  ml/s, and prostate volumes of 30–80 cm<sup>3</sup>. Of these men, 81.5% (846/1038) were sexually active at baseline (Tables 1 and 3).

Compared to MTOPS participants, PUL subjects were significantly older ( $64.6 \pm 7.61$  vs  $62.4 \pm 6.84$  yr;  $p = 0.0004$ ), had larger prostate volumes ( $44.3 \pm 11.7$  vs  $38.7 \pm 9.55$  cm<sup>3</sup>;  $p < 0.0001$ ), and had a greater symptom burden (IPSS 23.0 vs 20.0; QoL 4.65 vs 3.28; Qmax 7.83 vs 8.96 ml/s; Table 3). With regard to baseline sexual function,

**Table 3 – Baseline demographics for the combined PUL and MTOPS sexually active cohorts with IPSS  $\geq 13$ , Qmax  $\leq 12$  ml/s, and prostate volume of 30–80 cm<sup>3</sup>.**

Characteristic	PUL	Doxazosin	<i>p</i> value *	Finasteride	<i>p</i> value *	Combination	<i>p</i> value *	Placebo	<i>p</i> value *
Sexually active at baseline ( <i>n</i> )	188	223		211		221		191	
Age (yr)	64.6 $\pm$ 7.61	62.5 $\pm$ 6.90	0.0042	62.7 $\pm$ 6.98	0.0112	62.4 $\pm$ 6.69	0.0027	62.0 $\pm$ 6.81	0.0008
Body mass index (kg/m <sup>2</sup> )	28.4 $\pm$ 4.32	27.8 $\pm$ 3.75	0.1075	27.5 $\pm$ 3.78	0.0325	28.0 $\pm$ 4.71	0.3899	27.8 $\pm$ 3.89	0.1237
Prostate volume (cm <sup>3</sup> )	44.3 $\pm$ 11.7	39.5 $\pm$ 10.1	<0.0001	38.2 $\pm$ 9.32	<0.0001	38.1 $\pm$ 9.72	<0.0001	38.8 $\pm$ 8.86	<0.0001
IPSS	23.0 $\pm$ 5.52	19.9 $\pm$ 4.40	<0.0001	20.1 $\pm$ 4.39	<0.0001	19.8 $\pm$ 4.86	<0.0001	20.3 $\pm$ 4.61	<0.0001
Quality-of-life score	4.65 $\pm$ 1.02	3.17 $\pm$ 1.12	<0.0001	3.27 $\pm$ 1.18	<0.0001	3.23 $\pm$ 1.20	<0.0001	3.49 $\pm$ 1.22	<0.0001
BPHII	7.00 $\pm$ 2.85	4.39 $\pm$ 2.37	<0.0001	4.51 $\pm$ 2.60	<0.0001	4.43 $\pm$ 2.65	<0.0001	4.73 $\pm$ 2.65	<0.0001
Qmax (ml/s)	7.83 $\pm$ 2.59	8.97 $\pm$ 1.99	<0.0001	9.00 $\pm$ 1.99	<0.0001	8.99 $\pm$ 2.05	<0.0001	8.87 $\pm$ 2.05	<0.0001
<b>Erectile function</b>									
IIEF (range 0–25)	16.1 $\pm$ 7.4	–	–	–	–	–	–	–	–
BMSFI (range 0–12)	–	6.8 $\pm$ 3.1	–	6.6 $\pm$ 3.2	–	6.9 $\pm$ 3.2	–	6.9 $\pm$ 3.3	–
Percentage of maximum score (%)	64	57	–	55	–	58	–	58	–
<b>Ejaculatory function</b>									
MSHQ-EjD (range 0–15)	8.9 $\pm$ 3.1	–	–	–	–	–	–	–	–
BMSFI (range 0–8)	–	6.3 $\pm$ 1.8	–	6.2 $\pm$ 1.8	–	6.3 $\pm$ 1.8	–	6.4 $\pm$ 1.6	–
Percentage of maximum score (%)	59	79	–	78	–	79	–	80	–
<b>Sexual satisfaction</b>									
IIEF (range 0–10)	6.7 $\pm$ 2.7	–	–	–	–	–	–	–	–
BMSFI (range 0–4)	–	2.1 $\pm$ 1.2	–	2 $\pm$ 1.2	–	2.1 $\pm$ 1.1	–	2.2 $\pm$ 1.2	–
Percentage of maximum score (%)	67	53	–	50	–	53	–	55	–

BMSFI = Brief Male Sexual Function Inventory; BPHII = Benign Prostatic Hyperplasia Impact Index; IIEF = International Index of Erectile Function; IPSS = International Prostate Symptom Score; MSHQ-EjD = Male Sexual Health Questionnaire for Ejaculatory Function; PUL = prostatic urethral lift.  
\**p* value versus PUL.

the PUL group had a slightly higher percentage of maximum erectile (64% vs 55–58%) and sexual satisfaction scores (67% vs 50–55%) and lower ejaculatory scores (59% vs 78–80%).

