Real-world therapeutic management and evolution of patients with benign prostatic hyperplasia in primary care and urology in Spain

Bernardino Miñana1 | José Maria Molero2 | Alfonso Agra Rolán3 | Miguel Téllez Martínez-Fornes4 | Rafael Cuervo Pinto3 | David Lorite Mingot3 | Ágata Carreño5 | Juan Manuel Palacios-Moreno6

1Urology Department, University Clinic of Navarra, Pamplona, Spain | 2Primary Care Centre San Andrés, Madrid, Spain | 3Medical Department, GlaxoSmithKline, Madrid, Spain | 4Department of Urology, Severo Ochoa University Hospital, Madrid, Spain | 5Health Economics and Outcomes Research—Real World Insights (HEOR-RWI), IQVIA, Madrid, Spain | 6Global Medical Classic and Established Products, GlaxoSmithKline, Madrid, Spain

Correspondence
Juan Manuel Palacios-Moreno, Global Medical Classic and Established Products, GlaxoSmithKline, Tres Cantos, Madrid, Spain.
Email: juan-manuel.m.palacios@gsk.com

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Abstract
Objectives: This study aimed to describe the real-world therapeutic management of patients with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) (LUTS/BPH) attending primary care and urology clinics in Spain.

Methods: This observational, retrospective, multicentre study included men ≥50 years of age diagnosed with LUTS/BPH (≤8 years prior to study visit) (N = 670). Therapeutic management according to healthcare service (primary care vs. urology clinics) or progression criteria, proportion of patients with treatment change, patient profile according to therapy and evolution of LUTS severity were assessed.

Results: Overall differences were noticed in the management of patients between healthcare service (P < .001) and with or without progression criteria (P < .05). Most patients received pharmacological treatment at diagnosis (70.7%; 474/670), which increased at study visit (81.6%; 547/670) with overall similar profiles between primary care and urology clinics for each therapy. α1-Blockers were the most used pharmacological treatment across healthcare settings at diagnosis (61.8%; 293/474) and study visit (51%; 279/547). Only 27.1% (57/210) of patients with progression criteria at diagnosis and 35.6% (99/278) at study visit received 5α-reductase inhibitor (5ARI) alone or in combination with a α1-blocker. Overall, most patients did not change treatment (60%; 402/670) with a trend of more patients worsening in symptoms when not receiving α1-blocker plus 5ARI combination therapy.

Conclusion: Most patients with LUTS/BPH received pharmacological treatment; however, most men with progression criteria did not receive a 5ARI alone or in combination. These results support the need to reinforce both primary care and urologists existing clinical guideline recommendations for the appropriate medical management of patients with LUTS/BPH.
Benign prostatic hyperplasia (BPH) is a progressive, non-malignant overgrowth of the prostate gland and the most common cause of lower urinary tract symptoms (LUTS) in ageing men.\(^1\)\(^2\)\(^4\) The prevalence of BPH increases with age, affecting >50% of men ≥50 years of age,\(^5\)\(^6\) and is a significant burden on health-related quality of life (QoL) worldwide and in Spain.\(^2\)\(^4\)\(^7\)\(^8\) BPH may lead to long-term complications, such as acute urinary retention or the requirement for surgery.\(^9\) The progressive nature of BPH and the growth of the ageing population imposes a considerable socio-economic burden with regard to the treatment of BPH.\(^10\)\(^11\) The main aims of BPH therapy are to improve QoL and LUTS and minimise disease progression.\(^7\)\(^12\)\(^13\) Therapy choice should depend on the severity of LUTS, risk of progression, the type of symptoms, how bothersome they are and patient preference.\(^8\)\(^13\)\(^15\)

Clinical guidelines provide specific recommendations for management of mild-to-moderate and moderate-to-severe LUTS due to BPH (LUTS/BPH).\(^8\)\(^13\)\(^16\)\(^17\) For men with mild-to-moderate and nonbothersome LUTS/BPH, which do not warrant pharmacological or surgical intervention, are generally subject to watchful waiting. The recommended first-line treatment for patients with moderate-to-severe LUTS/BPH criteria is monotherapy with α1-blockers due to their rapid onset of action. Muscarinic receptor antagonists may be used for this group of patients presenting bladder storage symptoms and phosphodiesterase 5 inhibitors (PDE5Is) in individuals with or without erectile dysfunction. Combination therapy with an α1-blocker and a muscarinic receptor antagonist may be used in patients with moderate-to-severe LUTS/BPH if monotherapy with either agent did not relieve storage symptoms. For patients with moderate-to-severe LUTS/BPH at risk of disease progression (eg, prostate volume >40 mL or prostate-specific antigen [PSA] >1.4-1.6 ng/mL), 5α-reductase inhibitor (SARI) monotherapy or combination therapy with an α1-blocker is recommended where long-term treatment (>12 months) is intended. Surgical treatment is reserved for patients with bothersome moderate-to-severe LUTS/BPH who do not respond to pharmacological therapy. Phytotherapy has a history of use in treating LUTS/BPH; however, the European Association of Urology does not provide a specific recommendation on their use due to the lack of efficacy data and in vivo effects of these compounds.\(^8\)

Primary care is expected to have an increasingly important role in the management of LUTS/BPH.\(^10\)\(^11\)\(^13\)\(^18\) With this in mind, a joint consensus document has been developed between primary care and urology clinic settings in Spain, presenting evidence-based best practice recommendations for the appropriate management and referral of patients with LUTS/BPH between healthcare services.\(^15\)\(^17\) The therapeutic management of BPH may vary depending on the healthcare service attended; complex patients may require specialist care, and patients managed in urology services may have different treatment trajectories to those managed in primary care.\(^19\) To identify the areas for improvement and optimise efficiency of BPH management in Spain, comprehensive knowledge of the current BPH treatment landscape is key. However, there are a lack of available data describing the real-world management of patients with BPH in both primary care and urology clinic settings.

A study (208 444) investigating the real-world demographic and clinical characteristics of patients attending primary care and urology clinics in Spain observed that the characteristics of patients with BPH were largely similar between healthcare services.\(^19\) However, it was also noted that methods of LUTS evaluation and BPH diagnosis were not fully aligned with guideline recommendations, with differences discerned between healthcare settings.\(^19\) Here, we present additional secondary endpoints from Study 208 444 with the aim of describing the real-world therapeutic management of patients with LUTS/BPH attending primary care and urology clinics in Spain. Also, the relationship between therapeutic management and patient clinical characteristics, including progression criteria, and the evolution of symptom severity and treatment over time were assessed.

### 2 | METHODS

#### 2.1 | Study design

This was an observational, retrospective, multicentre study (208444) carried out in primary care and urology clinics in Spain. The study...
design has been described previously. Briefly, data from LUTS/BPH diagnosis and last follow-up visits were collected from patient healthcare records by 52 primary care physicians and 36 urologists who met feasibility criteria. Data were collected from May 2018 to September 2018, and data from May 2010 to September 2018 were analysed. Additionally, patients completed the eight-item International Prostate Symptom Score (IPSS) questionnaire at the time of study inclusion (ie, at the study visit) as described previously. The management and provision of clinical data were performed by IQVIA.

