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Real-world assessment and characteristics of men with benign prostatic hyperplasia (BPH) in primary care and urology clinics in Spain

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Abstract

Objectives: To describe the real-world demographic and clinical characteristics of patients with lower urinary tract symptoms (LUTS) as a result of benign prostatic hyperplasia (BPH) in Spain.

Methodology: This observational, retrospective, multicentre study conducted in primary care and urology clinics in Spain included men aged ≥50 years diagnosed (≤8 years prior to study visit) with LUTS caused by BPH. The primary endpoint was demographic and clinical characteristics; secondary endpoints included disease progression and diagnostic tests across both healthcare settings.

Results: A total of 670 patients were included (primary care: n = 435; urology: n = 235). Most patients had moderate/severe LUTS (74.6%) and prostate volume >30 cc (81.7%), with no differences between settings. More patients had prostate-specific antigen (PSA) ≥1.5 ng/mL in primary care (74.5%) versus urology (67.7%). Progression criteria were prevalent (48.9%). Clinical criteria were more commonly used than the International Prostate Symptom Score (IPSS) to evaluate LUTS at diagnosis (primary care: clinical criteria 73.0%; IPSS: 26.9%; urology: clinical criteria 76.5%; IPSS: 23.4%). Proportion of patients with moderate/severe LUTS at diagnosis was lower using clinical criteria than IPSS, and the proportion of patients with 'worsening' LUTS (diagnosis to study visit) was higher when using clinical criteria versus IPSS. In both healthcare settings, the most commonly used diagnostic tests were general and urological clinical history and PSA.

Conclusion: Demographic and clinical characteristics of patients with BPH in Spain were similar in primary care and urology; however, assessment criteria to evaluate LUTS severity differ and are not completely aligned with clinical guideline recommendations. Increased use of recommended assessments may enhance optimal BPH management.

1 | INTRODUCTION

Benign prostatic hyperplasia (BPH) is a progressive, non-malignant overgrowth of the prostate gland commonly observed in men over 50 years of age.[1,2] By obstructing urinary flow, BPH frequently causes lower urinary tract symptoms (LUTS), which are a significant burden in ageing men, and have a major negative impact on quality of life (QoL); it also increases the risk of disease progression.[1,3-7]

Although BPH is the most common cause of LUTS, other possible causes exist; therefore, comprehensive assessment facilitating an accurate diagnosis of BPH as a cause of LUTS is crucial.[8-11] As per clinical guidelines in Spain, the following assessments are mandatory: clinical history, physical exam, digital rectal exam (DRE) and urinalysis; and the following assessments are recommended: prostate-specific antigen (PSA) and International Prostate Symptom Score (IPSS).[12,13] Such comprehensive assessment also allows determination of LUTS severity and the identification of men at risk of progression to inform the choice of an appropriate treatment strategy and follow-up.[3,9,14]

The main aim of BPH therapy is to alleviate bothersome LUTS, improve QoL and minimise the risk of disease progression.[10,14-17] As a result of the progressive nature of BPH, the risk of LUTS deterioration, acute urinary retention (AUR) or the requirement for surgery will increase over time.[18] The most highly predictive measures for disease progression are age, LUTS severity, decreased urinary flow, prostatic enlargement and PSA (progression criteria defined as IPSS ≥ 8; prostate volume >30 cc and PSA ≥ 1.5 ng/mL).[1,15,19-21] Progression criteria are prevalent in patients with BPH, with many men already showing signs of progression at diagnosis.[1]

With the natural age-related progression of the disease and an ageing population, an increase in the prevalence of BPH and its associated social and economic impact on healthcare is foreseeable.[14,17,22,23] Therefore, primary care has an increasingly important role in the diagnosis and management of patients with BPH.[6,22,24] A 'shared care' approach between primary care and urology is advocated for the management of BPH; however, initial management may vary between primary care and urology.[16,23-25] A joint consensus document between primary care and urology settings in Spain, first published in 2010[26] with continuous updates[12,13,24] was developed in order to facilitate the appropriate and streamlined management of BPH across healthcare settings.[12,24,26]

There is insufficient evidence to confirm that the assessments and diagnostic tests recommended by clinical guidelines are being used in daily practice by primary care physicians and urologists. These tests are required to make a differential diagnosis of BPH and stratify patients, identifying those with risk of progression and ultimately informing the most optimal management strategy. Furthermore, although comprehensive knowledge of current BPH management in Spain is key to identifying areas for improvement and optimising BPH treatment and QoL, there is a lack of available data describing the real-world characteristics of patients with LUTS caused by BPH in both primary care and urology clinic settings. This study aimed to describe the real-world demographic and clinical characteristics of patients with LUTS caused by BPH attending primary care and urology clinics in Spain, and the assessments used for diagnosis and evaluation of disease severity to confirm alignment with guideline recommendations.

What's known

- Comprehensive assessment is key to the accurate diagnosis of benign prostatic hyperplasia (BPH) as a cause of lower urinary tract symptoms (LUTS) amidst diverse patient types, and for identification of patients at risk of progression to inform an appropriate treatment strategy.
- A 'shared care' approach between primary care and urology is advocated; however, BPH management may differ between healthcare settings, and insufficient evidence exists to confirm compliance with clinical guidelines.

What's new

- Although demographic and clinical characteristics of patients with BPH in Spain are similar in both primary care and urology, evaluation methods of BPH severity and diagnosis differ between healthcare settings and are not completely aligned with clinical guideline recommendations.
- Clinical criteria may underestimate LUTS severity and progression risk compared with the International Prostate Symptom Score (IPSS); increasing IPSS use and other recommended assessments may enhance optimal BPH management.