Baseline phosphodiesterase type 5 (PDE5) inhibitor use did not require washout as part of any study protocol. In the PUL group, 10% used a PDE5 inhibitor before treatment and usage remained steady: 11% of subjects used this type of drug at 48 mo after treatment. Conversely, no PDE5 inhibitor use was reported for subjects who were randomized to doxazosin, finasteride, or combination therapy; however, de novo PDE5 use increased for each medical therapy cohort once BPH treatment was initiated. At 48 mo, 23% of doxazosin, 25% of finasteride, and 24% of combination therapy subjects were using a PDE5 inhibitor.

### 3.2. Sexual function outcomes

IIEF and MSHQ scores after PUL have been previously reported in the LIFT, Crossover and MedLift trials. However, for the current analysis we observed no significant differences in erectile, ejaculatory or sexual satisfaction outcomes among PUL studies allowing for the results to be integrated into a combined PUL group.

### 3.3. Erectile function

Following PUL, subjects experienced a significant 17% (95% CI 3–30%; *p* = 0.015) and 21% (95% CI 2–39%; *p* = 0.029) improvement in erectile function at 12 and 24 mo, respectively. By contrast, doxazosin therapy had no significant effects on erectile function at any time point, while finasteride significantly reduced erectile function at 48 mo by 11%

(95% CI –20% to –1%; *p* = 0.024), and combination therapy led to a slight but nonsignificant 4% decrease (95% CI –11% to +3%; *p* = 0.272) in erectile function at 12 mo (Fig. 1 and Table 4). PUL was superior in preserving erectile function compared to doxazosin at 12 mo (*p* = 0.02) and 24 mo (*p* = 0.05), compared to finasteride at 24 mo (*p* = 0.02) and 48 mo (*p* = 0.03), and compared to combination therapy at 12 mo (*p* = 0.008).

Notably, the percentage of subjects from the combined PUL group who experiences a minimal clinically important difference (MCID) improvement in the erectile function domain (according to baseline ED severity: mild, 2; moderate, 5; severe, 7) was 42% at 12 mo, 44% at 24 mo, 46% at 36 mo, and 43% at 48 mo (Table 5). There is no similar analysis to estimate the MCID for the erectile function domain on the BMSFI in MTOPS drug cohorts.

### 3.4. Ejaculatory function

Subjects treated with PUL also experienced significant improvements in ejaculatory function over 48 mo, with mean percentage changes from baseline in ejaculatory function score reaching 35% (95% CI 22–48%; *p* < 0.0001) at 12 mo, 33% (95% CI 14–53%; *p* = 0.0009) at 24 mo, 14% (95% CI 4–24%; *p* = 0.007) at 36 mo, and 18% (95% CI 6–30%; *p* = 0.003) at 48 mo (Fig. 1 and Table 4).

Conversely, only men treated with finasteride or combination therapy experienced a decline in ejaculatory function. Among the drug therapy groups, combination therapy resulted in the greatest decrease in ejaculatory function, with a statistically significant reduction in mean ejaculatory function score relative to baseline of 17% (95% CI –23% to