The study protocol and procedures were reviewed and approved prior to study commencement by an Independent Review Board and Ethics Committee (CEIm del Hospital Universitario Severo Ochoa, Madrid, Spain). Classification from the Spanish Agency of Medicines and Medical Devices was obtained. Written informed consent was provided by each patient prior to study participation.

2.2 | Patient population

Male patients ≥50 years of age diagnosed with LUTS/BPH ≤8 years prior to the study visit were included. Full details on eligibility and exclusion criteria, diagnostic tests, and demographic and clinical characteristics have been described previously. Data regarding clinical diagnosis of LUTS/BPH and past follow-up visits (including PSA determination) had to be available in the patient’s health record. Patients attending the clinic (for any reason) who met the study eligibility criteria were also recruited, resulting in a total of 670 patients included in the study (435 patients were recruited in primary care and 235 patients from urology clinics).

2.3 | Endpoints and assessments

As previously reported, the primary endpoints of this study were to describe the demographic and clinical characteristics of patients with LUTS due to BPH. Secondary endpoints of this study, investigating the therapeutic management of patients with LUTS due to BPH attending primary care and urology clinics, are described here. The following secondary endpoints were assessed at diagnosis and study visit: therapeutic management according to healthcare service or progression criteria (protocol defined as moderate or severe LUTS and prostate volume ≥30 mL and/or PSA ≥1.5 ng/mL), proportion of patients with treatment change, patient profile according to therapy and healthcare service, and evolution of LUTS severity according to therapeutic management in patients that did not change treatment.

2.4 | Data analysis

An analysis of 601 patients was considered necessary based on the assumption that the real-world population prevalence of LUTS/BPH was 50%, estimating a proportion using an asymptotic normal 95% bilateral confidence interval with a maximum imprecision rate of 4%. To achieve this, 675 patients needed to be recruited, assuming a 10% dropout/missing rate. As a larger proportion of patients with LUTS/BPH are followed-up in primary care than in urology clinics, the sample distribution was approximately 2:1. All data were stratified according to level of care at the study visit (ie, primary care or urology clinic). All analyses were conducted by IQVIA and performed using SAS software statistics, Version 9.4.

The changes in treatment pattern were defined as a change of treatment according to when any recorded treatment at diagnosis was different from the study visit (ie, no treatment, watchful waiting, phytotherapy or pharmacological treatment) and a change of treatment according to when pharmacological treatment prescribed at diagnosis was different from the study visit (ie, α1-blocker, 5ARI, combination of α1-blocker and 5ARI, or combination of α1-blocker and antimuscarinic). The proportion of patients receiving each type of treatment (none, watchful waiting, monotherapy or combination therapy) and prescriptions (treatment with/without watchful waiting, phytotherapy, α1-blocker, 5ARI, combination of α1-blocker and 5ARI, or combination of α1-blocker and antimuscarinic) was presented according to healthcare service at diagnosis and study visit. For each treatment type at diagnosis and study visit, the following were described: age, time since diagnosis, symptom severity, prostate volume, PSA, QoL and progression criteria.

The proportion of patients with treatment modification between diagnosis and study visit was assessed at the therapeutic group level. Their relationship with the following independent variables was described: age, age at diagnosis, healthcare service, symptom severity, time since diagnosis, prostate volume, PSA and progression criteria. Bivariate relations with a P < 0.1 were included in the multivariate logistic regression models.

Statistical tests were used depending on whether response variables were discrete (treatment patterns and therapeutic management, PSA level, progression criteria, QoL categorised, symptom severity and prostate volume) or quantitative (age, time since diagnosis, symptom severity, prostate volume, PSA and progression criteria). Statistical tests were used depending on whether response variables were discrete (treatment patterns and therapeutic management, PSA level, progression criteria, QoL categorised, symptom severity and prostate volume) or quantitative (age, time since diagnosis, symptom severity, prostate volume, PSA and progression criteria). Statistical tests were used depending on whether response variables were discrete (treatment patterns and therapeutic management, PSA level, progression criteria, QoL categorised, symptom severity and prostate volume) or quantitative (age, time since diagnosis, symptom severity, prostate volume, PSA and progression criteria). The chi-squared test or Fisher’s exact test was used to analyse discrete variables, and Student’s t-test (if the data were normally distributed, as assessed by the Kolmogorov-Smirnov test of normality) or Wilcoxon signed-rank test or median test (if the data were not normally distributed) was used to analyse quantitative variables. A statistical significance level of 0.05 was used in all tests.

3 | RESULTS

3.1 | Therapeutic management according to healthcare service

There was a significant difference in the overall management of patients in primary care and urology clinics at diagnosis and study visit (both \( P < .001 \)) (Table 1).
Nonpharmacological treatment (which included only watchful waiting) was used by 10.3% (45/435) of patients in primary care and 6% (14/235) in urology clinics at diagnosis. At study visit, nonpharmacological treatment was used by 9% (39/435) of patients in primary care and 3% (7/235) of patients in urology clinics (Table 1).

| Treatment, n (%) | Primary care | Urology clinics | Total | P value<sup>a</sup> |
|-----------------|--------------|-----------------|-------|---------------------|
| Management<sup>b</sup> | | | | |
| Without active treatment | 78 (17.9) | 50 (11.5) | 59 (25.1) | 27 (11.5) | 137 (20.4) | 77 (11.5) | <.001 | <.001 |
| Nonpharmacological treatment | 45 (10.3) | 39 (9.0) | 14 (6.0) | 7 (3.0) | 59 (8.8) | 46 (6.9) |
| Monotherapy | 259 (59.5) | 228 (52.4) | 113 (48.1) | 103 (43.8) | 372 (55.5) | 331 (49.4) |
| Combination | 53 (12.2) | 118 (27.1) | 49 (20.9) | 98 (41.7) | 102 (15.2) | 216 (32.2) |

| Treatment (multiresponse<sup>c</sup>) | Primary care | Urology clinics | Total | P value<sup>d</sup> |
|-----------------|--------------|-----------------|-------|---------------------|
| Watchful waiting | 54 (12.4) | 46 (10.6) | 14 (6.0) | 7 (3.0) | 68 (10.1) | 53 (7.9) | .008 | .001 |
| Pharmacological treatment<sup>d</sup> | 312 (71.7) | 346 (79.5) | 162 (68.9) | 201 (85.5) | 474 (70.7) | 547 (81.6) |
| Phytotherapy | 50 (11.6) | 33 (9.5) | 17 (10.5) | 31 (13.6) | 67 (11.5) | 46 (8.4) | .079 | .316 |
| Monotherapy<sup>d</sup> | 259 (59.0) | 228 (52.4) | 113 (48.1) | 103 (43.8) | 372 (55.5) | 331 (59.5) |
| α1-blockers | 195 (75.3) | 190 (83.3) | 96 (86.7) | 89 (86.4) | 293 (78.5) | 331 (60.5) | .013 | .477 |
| Tamsulosin | 142 (72.8) | 134 (65.9) | 66 (67.3) | 50 (56.2) | 208 (71.0) | 184 (65.9) |
| Doxazosin | 11 (5.4) | 9 (4.7) | 5 (5.1) | 6 (6.7) | 16 (5.5) | 15 (5.4) |
| Silodosin | 30 (15.4) | 39 (20.5) | 24 (25.4) | 31 (34.8) | 54 (18.4) | 70 (25.1) |
| Terazosin | 3 (1.5) | 1 (0.5) | 2 (2.0) | 1 (1.1) | 5 (1.7) | 2 (0.7) |
| Alfuzosin | 9 (4.6) | 7 (3.7) | 1 (1.0) | 1 (1.1) | 10 (3.4) | 8 (2.9) |
| 5ARI | 19 (7.3) | 20 (8.8) | 3 (2.7) | 5 (4.9) | 22 (5.9) | 25 (7.6) | .095 | .212 |
| Finasteride | 6 (1.6) | 10 (5.0) | 0 (0) | 0 (0) | 6 (2.7) | 10 (4.0) |
| Dutasteride | 13 (6.4) | 10 (5.0) | 3 (100) | 5 (100) | 16 (72.7) | 15 (60.0) |
| PDE5I | 4 (1.5) | 3 (1.3) | 1 (0.9) | 0 (0) | 5 (1.3) | 3 (0.9) |
| Tadalafil | 2 (50.0) | 2 (66.7) | 0 (0) | 0 (0) | 2 (40.0) | 2 (66.7) |
| Other | 2 (50.0) | 1 (33.3) | 1 (100) | 0 (0) | 3 (60.0) | 1 (33.3) |
| Combination<sup>e</sup> | 53 (17.0) | 118 (34.1) | 49 (30.2) | 98 (48.8) | 102 (21.5) | 216 (39.5) |
| α1-blocker + 5ARI | 42 (79.2) | 95 (80.5) | 31 (63.3) | 65 (66.3) | 73 (71.6) | 160 (74.1) | .074 | .018 |
| Doxazosin + finasteride | 2 (4.8) | 2 (2.1) | 0 (0) | 0 (0) | 2 (2.7) | 2 (1.3) |
| Tamsulosin + dutasteride | 40 (95.2) | 93 (97.9) | 31 (100) | 64 (98.5) | 71 (97.3) | 157 (98.1) |
| Other | 0 (0) | 0 (0) | 0 (0) | 1 (1.5) | 0 (0) | 1 (0.6) |
| α1-blocker + antimuscarinic | 11 (20.8) | 23 (19.5) | 18 (36.7) | 33 (33.7) | 29 (28.4) | 56 (25.9) | .074 | .018 |
| Tamsulosin + solifenacin | 11 (100) | 23 (100) | 17 (94.4) | 30 (90.9) | 28 (96.6) | 53 (94.6) |
| Other | 0 (0) | 0 (0) | 1 (5.6) | 3 (9.1) | 1 (3.4) | 3 (5.4) |

Abbreviations: 5ARI, 5α-reductase inhibitor; BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms; PDE5I, phosphodiesterase 5 inhibitor.

The bold values indicate significant P values.

<sup>a</sup>Primary care versus urology clinics.

<sup>b</sup>If a patient received more than one treatment, management was grouped as the most restrictive treatment (eg, a patient receiving monotherapy and phytotherapy was considered as ‘monotherapy’). Without active treatment includes only patients with no watchful waiting or pharmacological treatment. Nonpharmacological treatment includes only watchful waiting. Monotherapy includes all patients treated with monotherapy pharmacological treatment including phytotherapy. Combination includes all pharmacological treatments in combination.

<sup>c</sup>Multiresponse variable; for example, a patient who received phytotherapy and α1-blockers was included in both groups.

<sup>d</sup>Percentages for named agents use the number of patients receiving a treatment in that drug class as the denominator.

<sup>e</sup>Percentage for monotherapy and combination therapy subcategories use the number of patients receiving each monotherapy or combination therapy type, respectively, as the denominator.
Most patients (total diagnosis: 70.7% [474/670]; study visit: 81.6% [547/670]) received pharmacological treatment (monotherapy or combination) for LUTS/BPH, with a trend for primary care to prescribe more monotherapy and less combination compared with urology clinics at either diagnosis or study visit. Of the patients receiving pharmacological treatment, monotherapy was the most
common in both primary care (diagnosis: 83% [259/312]; study visit: 65.9% [228/346]) and urology clinics (diagnosis: 69.8% [113/162]; study visit: 51.2% [103/201]) (Table 1).

Of the monotherapy treatments assessed, α1-blockers were the most used across both healthcare settings (diagnosis: 78.8% [293/372]; study visit: 84.3% [279/331]) and were significantly greater in urology clinics at diagnosis (P = .013). Of the α1-blockers used, tamsulosin was the most used across both healthcare settings (diagnosis: 71.0% [208/293]; study visit: 65.9% [184/279]) (Table 1).

Monotherapy with a 5ARI was used at a much lower rate (diagnosis: 5.9% [22/372]; study visit: 7.6% [25/331]) with no significant difference between healthcare settings (Table 1).

Combination therapy was used at diagnosis by 17% (53/312) in primary care and 30.2% (49/162) in urology clinics. At study visit, combination therapy was used by 34.1% (118/346) in primary care and 48.8% (98/201) in urology clinics. No statistical analysis was performed. The most common combination therapy in both healthcare settings was α1-blocker plus 5ARIs (total diagnosis: 71.6% [73/102]; study visit: 74.1% [160/216]), which was significantly greater in primary care versus urology clinics at study visit (P = .018). Tamsulosin and dutasteride appeared to be the most prescribed α1-blocker plus 5ARIs combination therapy; however, no statistical analysis was performed. At study visit, use of α1-blocker plus antimuscarinic combination therapy was significantly greater (P = .018) in urology clinics (33.7% [33/98]) than in primary care (19.5% [23/118]). Specifically, tamsulosin and solifenacin accounted for nearly all α1-blocker plus antimuscarinic combination therapy used (Table 1).

### 3.2 | Therapeutic management according to progression criteria

There was a significant difference in the overall management of patients showing progression criteria and those who did not at both diagnosis (P < .001) and study visit (P = .033). The proportion of patients with progression criteria that received no active treatment was 8.4% (20/239) and 8% (26/324) at diagnosis and study visit, respectively. Similarly, only 3.8% (9/239) and 6.2% (20/324) had nonpharmacological treatment, that is, only watchful waiting, at diagnosis and study visit, respectively (Table 2).