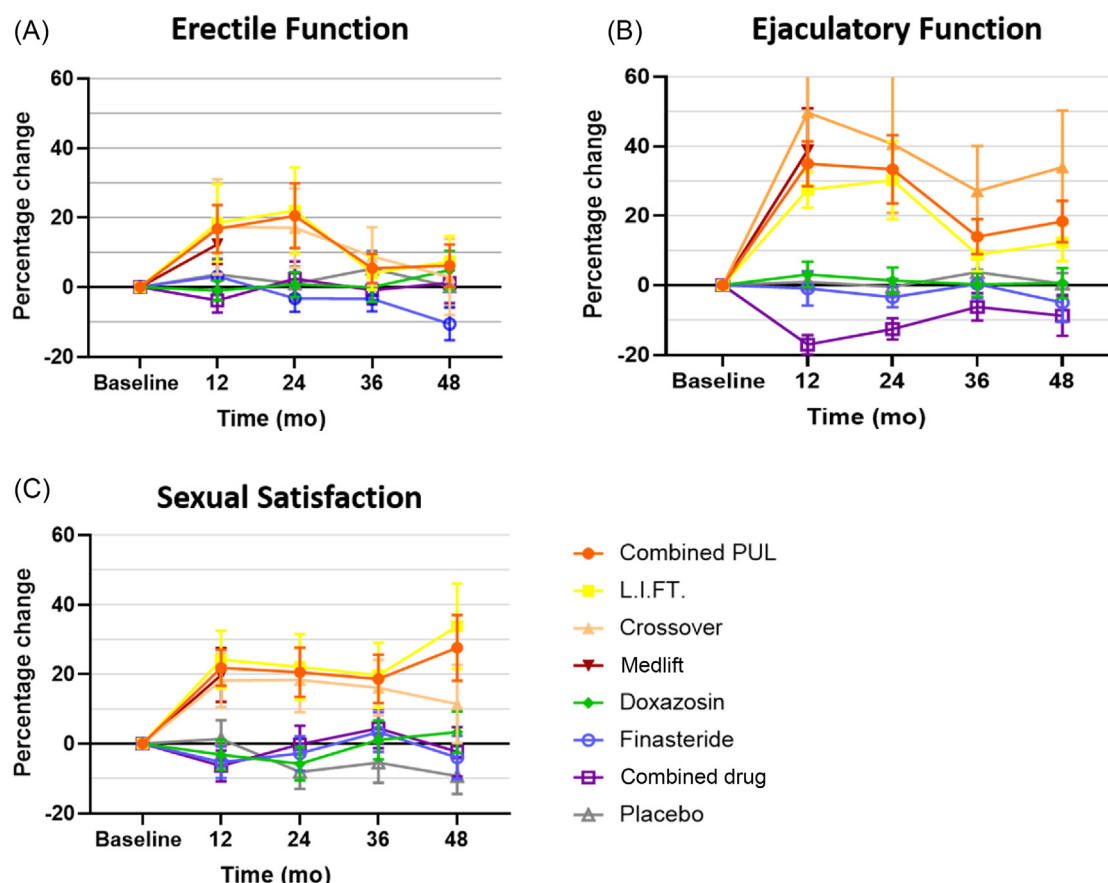


Fig. 1 – Sexual function profiles among men with lower urinary tract symptoms/benign prostatic hyperplasia treated with prostatic urethral lift (PUL) versus a daily dose of medical therapy: (A) erectile function, (B) ejaculatory function, and (C) sexual satisfaction.

–12%;  $p < 0.0001$ ) at 12 mo and 13% (95% CI –19% to –7%;  $p < 0.0001$ ) at 24 mo. In the finasteride group, ejaculatory scores decreased by between 1% (95% CI –11% to +9%;  $p = 0.8$ ) and 5% (95% CI –16% to +6%;  $p = 0.375$ ) relative to baseline, but the changes were not statistically significant. The comparative analysis between PUL and medical therapy demonstrated that only PUL significantly improved ejaculatory function at all time points (Fig. 1 and Table 4).

### 3.5. Sexual satisfaction

Subjects in the combined PUL group reported significant improvements in sexual satisfaction through 48 mo after treatment. Relative to baseline, the mean sexual satisfaction domain score following PUL increased by 22% (95% CI 12–32%;  $p < 0.0001$ ) at 12 mo, 21% (95% CI 7–35%;  $p = 0.0043$ ) at 24 mo, 19% (95% CI 5–33%;  $p = 0.009$ ) at 36 mo, and 28% (95% CI 9–46%;  $p = 0.005$ ) at 48 mo (Fig. 1 and Table 4). By contrast, subjects treated with doxazosin, finasteride, or combination therapy experienced an overall decrease in sexual satisfaction during follow-up; however, differences in the mean percentage change from baseline were not statistically significant. Overall, sexual satisfaction was

significantly enhanced in men treated with PUL versus those treated with medical therapy.

## 4. Discussion

This report is the first meta-analysis of sexual function outcomes across multiple PUL studies and the first longitudinal comparison of changes in sexual function between BPH patients treated with PUL or once-daily medical therapy from the MTOPS trial. Our findings reveal that men who received PUL experienced positive treatment effects in the three sexual function domains we examined: erectile function, ejaculatory function, and sexual satisfaction. Notably, we show that PUL not only preserved sexual function but also led to significant improvements in erectile and ejaculatory function and overall sexual satisfaction compared to baseline (Fig. 1 and Table 4).

### 4.1. $\alpha$ blockers

Ejaculation disorders are the most common side effects as a result of  $\alpha$  blocker therapy. It has been estimated that rates of EjD, including retrograde ejaculation and anejaculation,