Most patients showing progression criteria received pharmacological treatment for LUTS/BPH (at diagnosis: progression 87.9% [210/239] compared with no progression 64.1% [234/365], P < .001; at study visit: 85.8% [278/324] compared with no progression 77.7% [269/346], P = .007). At diagnosis, the most frequently prescribed pharmacological treatment for patients showing progression criteria was α1-blocker monotherapy (59.5% [125/210]) that decreased by study visit (51.4% [143/278]). The second most frequently prescribed therapy at diagnosis was α1-blocker plus 5ARI combination therapy (20.5% [43/210]) that increased at study visit (28.8% [80/278]). At diagnosis and study visit, phytotherapy as a monotherapy alone (7.1% [15/210]) and 2.9% [8/278], respectively), 5ARI monotherapy (6.7% [14/210] and 6.8% [19/278], respectively) and α1-blocker plus antimuscarinic (5.2% [11/210] and 9.4% [26/278], respectively) were prescribed in patients with progression criteria (Table 2).

There was a significantly larger proportion of 5ARI monotherapy used in patients with progression criteria at either diagnosis (P = .021) or study visit (P = .012) versus those with no progression criteria. At diagnosis, there was also a larger proportion of patients with progression criteria receiving α1-blocker plus 5ARI combination therapy (P = .047); at study visit, this was not significantly different between patients with and without progression criteria. At diagnosis, significantly more patients with no progression criteria received α1-blocker plus antimuscarinic combination therapy than patients with progression criteria (P = .047) (Table 2).

### 3.3 | Proportion of patients with treatment change from diagnosis to study visit

Overall, 40% (268/670) of patients had a change in treatment between diagnosis and study visit (P = .869). The mean (standard deviation [SD]) time from diagnosis to study visit was 3.47 (2.38) years. Treatment change proportions were similar in primary care (39.8% [173/435]) and urology clinics (40.4% [95/235]). The factors influencing a change in treatment from diagnosis to study visit in primary care were time since diagnosis, prostate volume at study visit and PSA at study visit. In urology services, however, increasing age, symptom severity and prostate volume at study visit had a significant effect on change in treatment (Table S1).

### 3.4 | Patient profile according to therapy at diagnosis and study visit, according to healthcare service

#### 3.4.1 | Monotherapy with α1-blocker

At diagnosis, patients treated with α1-blocker therapy showed similar profiles across healthcare settings with no significant differences observed (Table 3). Most patients receiving α1-blocker therapy at diagnosis had moderate-to-severe symptoms (total diagnosis: 71.3% [204/286] and a mean (SD) IPSS of 16.9 (7.0). In total at diagnosis, 76.5% (153/200) of patients had a prostate volume ≥30 mL. 45.7% (122/267) of patients showed progression criteria and the median PSA value was 2.7 ng/mL. Several patient profile differences were observed between healthcare settings among those receiving α1-blockers at the study visit. Mean age (mean [SD] age: primary care, 69.9 [8.6] years; urology clinics, 66.7 [6.7] years; P = .002) and time since diagnosis (mean [SD] time since diagnosis: [SD] primary care, 3.7 [2.4] years; urology clinics, 2.8 [2.3] years; P = .003) were significantly higher in primary care than in urology clinics at study visit. Also, mean PSA values were significantly higher in primary care (7.3 [14.2] ng/mL) than in urology clinics (2.8 [2.0] ng/mL) at study visit (P = .022) (Table 3).
3.4.2 | Monotherapy with 5ARI

At diagnosis and study visit, patients treated with 5ARI therapy showed similar profiles across healthcare settings, with no significant differences observed (Table 4). Most patients receiving monotherapy with 5ARI at diagnosis had moderate-to-severe symptoms (total diagnosis: 95.3% [20/21]) and a mean (SD) IPSS of 21.6 (5.5). In total at diagnosis, 100% (11/11) of patients had a prostate volume ≥30 mL, 73.7% (14/19) showed progression criteria and the median PSA value was 4.2 ng/mL. Similar results were observed at study visit (Table 4).

### TABLE 3 Profile of patients treated with α1-blockers at diagnosis and study visit, according to healthcare service

| Primary care | Urology clinics | Total | P valuea |
|--------------|----------------|-------|----------|
| Diagnosis    | Study visit    | Diagnosis | Study visit |
| Primary care | n = 190        | n = 97  | n = 287  | n = 271  |
| Study visit  | n = 183        | n = 88  |           |          |
| Age (y), mean (SD) | 66.6 (8.0)     | 64.7 (7.5) | 65.9 (7.9) | 68.9 (8.2) | **.052**  | **.002**  |
| Age group, n (%) | <60 y    | 38 (20.0) | 27 (27.8) | 65 (22.6) | 41 (15.1) | .314  | .061  |
|          | 60-65 y | 54 (28.4) | 21 (21.6) | 75 (26.1) | 54 (19.9) |       |       |
|          | 66-70 y | 41 (21.6) | 24 (24.7) | 65 (22.6) | 68 (25.1) |       |       |
|          | >70 y   | 57 (30.0) | 25 (25.8) | 82 (28.6) | 108 (39.9) |       |       |
| Time since diagnosis, mean (SD) | — | 3.7 (2.4) | 2.8 (2.3) | 3.4 (2.4) | — | .003  |       |
| IPSS, mean (SD)b | 16.4 (7.2) | 18.0 (6.5) | 16.9 (7.0) | 12.9 (6.6) | .248  | .733  |       |
| Symptom severity, n (%) | Mild | 59 (31.2) | 23 (23.7) | 82 (28.7) | 62 (22.9) | .414  | .565  |
|          | Moderate | 102 (54.0) | 58 (59.8) | 160 (55.9) | 163 (60.1) |       |       |
|          | Severe | 28 (14.8) | 16 (16.5) | 44 (15.4) | 46 (17.0) |       |       |
| Missing, n | 1 | 0 | 0 | 1 | 0 |       |       |
| QoL (IPSS Item 8), mean (SD) | 3.6 (1.4) | 3.9 (1.3) | 3.7 (1.4) | 2.5 (1.4) | .372  | .618  |       |
| Prostate volume, n (%) | I (<30 mL) | 25 (20.7) | 22 (27.8) | 47 (23.5) | 39 (21.2) | .355  | .518  |
|          | II (30-50 mL) | 48 (39.7) | 34 (43.0) | 82 (41.0) | 85 (46.2) |       |       |
|          | III (51-75 mL) | 31 (25.6) | 17 (21.5) | 48 (24.0) | 33 (17.9) |       |       |
|          | IV (>75 mL) | 17 (14.0) | 6 (7.6) | 23 (11.5) | 27 (14.7) |       |       |
| Missing, n | 69 | 18 | 7 | 87 | 87 |       |       |
| PSA value (ng/mL), mean (SD) | 4.17 (5.5) | 3.18 (2.2) | 3.84 (4.7) | 5.9 (11.9) | .812  | .022  |       |
| PSA value (ng/mL), median (P25, P75) | 2.7 (1.4, 4.9) | 2.6 (1.4, 5.3) | 2.6 (1.4, 3.7) | 2.7 (1.4, 4.7) | 2.8 (1.5, 4.9) | .459  | .435  |       |
| PSA value, n (%) | PSA < 1.5 ng/mL | 49 (27.2%) | 20 (23.0%) | 69 (25.8) | 63 (23.2) | .459  | .435  |       |
|          | PSA ≥ 1.5 ng/mL | 131 (72.8%) | 67 (77.0%) | 198 (74.2) | 208 (76.8) |       |       |
| Missing, n | 10 | 0 | 0 | 20 | 0 |       |       |
| Progression criteria, n (%) | 81 (45.0) | 41 (47.1) | 122 (45.7) | 137 (50.6) | .744  | .244  |       |
| Missing, n | 10 | 0 | 0 | 20 | 0 |       |       |

Abbreviations: IPSS, International Prostate Symptom Score; P25, percentile 25; P75, percentile 75; PSA, prostate-specific antigen; QoL, quality of life; SD, standard deviation.

The bold values indicate significant P values.

aPrimary care versus urology clinics.

bNumbers can vary due to missing values and selected patients. Information has been calculated for nonmissing values.
3.4.3 | Combination therapy with α1-blocker plus 5ARI

At diagnosis, patients treated with α1-blocker plus 5ARI therapy showed similar profiles across healthcare settings, with no significant differences observed (Table 5). Most patients treated with α1-blocker plus 5ARI therapy at diagnosis had moderate-to-severe symptoms (total diagnosis: 77.8% [56/72]) and a mean (SD) IPSS of 13.1 (6.0). In total at diagnosis, 92.2% (47/51) of patients had a prostate volume ≥30 mL, 61.4% (43/70) had progression criteria and the median PSA value was 3.7 ng/mL. Patient profiles at the study visit were generally similar between healthcare settings, with the exception that significantly more patients treated in primary care versus urology clinics had a longer time since diagnosis (P = .049) and the

TABLE 4 Profile of patients treated with 5ARI at diagnosis and study visit, according to healthcare service

| Primary care | Urology clinics | Total | P value<sup>a</sup> |
|--------------|----------------|-------|-------------------|
| **Diagnosis** | **Study visit** | **Diagnosis** | **Study visit** |
| Age (y), mean (SD) | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| 70.1 (10.2) | 72.9 (8.2) | 68.0 (0.0) | 70.0 (4.7) | 69.86 (9.7) | 72.3 (7.6) | — | .462 |
| **Age group, n (%)** | | | |
| <60 y | | 3 (15.8) | 2 (11.1) | 0 (0) | 0 (0) | 3 (14.3) | 2 (8.7) |
| 60-65 y | | 3 (15.8) | 1 (5.6) | 0 (0) | 1 (20.0) | 3 (14.3) | 2 (8.7) |
| 66-70 y | | 5 (26.3) | 3 (16.7) | 2 (100) | 2 (40.0) | 7 (33.3) | 5 (21.7) |
| >70 y | | 8 (42.1) | 12 (66.7) | 0 (0) | 2 (40.0) | 8 (38.1) | 14 (60.9) |
| **Time since diagnosis, mean (SD)** | | | |
| | | — | 3.9 (2.5) | — | 4.3 (2.9) | — | .852 |
| **IPSS, mean (SD)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| 21.6 (5.5) | 14.5 (6.9) | 0 (0) | 18.8 (8.0) | 21.6 (5.5) | 15.4 (7.2) | — | .313 |
| **Symptom severity, n (%)** | | | |
| Mild | | 1 (5.3) | 3 (16.7) | 0 (0) | 0 (0) | 1 (4.8) | 3 (13.0) |
| Moderate | | 16 (84.2) | 12 (66.7) | 1 (50.0) | 2 (40.0) | 17 (81.0) | 14 (60.9) |
| Severe | | 2 (10.5) | 3 (16.7) | 1 (50.0) | 3 (60.0) | 3 (14.3) | 6 (26.1) |
| **QoL (IPSS Item 8), mean (SD)** | | | |
| | | 5.2 (0.8) | 2.8 (1.4) | 0 (0) | 3.6 (1.1) | 5.2 (0.8) | 3 (1.4) | .222 |
| **Prostate volume, n (%)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| I (<30 mL) | | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0) | 0 (0.0) | 1 (7.1) |
| II (30-50 mL) | | 4 (44.4) | 4 (44.4) | 1 (50.0) | 1 (20) | 5 (45.5) | 5 (25.7) |
| III (51-75 mL) | | 2 (22.2) | 0 (0) | 0 (0.0) | 2 (40) | 2 (18.2) | 2 (13.4) |
| IV (>75 mL) | | 3 (33.3) | 4 (44.4) | 1 (50.0) | 2 (40) | 4 (36.4) | 6 (42.9) |
| Missing, n | | 10 | 9 | 0 | 0 | 10 | 9 |
| **PSA value (ng/mL), mean (SD)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| 6.8 (8.2) | 9.4 (16.5) | 1.8 (0.0) | 2.6 (2.1) | 6.5 (8.1) | 7.9 (14.8) | — | .146 |
| **PSA value (ng/mL), median (P25, P75)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| 4.5 (1.5, 9.1) | 4.1 (2.1, 7.3) | 1.8 (1.8, 1.8) | 1.8 (1.2, 2.5) | 4.2 (1.5, 9.1) | 3.9 (1.8, 6.1) | — | — |
| **PSA value, n (%)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| PSA < 1.5 ng/mL | | 4 (22.2%) | 2 (11.1) | 0 | 2 (40.0) | 4 (21.1) | 4 (17.4) |
| PSA ≥ 1.5 ng/mL | | 14 (77.8%) | 16 (88.9) | 1 (100%) | 3 (60.0) | 15 (78.9) | 19 (82.6) |
| Missing, n | | 1 | 0 | 1 | 0 | 2 | 0 |
| **Progression criteria, n (%)** | | | |
| (n = 19) | (n = 18) | (n = 2) | (n = 5) | (n = 21) | (n = 23) | Diagnosis | Study visit |
| 13 (72.2) | 14 (77.8) | 1 (100) | 3 (60.0) | 14 (73.7) | 17 (73.9) | .539 | .423 |
| Missing, n | | 1 | 0 | 1 | 0 | 2 | 0 |

Abbreviations: 5ARI, 5α-reductase inhibitor; IPSS, International Prostate Symptom Score; P25, percentile 25; P75, percentile 75; PSA, prostate-specific antigen; QoL, quality of life; SD, standard deviation.

<sup>a</sup>Primary care versus urology clinics.