**Table 4 – Sexual function outcomes over 4 yr after treatment with PUL or medical therapy.**

Domain	Intervention	Questionnaire	Statistic	Time point			
				12 mo	24 mo	36 mo	48 mo
Erectile function	PUL	IIEF (range 0–25)	N	159	103	93	74
			Baseline	16.2 ± 7.31	15.8 ± 7.28	16.2 ± 7.05	16.1 ± 6.78
			Follow-up	17.3 ± 7.67	16.8 ± 7.79	17.2 ± 7.86	17.2 ± 7.13
			Change	0.81	0.97	0.49	0.16
			Percentage change	17% ± 87%	21% ± 94%	5% ± 40%	6% ± 52%
			95% CI	3.24% to 30.34%	2.11% to 38.95%	–2.86% to 13.68%	–6.01% to 18.30%
			p vs baseline	0.0154	0.0293	0.1970	0.3169
	Doxazosin	BMSFI (range 0–12)	N	177	169	155	137
			Baseline	7.17 ± 2.97	7.34 ± 2.86	7.49 ± 2.81	7.12 ± 2.75
			Follow-up	6.75 ± 3.06	6.90 ± 3.07	6.83 ± 3.13	6.69 ± 3.17
			Change	–0.46	–0.46	–0.66	–0.42
			Percentage change	–1% ± 38%,	1% ± 46%	0% ± 53%	5% ± 65%
			95% CI	–6.61% to 4.61%	–6.29% to 7.78%	–8.37% to 8.31%	–6.06% to 15.86%
			p vs baseline	0.7263	0.8347	0.9944	0.3781
			p vs PUL	0.0174	0.0487	0.3598	0.8801
	Finasteride	BMSFI (range 0–12)	N	172	159	154	133
			Baseline	6.87 ± 3.24	6.77 ± 3.12	6.59 ± 3.04	6.85 ± 3.07
			Follow-up	6.46 ± 3.36	6.18 ± 3.37	6.08 ± 3.36	5.65 ± 3.25
			Change	–0.40	–0.59	–0.51	–1.2
			Percentage change	3% ± 60%	–3% ± 49%	–4% ± 44%	–11% ± 54%
			95% CI	–5.85% to 12.11%	–10.90% to 4.43%	–10.44% to 3.72%	–19.78% to –1.38%
			p vs baseline	0.4924	0.4054	0.3497	0.0244
			p vs PUL	0.0981	0.0196	0.1118	0.0306
	Combination	BMSFI (range 0–12)	N	170	170	173	127
			Baseline	7.35 ± 3.02	7.25 ± 3.05	6.97 ± 3.11	7.28 ± 3.08
			Follow-up	6.66 ± 3.27	6.58 ± 3.03	6.28 ± 3.19	6.49 ± 3.09
			Change	–0.68	–0.68	–0.70	–0.80
			Percentage change	–4% ± 45%	2% ± 64%	–1% ± 53%	1% ± 66%
			95% CI	–10.65% to 3.02%	–7.26% to 12.12%	–8.85% to 7.08%	–10.32% to 2.84%
			p vs baseline	0.2720	0.6209	0.8270	0.8301
			p vs PUL	0.0078	0.0868	0.2788	0.5637
	Placebo	BMSFI (range 0–12)	N	153	140	138	113
			Baseline	7.24 ± 3.24	7.29 ± 3.20	7.45 ± 3.15	7.51 ± 3.00
			Follow-up	6.84 ± 3.17	6.82 ± 3.31	7.17 ± 3.12	6.83 ± 3.04
			Change	–0.40	–0.48	–0.28	–0.69
			Percentage change	4% ± 57%	1% ± 58%	5% ± 60%	0% ± 62%
			95% CI	–5.38% to 12.68%	–8.72% to 10.61%	–4.80% to 15.47%	–11.36% to 11.75%
			p vs baseline	0.4258	0.8470	0.2999	0.9739
			p vs PUL	0.1120	0.0639	0.9906	0.4813

**Table 4 (Continued)**

Domain	Intervention	Questionnaire	Statistic	Time point			
				12 mo	24 mo	36 mo	48 mo
Ejaculatory function	PUL	MSHQ-EjD (range 0–15)	N	159	103	93	75
			Baseline	8.81 ± 3.18	8.81 ± 3.16	8.96 ± 3.07	8.98 ± 3.01
			Follow-up	10.7 ± 3.1	10.1 ± 3.2	9.83 ± 3.40	10.1 ± 3.4
			Change	1.78	1.27	0.73	1.01
			Percentage change	35% ± 81%	33% ± 99%	14% ± 49%	18% ± 51%
			95% CI	22.23% to 47.65%	13.95% to 52.79%	4.03% to 24.26%	6.37% to 29.82%
			p vs baseline	<0.0001	0.0009	0.0067	0.0029
	Doxazosin	BMSFI (range 0–8)	N	178	170	155	137
			Baseline	6.45 ± 1.68	6.53 ± 1.58	6.53 ± 1.60	6.44 ± 1.67
			Follow-up	6.28 ± 1.69	6.26 ± 1.75	6.20 ± 1.74	6.04 ± 1.87
			Change	–0.17	–0.27	–0.33	–0.40
			Percentage change	3% ± 49%	1% ± 49%	0% ± 44%	1% ± 50%
			95% CI	–4.06% to 10.31%	–6.03% to 8.71%	–6.74% to 7.14%	–7.88% to 9.08%
			p vs baseline	0.3916	0.7202	0.9544	0.8886
	Finasteride	BMSFI (range 0–8)	p vs PUL	<0.0001	0.0027	0.0254	0.0175
			N	174	160	156	134
			Baseline	6.26 ± 1.81	6.21 ± 1.80	6.05 ± 1.88	6.30 ± 1.73
			Follow-up	5.67 ± 1.97	5.66 ± 1.88	5.56 ± 1.93	5.43 ± 1.94
			Change	–0.59	–0.56	–0.49	–0.87
			Percentage change	–1% ± 65%	–3% ± 37%	0% ± 51%	–5% ± 64%
			95% CI	–10.73% to 8.65%	–9.16% to 2.33%	–7.75% to 8.44%	–15.98% to 6.06%
	Combination	BMSFI (range 0–8)	p vs baseline	0.8326	0.2416	0.9331	0.3750
			p vs PUL	<0.0001	0.0004	0.0359	0.0049
			N	170	170	174	127
			Baseline	6.42 ± 1.67	6.34 ± 1.74	6.24 ± 1.78	6.23 ± 1.78
			Follow-up	5.11 ± 2.11	5.17 ± 1.90	5.33 ± 2.11	5.11 ± 2.08
			Change	–1.3	–1.2	–0.90	–1.1
			Percentage change	–17% ± 36%	–13% ± 39%	–6% ± 52%	–9% ± 65%
	Placebo	BMSFI (range 0–8)	95% CI	–22.51% to –1.60%	–18.51% to –6.58%	–14.05% to 1.57%	–20.12% to 2.58%
			p vs baseline	<0.0001	<0.0001	0.1166	0.1287
			p vs PUL	<0.0001	<0.0001	0.0018	0.0012
			N	154	141	139	114
			Baseline	6.47 ± 1.56	6.57 ± 1.44	6.54 ± 1.51	6.57 ± 1.48
			Follow-up	6.33 ± 1.68	6.35 ± 1.57	6.45 ± 1.74	6.34 ± 1.71
			Change	–0.14	–0.22	–0.09	–0.23
			Percentage change	1% ± 28%	0% ± 27%	4% ± 43%	1% ± 33%
			95% CI	–3.57% to 5.47%	–4.98% to 4.16%	–3.45% to 11.00%	–5.71% to 6.55%
			p vs baseline	0.6792	0.8607	0.3033	0.8926
			p vs PUL	<0.0001	0.0010	0.0997	0.0089