<sup>b</sup>Numbers can vary due to missing values and selected patients. Information has been calculated for nonmissing values.
| TABLE 5  | Profile of patients treated with α1-blockers and 5ARI combination therapy at diagnosis and study visit, according to healthcare service |
|-----------|--------------------------------------------------------------------------------------------------------|
|           | Primary care | Urology clinics | Total |           |           |
|           | Diagnosis    | Study visit     | Diagnosis | Study visit | Diagnosis | Study visit |
|           | (n = 42)     | (n = 95)        | (n = 31)  | (n = 65)    | (n = 73)  | (n = 160)   |
| Age (y), mean (SD) | 68.4 (8.6) | 72.6 (8.8) | 69.9 (7.0) | 73.5 (7.1) | 69.0 (8.0) | 73.0 (8.1) | .413 | .533 |
| Age group, n (%) |               |               |         |             |           |             |
| <60 y     | 6 (14.3)     | 5 (5.3)       | 3 (9.7)  | 2 (3.1)     | 9 (12.3)  | 7 (4.4)    |
| 60-65 y   | 9 (21.4)     | 15 (15.8)     | 4 (12.9) | 8 (12.3)    | 13 (17.8) | 23 (14.4)  |
| 66-70 y   | 12 (28.6)    | 18 (18.9)     | 9 (29.0) | 10 (15.4)   | 21 (28.8) | 28 (17.5)  |
| >70 y     | 15 (35.7)    | 57 (60.0)     | 15 (48.4) | 45 (69.2)   | 30 (41.1) | 102 (63.8) |
| Time from diagnosis, mean (SD) |           |               |         |             |           |             |
|           | –            | 4.1 (2.2)     | –       | 3.4 (2.3)   | –         | 3.8 (2.3)  |
| IPSS, mean (SD) | 12.6 (7.1) | 12.3 (7.4) | 14.0 (4.1) | 14.1 (7.4) | 13.1 (6.0) | 13.0 (7.4) | .397 | .087 |
| Symptom severity, n (%) |               |               |         |             |           |             |
| Mild      | 13 (31.0)    | 27 (28.4)     | 3 (10.0) | 10 (15.4)   | 16 (22.2) | 37 (23.1)  |
| Moderate  | 25 (59.5)    | 54 (56.8)     | 23 (76.7) | 37 (56.9)   | 48 (66.7) | 91 (56.9)  |
| Severe    | 4 (9.5)      | 14 (14.7)     | 4 (13.3) | 18 (27.7)   | 8 (11.1)  | 32 (20.0)  |
| Missing, n | 0            | 0             | 1       | 0           | 1         | 0          |
| QoL (IPSS Item 8), mean (SD) | 3.3 (1.1)  | 2.6 (1.4)   | 3.2 (0.6) | 2.4 (1.5)   | 3.2 (1.0) | 2.5 (1.5)  |
| Prostate volume, n (%) |               |               |         |             |           |             |
| I (<30 mL) | 3 (13.0)     | 4 (7.7)       | 1 (3.6)  | 3 (5.3)     | 4 (7.8)   | 7 (6.4)    |
| II (30-50 mL) | 7 (30.4)   | 17 (32.7)     | 4 (14.3) | 20 (35.1)   | 11 (21.6) | 37 (33.9)  |
| III (51-75 mL) | 4 (17.4)  | 17 (32.7)     | 12 (42.9) | 19 (33.3)   | 16 (31.4) | 36 (33.0)  |
| IV (>75 mL) | 9 (39.1)    | 14 (26.9)     | 11 (39.3) | 15 (26.3)   | 20 (39.2) | 29 (26.6)  |
| Missing, n | 19           | 43            | 3       | 8           | 22        | 51         |
| PSA value (ng/mL), mean (SD) | 4.8 (3.0)  | 3.1 (3.0)   | 4.0 (3.7) | 3.0 (2.9)   | 4.5 (3.3) | 3.0 (2.9)  |
| PSA value (ng/mL), median (P25, P75) | 4.2 (2.6, 6.0) | 2.3 (1.3, 4.0) | 2.7 (2.3, 5.4) | 2.3 (1.1, 3.6) | 3.7 (2.3, 5.8) | 2.3 (1.3, 3.8) |
| PSA value, n (%) |               |               |         |             |           |             |
| PSA < 1.5 ng/mL | 3 (7.5%)   | 27 (28.4)     | 7 (22.6%) | 21 (32.3)   | 10 (14.1) | 48 (30.0)  |
| PSA ≥ 1.5 ng/mL | 37 (92.5%) | 68 (71.6)     | 24 (77.4%) | 44 (67.7)   | 61 (85.9) | 112 (70.0) |
| Missing, n | 2            | 0             | 0       | 0           | 2         | 0          |
| Progression criteria, n (%) | 23 (57.5)  | 46 (48.4)    | 20 (66.7) | 34 (52.3)   | 43 (61.4) | 80 (50.0)  |
| Missing, n | 2            | 0             | 1       | 0           | 3         | 0          |

Abbreviations: 5ARI, 5α-reductase inhibitor; IPSS, International Prostate Symptom Score; P25, percentile 25; P75, percentile 75; PSA, prostate-specific antigen; QoL, quality of life; SD, standard deviation.

The bold values indicate significant P values.

*aPrimary care versus urology clinics.

*bNumbers can vary due to missing values and selected patients. Information has been calculated for nonmissing values.
incidence of mild, moderate and severe symptom severities was different between settings \((P = .048)\) (Table 5).

### 3.4.4 | Combination therapy with α1-blocker and antimuscarinic

For patients receiving combination therapy with α1-blockers and antimuscarinic therapies, no significant differences in patient profile were observed at both diagnosis and study visit, other than lower IPSS Item 8 in primary care than in urology clinics at study visit (mean [SD] 2.5 [1.59] vs. 3.45 [1.39], respectively; \(P = .017\)) (Table S2).

Evolution of LUTS from diagnosis to study visit according to therapeutic management in patients that did not change treatment assessed at diagnosis and study visit.

| Symptoms at diagnosis | Treatment at diagnosis | Symptoms at study visit, n (%)\(^a\) |
|-----------------------|------------------------|-------------------------------------|
| IPSS                  |                        | Mild | Moderate | Severe |
| Mild (\(n = 26\))     | α1-blocker             | 7 (70.0) | 3 (30.0) | 0 |
|                       | α1-blocker + 5ARI      | 3 (75.0) | 1 (25.0) | 0 |
|                       | No treatment           | 7 (70.0) | 3 (30.0) | 0 |
|                       | Phytotherapy           | 2 (100.0) | 0 | 0 |
| Moderate (\(n = 99\)) | α1-blocker             | 7 (14.3) | 37 (75.5) | 5 (10.2) |
|                       | α1-blocker + 5ARI      | 5 (26.3) | 14 (73.7) | 0 |
|                       | No treatment           | 2 (10.5) | 14 (73.7) | 3 (15.8) |
|                       | Other treatment        | 0 | 4 (80.0) | 1 (20.0) |
|                       | Phytotherapy           | 0 | 6 (85.7) | 1 (14.3) |
| Severe (\(n = 47\))   | α1-blocker             | 3 (7.9) | 12 (31.6) | 23 (60.5) |
|                       | α1-blocker + 5ARI      | 0 | 1 (25.0) | 3 (75.0) |
|                       | No treatment           | 0 | 2 (66.7) | 1 (33.3) |
|                       | Other treatment        | 0 | 0 | 2 (100.0) |