**Table 4 (Continued)**

Domain	Intervention	Questionnaire	Statistic	Time point			
				12 mo	24 mo	36 mo	48 mo
Sexual satisfaction	PUL	IIEF (range 0–10)	N	156	98	89	72
			Baseline	6.73 ± 2.68	6.58 ± 2.68	6.63 ± 2.68	6.74 ± 2.67
			Follow-up	7.33 ± 2.39	7.04 ± 2.72	7.15 ± 2.45	7.51 ± 1.99
			Change	0.56	0.46	0.33	0.50
			Percentage change	22% ± 64%	21% ± 71%	19% ± 66%	28% ± 80%
			95% CI	11.69% to 31.97%	6.74% to 35.25%	4.79% to 32.52%	8.80% to 46.41%
			p vs baseline	<0.0001	0.0043	0.0089	0.0046
	Doxazosin	BMSFI (range 0–4)	N	159	154	146	120
			Baseline	2.15 ± 1.13	2.20 ± 1.09	2.29 ± 1.03	2.12 ± 1.10
			Follow-up	2.03 ± 1.13	2.09 ± 1.13	2.14 ± 1.09	2.18 ± 1.06
			Change	−0.12	−0.11	−0.15	0.06
			Percentage change	−3% ± 55%	−6% ± 60%	1% ± 68%	3% ± 66%
			95% CI	−11.87% to 5.47%	−15.24% to 3.77%	−9.98% to 12.14%	−8.53% to 15.20%
			p vs baseline	0.4675	0.2350	0.8466	0.5791
			p vs PUL	0.0002	0.0023	0.0509	0.0317
	Finasteride	BMSFI (range 0–4)	N	152	140	134	114
			Baseline	2.02 ± 1.16	1.98 ± 1.14	1.94 ± 1.15	1.92 ± 1.16
			Follow-up	1.94 ± 1.18	1.98 ± 1.09	1.86 ± 1.04	1.78 ± 1.11
			Change	−0.07	0.00	−0.08	−0.13
			Percentage change	−5% ± 56%	−3% ± 59%	3% ± 66%	−4% ± 67%
			95% CI	−14.34% to 3.70%	−12.59% to 6.99%	−7.95% to 14.67%	−16.33% to 8.43%
			p vs baseline	0.2458	0.5730	0.5580	0.5288
			p vs PUL	<0.0001	0.0070	0.0915	0.0060
	Combination	BMSFI (range 0–4)	N	155	155	157	115
			Baseline	2.16 ± 1.10	2.14 ± 1.11	2.07 ± 1.10	2.13 ± 1.10
			Follow-up	1.93 ± 1.03	1.93 ± 1.04	1.97 ± 1.03	1.90 ± 1.03
			Change	−0.24	−0.21	−0.10	−0.23
			Percentage change	−6% ± 55%	0% ± 66%	4% ± 72%	−2% ± 76%
			95% CI	−15.10% to 2.30%	−10.67% to 10.35%	−6.89% to 15.70%	−16.36% to 11.72%
			p vs baseline	0.1484	0.9758	0.4421	0.7440
			p vs PUL	<0.0001	0.0189	0.1157	0.0122
	Placebo	BMSFI (range 0–4)	N	141	128	126	104
			Baseline	2.34 ± 1.19	2.30 ± 1.21	2.33 ± 1.21	2.35 ± 1.16
			Follow-up	2.28 ± 1.13	2.11 ± 1.16	2.16 ± 1.16	2.18 ± 1.16
			Change	−0.06	−0.19	−0.16	−0.17
			Percentage change	1% ± 64%	−8% ± 55%	−5% ± 65%	−9% ± 53%
			95% CI	−9.28% to 12.00%	−17.73% to 1.59%	−16.88% to 6.04%	−19.51% to 0.92%
			p vs baseline	0.8009	0.1006	0.3507	0.0741
			p vs PUL	0.0062	0.0009	0.0085	0.0008

BMSFI = Brief Male Sexual Function Inventory; CI = confidence interval; IIEF = International Index of Erectile Function; MSHQ-EjD = Male Sexual Health Questionnaire for Ejaculatory Function; PUL = prostatic urethral lift.