**Clinical criteria**

| Symptoms at diagnosis | Treatment at diagnosis | Symptoms at study visit, n (%)\(^a\) |
|-----------------------|------------------------|-------------------------------------|
| Mild (\(n = 249\))    | α1-blocker             | 28 (35.9) | 41 (52.6) | 9 (11.5) |
|                       | α1-blocker + 5ARI      | 6 (50.0) | 6 (50.0) | 0 |
|                       | No treatment           | 46 (36.8) | 70 (56.0) | 9 (7.2) |
|                       | Other treatment        | 1 (33.3) | 2 (66.7) | 0 |
|                       | Phytotherapy           | 7 (22.6) | 20 (64.5) | 4 (12.9) |
| Moderate (\(n = 227\))| α1-blocker             | 22 (17.3) | 78 (61.4) | 27 (21.3) |
|                       | α1-blocker + 5ARI      | 4 (11.8) | 24 (70.6) | 6 (17.7) |
|                       | No treatment           | 7 (18.9) | 25 (67.6) | 5 (13.5) |
|                       | Other treatment        | 1 (10.0) | 8 (80.0) | 1 (10.0) |
|                       | Phototherapy           | 8 (42.1) | 8 (42.1) | 3 (15.8) |
| Severe (\(n = 20\))   | α1-blocker             | 1 (8.3) | 2 (16.7) | 9 (75.0) |
|                       | α1-blocker + 5ARI      | 0 | 4 (66.7) | 2 (33.3) |
|                       | No treatment           | 2 (100.0) | 0 | 0 |

**Abbreviations:** 5ARI, 5α-reductase inhibitor; IPSS, International Prostate Symptom Score.

\(^a\)Percentages use the row n value as the denominator.

Most patients appeared to remain in the same symptom category at study visit, irrespective of symptom severity and treatment received at diagnosis. There appeared to be a trend for more patients experiencing worsening symptoms when not receiving α1-blocker plus 5ARI combination therapy; however, no statistical analysis was performed (Table 6 and Figure S1). Overall, most patients tended to maintain or improve in symptom severity when assessed by IPSS at diagnosis. Conversely, those that were assessed by clinical criteria at diagnosis showed a tendency to maintain or worsen in symptom severity. However, no statistical comparison was performed (Table 6).

### 4 | DISCUSSION

This was a real-world, observational study in men with LUTS/BPH consulting primary care and urology clinics in Spain. This study was
aimed at assessing therapeutic management according to progression criteria and to inform on patient clinical characteristics in response to medical treatment in addition to assessing the evolution of symptom severity.

A significant difference in the management of patients between healthcare settings was noted, at both diagnosis and study visit, with a trend for primary care to include more patients on watchful waiting as well as more monotherapy and less combination therapy prescription. Over 70% to 80% of patients received pharmacological treatment at diagnosis and study visit, respectively, confirming this as a standard of care for men with LUTS/BPH. The most frequently used pharmacological treatment in both healthcare services was α1-blocker monotherapy, with 62% at diagnosis and 51% at study visit. Although being the second most prescribed pharmacological treatment, combination therapy with α1-blocker plus 5ARI was used at a much lower rate than α1-blocker monotherapy (15% at diagnosis and 29% at study visit vs. 62% at diagnosis and 51% at study visit, respectively). These results are similar to those recently published from a population-based cohort in the United Kingdom.21 5ARI monotherapy (5%), PDE5i (1%) and α1-blocker plus antimuscarinics (6-10%) comprised a much lower proportion of pharmacological treatment used at both diagnosis and study visit.

This study also looked at the therapeutic management of men with LUTS/BPH according to the presence of progression criteria, that is, moderate-to-severe symptom severity, prostate volume ≥30 mL and/or PSA ≥ 1.5 ng/mL19 at diagnosis and study visit. As recommended by clinical guidelines, LUTS/BPH men at risk of disease progression should be receiving a disease-modifying pharmacological therapy (5ARI in monotherapy or in combination).8,13,15,16 However, α1-blockers as monotherapy were still the most prescribed pharmacological treatment at both diagnosis (60%) and study visit (51%) in men with progression criteria. In fact, only 27% (at diagnosis) and 36% (at study visit) of patients at risk of disease progression receiving pharmacological treatment were prescribed with 5ARI in monotherapy or in combination. Therefore, these findings indicate that despite a marginal increase in the proportion of patients with progression criteria receiving a 5ARI-based treatment from diagnosis to the study visit, the majority of patients are still receiving suboptimal treatment.

This study showed that 40% of men changed treatment between diagnosis and study visit (average duration roughly 3.5 years). The factors affecting treatment change from diagnosis to study visit were mainly linked to disease progression (i.e., increasing time since diagnosis, prostate volume and symptom severity), rather than the healthcare service attended. These findings indicate that therapeutic approach is, in part, governed by the patient profile as opposed to level of care. Similarly, in a previous study, medication changes were reported to be similar in patients managed by primary care physicians and those managed by urologists.10

Overall, patient profiles were similar between primary care and urology clinics for each therapy. Focusing on α1-blocker monotherapy as the most frequently used treatment, about half of patients (46% at diagnosis and 51% at study visit) had progression criteria. According to clinical guidelines, patients would have been most appropriately treated with a 5ARI in monotherapy or in combination due to their progression profile risk. It is interesting to note that 24% (6/25) of men receiving 5ARI monotherapy and 50% (80/160) of men receiving combination therapy with α1-blocker plus 5ARI at study visit did not have progression criteria as defined in the study protocol. Therefore, this study shows that the medical treatment recommendations by clinical guidelines are not closely followed by either primary care or urology clinics, demonstrating suboptimal medical management of patients with LUTS/BPH.

Overall, most patients appeared to remain in the same symptom category at study visit, irrespective of the symptom severity and treatment received at diagnosis. Despite the low sample size, an increase in patients with worsening in symptoms when not receiving α1-blocker plus 5ARI combination therapy was observed. The proportion of patients with worsening symptoms from diagnosis to study visit appeared to be lower when IPSS was used instead of clinical criteria. It is possible that clinical criteria, which are a more subjective assessment of severity compared with IPSS, may be less accurate in evaluating severity. Despite the known limitations of IPSS, such as reproducibility of responses,22 it remains the consensus approach to evaluate LUTS/BPH severity. Previous work has suggested that objective variables such as IPSS and PSA (as recommended by European Urology Association guidelines)8 enable the accurate diagnosis of patients with LUTS/BPH in primary care.4 In another study, a high correlation was observed between diagnoses using medical history, serum PSA, digital rectal examination and IPSS and those based on a full battery of tests including ultrasonography and uroflowmetry.23 Therefore, the initial evaluation of LUTS/BPH using simple diagnostic tools available in the primary care setting is an appropriate strategy to facilitate the diagnosis. Furthermore, this approach might minimise delays in the management of LUTS/BPH and inform on the appropriate referral to specialised care.23,24

As this study utilised real-world clinical data, important information, which may help address the study objectives, could have been missing; this is a well-known limitation of real-world studies.25 To mitigate this, feasibility tests helped ensure investigators could provide the required study data, as described previously.19 An important limitation to recognise is the low number of patients when evaluating the management by progression criteria or the evolution of symptoms by method of assessing severity, as such limiting robust interpretations and conclusions derived from this study. A strength of using real-world data is that the results are generalisable to a wide patient population. Additionally, as patient baseline demographics are similar to other studies in patients with LUTS/BPH,12,26 the patient population is likely to be representative of the wider population and results are therefore applicable to other countries.
5 | CONCLUSION

This study demonstrates a significant difference in the overall management of patients with LUTS/BPH according to healthcare service and progression criteria. Most patients received pharmacological treatment with similar profiles between primary care and urology clinics for each therapy. α1-Blockers were the most used treatment across healthcare settings, and the majority of patients with progression criteria did not receive disease-modifying pharmacological therapy (ie, 5ARI) in monotherapy or in combination, with this pattern persisting throughout the study observation period. Overall, most patients did not change treatment, and there was a general trend of symptom worsening when not receiving α1-blocker plus 5ARI combination therapy.