**Table 5 – MCID improvement in erectile function over 4 yr after treatment with prostatic urethral lift.<sup>a</sup>**

Baseline	N	12 mo		24 mo		36 mo		48 mo	
ED severity (score range)	117	n/N	MCID increase	n/N	MCID increase	n/N	MCID increase	n/N	MCID increase
Severe (1–10)	33	3/24	15.6 (13) [13–21]	2/19	16.5 (16.5) [15–18]	0/13	NA	1/8	18
Moderate (11–16)	32	11/28	8.6 (9) [5–15]	9/18	11.7 (11) [6–17]	7/14	10.4 (9) [8–15]	6/12	10.1 (10) [5–15]
Mild (17 to <25)	52	26/44	5 (5) [2–10]	19/31	4.1 (4) [2–9]	20/32	4.6 (4.5) [2–9]	14/29	4.4 (5) [2–6]
Improved by MCID, % (n/N)		42 (40/96)		44 (30/68)		46 (27/59)		43 (21/49)	
MCID = minimal clinically important difference.									
<sup>a</sup> Results for the MCID increase are presented as mean (median) [range].									

range from 1.5% among men taking nonselective  $\alpha$  blockers, such as doxazosin, terazosin, and alfuzosin, to 4–26% among men taking tamsulosin, which exerts its greatest effect in the prostate and bladder [22]. It is thought that these effects occur via peripheral inhibition of  $\alpha_{1A}$  subtype receptors in the seminal vesicles and vas deferens, and a central effect on brain dopaminergic and serotonergic receptors [23]. Alpha blocker therapy can also result in a decrease in libido (1–4.7%) of men and ED in (0.6–6.3%) [24]. In a survey of 354 patients taking tamsulosin, 40.7% indicated that their sexual function had deteriorated within 6 mo of starting therapy [25].

Despite robust evidence demonstrating the impact of  $\alpha$  blockers on sexual function, we and others have found that men taking doxazosin in the MTOPS trial did not experience significant reductions in BMSFI erectile or ejaculatory function domains when compared to baseline (as shown here) or placebo [26]. Although these results appear to be in contrast to what we understand about  $\alpha$  blocker treatment, it is important to note that we are reporting mean questionnaire scores that may mask low adverse-event rates. For example, if 2–5% of patients experience anejaculation, the BMSFI may not show an effect, yet these percentages of patients may experience dysfunction and should be counseled appropriately. Moreover, de novo PDE5 inhibitor use was high among MTOPS subjects taking doxazosin, increasing to 23% at 48-mo follow-up, and may have contributed to the response seen in this cohort. It has also been reported that adherence rates among men taking  $\alpha$  blockers for BPH are 38.8% at 6 mo and 31.0% at 12 mo [27], potentially reflecting discontent with the therapy.

#### 4.2. 5-ARIs

Several large randomized controlled trials have shown increased incidence of erectile and EjD among subjects taking 5-ARIs in the management of LUTS/BPH [28–30]. It is believed that the mechanism underlying the sexual dysfunction induced by 5-ARIs is mediated by reduced levels of dihydrotestosterone and decreased nitric oxide synthase expression [5]. It is estimated that the prevalence of de novo sexual dysfunction following 5-ARI use ranges from 5% to 9% for ED [5] and from 1% to 5% for EjD [31].

Our findings are in line with these results, as well with outcomes reported by Fwu et al [26], who found that MTOPS subjects assigned to finasteride had significantly worsening

BMSFI scores compared to those taking placebo. Although the long-term effects after cessation remain to be elucidated, adherence rates among patients taking 5-ARIs for BPH symptoms are even lower than for patients on  $\alpha$  blockers, and have been reported to be 18% at 12 mo and only 8% at 60 mo [32].

#### 4.3. Combination therapy

Perhaps due to the combined synergistic effect of  $\alpha$  blockers and 5-ARIs, combination therapy can lead to a higher incidence of sexual dysfunction compared to either drug alone [9,8,13,33]. In a prospective study evaluating sexual adverse events among 156 BPH patients treated with medication therapy, complete absence of ejaculation was experienced by 23% of men on combined therapy, compared with 15% of those on tamsulosin alone and 5% of those on finasteride alone [34]. In the MTOPS trial, rates of ED and EjD adverse events reported were higher for combination therapy than for monotherapy and subjects assigned to combination therapy experienced the largest decrease in BMSFI scores compared to placebo [18,26]. Here we report similar results for subjects treated with combination therapy who experienced a notable decline in ejaculatory function at 12 and 24 mo ( $p < 0.0001$ ). As such, adherence rates for combination therapy are estimated to be lower than for either monotherapy, with 9% adherence at 1 yr and only 3% at 5 yr [32].

#### 4.4. PUL

In clinical studies to date, no de novo sustained ED or EjD has been reported after PUL [11–15]. The results from this indirect comparison not only support previous findings but also demonstrate that PUL can enhance erectile and ejaculatory function and sexual satisfaction after treatment. It is believed that the mechanical nature and tissue-sparing approach of PUL play a key role in preservation of sexual function. Since the bladder neck is left intact during PUL, antegrade ejaculation is preserved, and with the absence of thermal tissue damage, the risk of ED is minimal [13].