Therefore, this study shows that the clinical guideline recommendations for patients with LUTS/BPH are not closely adhered by either primary care or urology clinics. As such, a significant proportion of patients with LUTS/BPH receive inadequate medical management. Moreover, this reveals a need to further emphasize existing guideline criteria for the use of 5ARI combination therapy in both healthcare settings.

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DISCLOSURES

BM has participated in advisory boards and speaker’s bureaus and has received compensation for travel expenses and for being a trial investigator from GSK, Janssen, Astellas, Werfen, Bayer, Sanofi and IPSEN. JMM has received financial compensation from GSK for scientific advice on the design and development of the study protocol and from IQVIA for participating as a researcher. JMM has also participated in advisory boards for GSK and Astellas and in speaker’s bureaus for GSK and has received compensation from GSK and Pierre Fabre for being a trial investigator. AAR, RCP, DLM and JMP-M are employees of GSK and hold shareholder status in the company. MTM-F received financial compensation from GSK for travel expenses and for being trial investigator. AC is an employee of IQVIA.

DATA AVAILABILITY STATEMENT

Anonymised individual participant data and study documents can be requested for further research from www.clinicalstudydatarequest.com.

ORCID

Juan Manuel Palacios-Moreno https://orcid.org/0000-0001-9946-4005

REFERENCES

1. Lim KB. Epidemiology of clinical benign prostatic hyperplasia. Asian J Urol. 2017;4:148-151.
2. Minana B, Rodríguez-Antolin A, Prieto M, Pedrosa E. Severity profiles in patients diagnosed of benign prostatic hyperplasia in Spain. Actas Urol Esp. 2013;37:544-548.
3. Roehrborn CG. Benign prostatic hyperplasia: an overview. Rev Urol. 2005;7(Suppl 9):S3-S14.
4. Carballido J, Fournade R, Pagliarulo A, et al. Can benign prostatic hyperplasia be identified in the primary care setting by using only simple tests? Results of the Diagnosis Improvement in PrimArty Care Trial. Int J Clin Pract. 2011;65:989-996.
5. Andriole G. Benign prostatic hyperplasia (BPH). [Online] 2018. https://www.msdmanuals.com/en-en/professional/genitourinary-disorders/benign-prostate-disease/benign-prostatic-hyperplasia-bph. Accessed July 8, 2019.
6. 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.
7. 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;115:508-519.
8. Gravas S, Cornu JN, Gacci M, et al. EAU guidelines on management of non-neurogenic male LUTS [online] 2020. https://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/. Accessed November 2, 2020.
9. O’Leary MP. Lower urinary tract symptoms/benign prostatic hyperplasia: maintaining symptom control and reducing complications. Urology. 2003;62:15-23.
10. Rensing AJ, Kuxhausen A, Vetter J, Strope SA. Differences in the treatment of benign prostatic hyperplasia: comparing the primary care physician and the urologist. Urol Pract. 2017;4:193-199.
11. Kirby RS, Kirby M, Fitzpatrick JM. Benign prostatic hyperplasia: counting the cost of its management. BJU Int. 2010;105:901-902.
12. Roehrborn CG. BPH progression: concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. BJU Int. 2008;101 (Suppl 3):17-21.
13. Tanguay S, Awde M, Brock G, et al. Diagnosis and management of benign prostatic hyperplasia in primary care. Can Urol Assoc J. 2009;3:592-510.
14. Nickel JC, Méndez-Probst CE, Whelan TF, et al. 2010 Update: guidelines for the management of benign prostatic hyperplasia. Can Urol Assoc J. 2010;4:310-316.
15. Brenes Bermúdez FJ, Brotons Munto F, Castineiras Fernandez J, et al. Consensus document on the management and follow-up of the male with lower urinary tract symptoms secondary to benign prostate hyperplasia. Semergen. 2016;42:547-556.
16. Bartsch G, Fitzpatrick JM, Schalken JA, et al. Consensus statement: the role of prostate-specific antigen in managing the patient with benign prostatic hyperplasia. BJU Int. 2004;93:27-29.
17. Brenes FJ, Brotons F, Cozar JM, et al. Criterios de derivación en HBP para AP–5G (4a ed.). [Online] 2019. http://mgf.org/criterios-de-derivacion-en-hiperplasia-benigna-de-prostata-para-atencion-primaria-5g-4a-ed/. Accessed July 6, 2020.
18. López BM, Romero AH, Ortín EO, García IL. Can primary care physicians manage benign prostatic hyperplasia patients as urologists do? Eur Med J. 2014. https://www.emjreviews.com/urology/article/can-primary-care-physicians-manage-benign-prostatic-hyperplasia-patients-as-urologists-do/. Accessed July 8, 2020.
19. Maria Molero J, Minana B, Palacios-Moreno JM, et al. Real-world assessment and characteristics of men with benign prostatic hyperplasia (BPH) in primary care and urology clinics in Spain. Int J Clin Pract. 2020;74(11):13602.
20. AEMPS. Spanish Agency of Drugs and Medical Devices [Online] 2020. https://www.aemps.gob.es. Accessed November 2, 2020.
21. Ayele HT, Reynier P, Azoulay L, et al. Trends in the pharmacological treatment of benign prostatic hyperplasia in the UK from 1998 to 2016: a population-based cohort study. World J Urol. 2020. https://doi.org/10.1007/s00345-020-03429-2.
22. Johnson TV, Abbasi A, Erlich SS, et al. Patient misunderstanding of the individual questions of the American Urological Association symptom score. J Urol. 2008;179(6):2291-2295; discussion 2294-2295.
23. Carballido Rodríguez J, Badia Llach X, Gimeno Collado A, et al. Validity of tests for initial diagnosis and its concordance with final diagnosis in patients with suspected benign prostatic hyperplasia. *Actas Urol Esp*. 2006;30:667-674.

24. Emberton M, Cornet EB, Bassi PF, et al. Benign prostatic hyperplasia as a progressive disease: a guide to the risk factors and options for medical management. *Int J Clin Pract*. 2008;62:1076-1086.

25. Kim HS, Kim JH. Proceed with caution when using real world data and real world evidence. *J Korean Med Sci*. 2019;34:e28.

26. 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;349:2387-2398.

**SUPPORTING INFORMATION**

Additional Supporting Information may be found online in the Supporting Information section.

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