Enhancement of sexual function after PUL may be associated with improvements in urinary symptoms, with evidence suggesting significant correlations between improvements in IPSS obstructive and irritative scores and increase in sexual function and satisfaction with sex life [35,36]. Of

note, our data show that the gains in erectile and ejaculatory function domains achieved after PUL were most pronounced at 12 and 24 mo following treatment and became less significant at later time points (Fig. 1). This observation may be attributed in part to a decline in sexual function associated with age and regression to the mean [37].

A key strength of this study is the use of high-quality evidence, as demonstrated by the meta-analysis comparing sexual function outcomes from three independent PUL studies. Some limitations include the use of distinct sexual health questionnaires between the treatments compared. We relied on shared similarities between questionnaires and analyzed sexual function by assessing the percentage change between baseline and post-treatment scores in each domain, thus maintaining questionnaire integrity. The adherence rate to medical treatment in the MTOPS trial was exceptionally good, perhaps due in some part to the increase in PDE5 use that was observed for each MTOPS cohort once medical therapy was initiated. In a real-world setting, up to 70–77% of patients opt out of medical therapy during the first year of treatment [38,39] and many are dissatisfied with medication therapy because of limited therapeutic effectiveness or a suboptimal effect [40]. Despite these high rates of discontinuation reported, the choice to undergo a BPH procedure, although minimally invasive, may be unappealing for patients who wish to avoid surgery and the potential postoperative side effects that may occur such as dysuria, hematuria, and pelvic pain. Lastly, limited data were available from MTOPS and PUL studies regarding comorbidities that may influence male sexual function, including depression, diabetes, hypertension, and heart disease [37].

## 5. Conclusions

The long-term effects on sexual health in BPH patients following treatment with PUL or once-daily medical therapy reveal that PUL provides a safe and effective alternative for men who are currently underserved by medical therapy and who wish to maintain and possibly improve sexual function, a key aspect of an individual's health and QoL.

**Author contributions:** Claus G. Roehrborn had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Roehrborn.

*Acquisition of data:* Roehrborn.

*Analysis and interpretation of data:* Roehrborn, Rukstalis.

*Drafting of the manuscript:* Roehrborn.

*Critical revision of the manuscript for important intellectual content:* Roehrborn, Rukstalis.

*Statistical analysis:* Roehrborn.

*Obtaining funding:* Roehrborn.

*Administrative, technical, or material support:* Roehrborn.

*Supervision:* Roehrborn.

*Other:* None.

**Financial disclosures:** Claus G. Roehrborn certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Claus G. Roehrborn and Daniel B. Rukstalis are paid consultants for NeoTract Inc./Teleflex.

**Funding/Support and role of the sponsor:** The study was sponsored by NeoTract Inc./Teleflex. The sponsor played a role in the collection, management, analysis, and interpretation of the data, and in manuscript preparation and review.

**Acknowledgments:** We would like to thank Roula Antoon and the team at NeoTract Inc./Teleflex, especially Jacqueline Nerney Welch, Emma Flores-Kim, and Allison Najafi for their support in the preparation of this manuscript.

## References

- [1] 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;44:637–49.
- [2] Dunphy C, Laor L, Te A, Kaplan S, Chughtai B. Relationship between depression and lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Rev Urol* 2015;17:51–7.
- [3] Speakman M, Kirby R, Doyle S, Ioannou C. Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH)—focus on the UK. *BJU Int* 2015;115:508–19.
- [4] Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. *J Urol* 1984;132:474–9.
- [5] Gur S, Kadowitz PJ, Hellstrom WJ. Effects of 5- $\alpha$  reductase inhibitors on erectile function, sexual desire and ejaculation. *Expert Opin Drug Saf* 2013;12:81–90.
- [6] Vallancien G, Emberton M, Harving N, van Moorselaar RJ, Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. *J Urol* 2003;169:2257–61.
- [7] Foster HE, Dahm P, Kohler TS, et al. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline amendment 2019. *J Urol* 2019;202:592–8.
- [8] Gravas S, Cornu JN, Gacci M, et al. EAU guidelines: management of non-neurogenic male LUTS. Arnhem, The Netherlands: European Association of Urology; 2020. <https://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/>
- [9] DeLay KJ, Nutt M, McVary KT. Ejaculatory dysfunction in the treatment of lower urinary tract symptoms. *Transl Androl Urol* 2016;5:450–9.
- [10] Trost L, Saitz TR, Hellstrom WJ. Side effects of 5- $\alpha$  reductase inhibitors: a comprehensive review. *Sex Med Rev* 2013;1:24–41.
- [11] Roehrborn CG, Barkin J, Gange SN, et al. Five year results of the prospective randomized controlled prostatic urethral L.I.F.T. study. *Can J Urol* 2017;24:8802–13.
- [12] Sonksen J, Barber NJ, Speakman MJ, et al. Prospective, randomized, multinational study of prostatic urethral lift versus transurethral resection of the prostate: 12-month results from the BPH6 study. *Eur Urol* 2015;68:643–52.
- [13] Woo HH, Bolton DM, Laborde E, et al. Preservation of sexual function with the prostatic urethral lift: a novel treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Sex Med* 2012;9:568–75.

- [14] Ruktalis D, Rashid P, Bogache WK, et al. 24-Month durability after crossover to the prostatic urethral lift from randomised, blinded sham. *BJU Int* 2016;118(Suppl 3):14–22.
- [15] Ruktalis D, Grier D, Stroup SP, et al. Prostatic urethral lift (PUL) for obstructive median lobes: 12 month results of the MedLift study. *Prostate Cancer Prostat Dis* 2019;22:411–9.
- [16] Eure G, Gange S, Walter P, et al. Real-world evidence of prostatic urethral lift confirms pivotal clinical study results: 2-year outcomes of a retrospective multicenter study. *J Endourol* 2019;33:576–84.
- [17] Roehrborn CG. Current medical therapies for men with lower urinary tract symptoms and benign prostatic hyperplasia: achievements and limitations. *Rev Urol* 2008;10:14–25.
- [18] McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349:2387–98.
- [19] 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;49:822–30.
- [20] Rosen RC, Catania JA, Althof SE, et al. Development and validation of four-item version of Male Sexual Health Questionnaire to assess ejaculatory dysfunction. *Urology* 2007;69:805–9.
- [21] O'Leary MP, Fowler FJ, Lenderking WR, et al. A brief male sexual function inventory for urology. *Urology* 1995;46:697–706.
- [22] Kaplan SA. Side effects of alpha-blocker use: retrograde ejaculation. *Rev Urol* 2009;11(Suppl 1):S14–8.
- [23] Gacci M, Eardley I, Giuliano F, et al. Critical analysis of the relationship between sexual dysfunctions and lower urinary tract symptoms due to benign prostatic hyperplasia. *Eur Urol* 2011;60:809–25.
- [24] van Dijk MM, de la Rosette JJ, Michel MC. Effects of alpha<sub>1</sub>-adrenoceptor antagonists on male sexual function. *Drugs* 2006;66:287–301.
- [25] Zlotta AR, Teillac P, Raynaud JP, Schulman CC. Evaluation of male sexual function in patients with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), tamsulosin or finasteride. *Eur Urol* 2005;48:269–76.
- [26] Fwu CW, Eggers PW, Kirkali Z, McVary KT, Burrows PK, Kusek JW. Change in sexual function in men with lower urinary tract symptoms/benign prostatic hyperplasia associated with long-term treatment with doxazosin, finasteride and combined therapy. *J Urol* 2014;191:1828–34.
- [27] Schoenfeld MJ, Shortridge EF, Gelwicks SC, Cui Z, Wong DG. Treatment patterns in alpha-blocker therapy for benign prostatic hyperplasia. *Am J Mens Health* 2014;8:267–72.
- [28] Gormley GJ, Stoner E, Bruskewitz RC, et al. The effect of finasteride in men with benign prostatic hyperplasia. The Finasteride Study Group. *N Engl J Med* 1992;327:1185–91.
- [29] McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. Finasteride Long-Term Efficacy and Safety Study Group. *N Engl J Med* 1998;338:557–63.
- [30] Roehrborn CG, Boyle P, Nickel JC, et al. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. *Urology* 2002;60:434–41.
- [31] Kapoor A. Benign prostatic hyperplasia (BPH) management in the primary care setting. *Can J Urol* 2012;19(Suppl 1):10–7.
- [32] Cindolo L, Pirozzi L, Fanizza C, et al. Drug adherence and clinical outcomes for patients under pharmacological therapy for lower urinary tract symptoms related to benign prostatic hyperplasia: population-based cohort study. *Eur Urol* 2015;68:418–25.
- [33] Roehrborn CG, Siami P, Barkin J, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. *Eur Urol* 2010;57:123–31.
- [34] Stojanovic N, Ignjatovic I, Djenic N, Bogdanovic D. Adverse effects of pharmacological therapy of benign prostatic hyperplasia on sexual function in men. *Srp Arh Celok Lek* 2015;143:284–9.
- [35] Nakamura M, Fujimura T, Nagata M, et al. Association between lower urinary tract symptoms and sexual dysfunction assessed using the core lower urinary tract symptom score and International Index of Erectile Function-5 questionnaires. *Aging Male* 2012;15:111–4.
- [36] Jung JH, Jae SU, Kam SC, Hyun JS. Correlation between lower urinary tract symptoms (LUTS) and sexual function in benign prostatic hyperplasia: impact of treatment of LUTS on sexual function. *J Sex Med* 2009;6:2299–304.
- [37] Camacho ME, Reyes-Ortiz CA. Sexual dysfunction in the elderly: age or disease? *Int J Impot Res* 2005;17(Suppl 1):S52–6.
- [38] Cindolo L, Pirozzi L, Sountoulides P, et al. Patient's adherence on pharmacological therapy for benign prostatic hyperplasia (BPH)-associated lower urinary tract symptoms (LUTS) is different: is combination therapy better than monotherapy? *BMC Urol* 2015;15:96.
- [39] Zabkowski T, Saracyn M. Drug adherence and drug-related problems in pharmacotherapy for lower urinary tract symptoms related to benign prostatic hyperplasia. *J Physiol Pharmacol* 2018;69:639–45.
- [40] Fourcade RO, Lacoïn F, Roupert M, et al. Outcomes and general health-related quality of life among patients medically treated in general daily practice for lower urinary tract symptoms due to benign prostatic hyperplasia. *World J Urol* 2012;30:419–26.