2 | METHODS

2.1 | Study design

This was an observational, retrospective, cross-sectional, multicentre study carried out in primary care and urology clinics in Spain. The period of data collection was from May 2018 to September 2018 and data from May 2010 to September 2018 were analysed (Figure 1). Prior to patient enrolment at study sites, a feasibility test was conducted to assess whether study investigators had access to the required information in patient health records.

The provision and management of clinical data were performed by IQVIA.[27] Data were collected retrospectively from patient health records at BPH diagnosis and at the last available BPH follow-up visit. Additionally, patients completed in a single presential visit, the 8-item IPSS questionnaire at the time of study inclusion (study visit) to assess LUTS severity and QoL; no other study-specific tests were performed at the study visit (Figure 1).

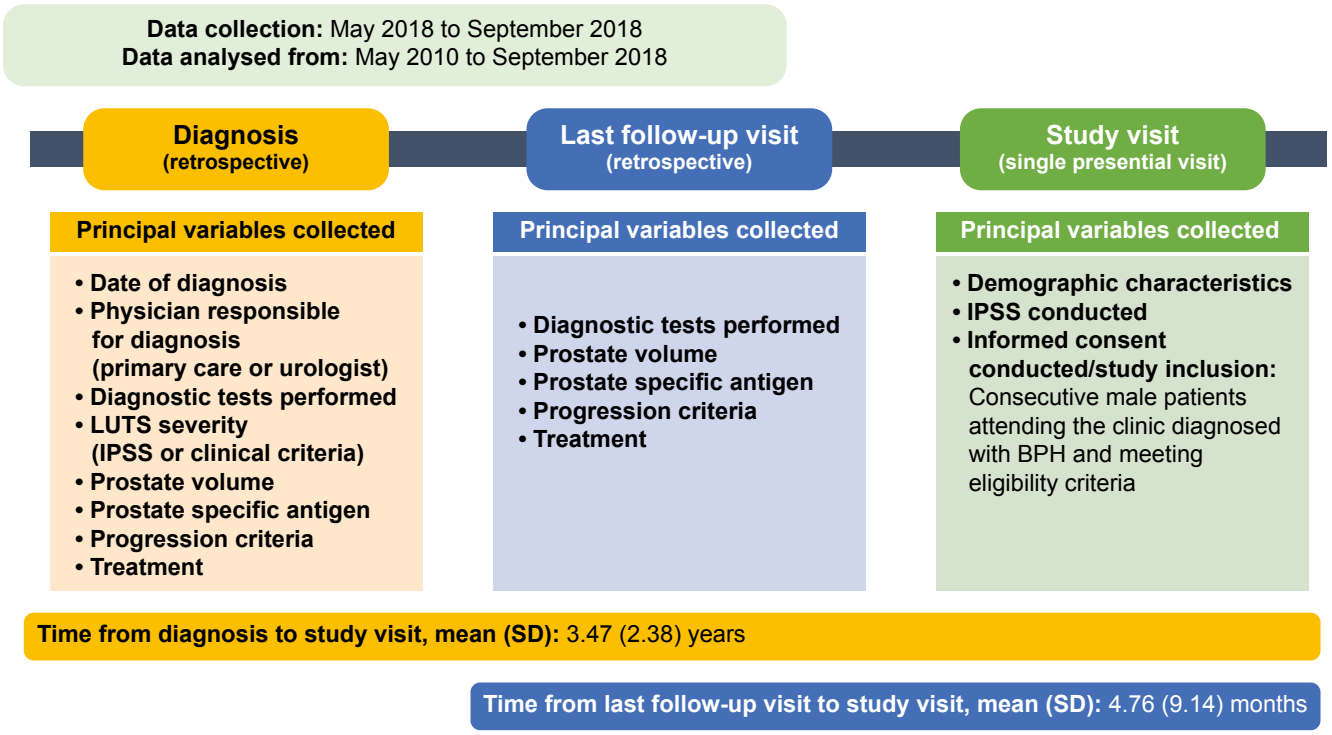

FIGURE 1 Study design. BPH, benign prostatic hyperplasia; IPSS, international prostate symptom score; LUTS, lower urinary tract symptom; SD, standard deviation

The study protocol and procedures were reviewed and approved by an Independent Review Board and ethics committee (CElm del Hospital Universitario Severo Ochoa, Madrid, Spain) prior to commencement. The study was conducted in accordance with Good Clinical Practice ethical principles, as outlined in the Declaration of Helsinki concerning this type of study.[28] Classification from the Spanish Agency of Medicines and Medical Devices[29] was obtained and 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 caused by BPH ≤ 8 years prior to the study visit were included. Data regarding clinical diagnosis of BPH and last available follow-up visit including a PSA determination were required to be available in the patient's health record. Patients were excluded if presenting with LUTS caused by conditions other than BPH, or with prostatic, bladder or pelvic neoplasia, history of pelvic surgery (including bladder, prostate or urethra) or an absolute indication for surgical treatment of BPH (defined as recurrent/refractory AUR, recurrent urinary infections, overflow incontinence, dilated upper urinary tract, bladder stones or diverticula and macrohaematuria resistant to BPH treatment rendering the patient unsuitable for medical treatment at the current disease stage).[9] Patients attending the clinic (for any reason) who met the study eligibility criteria were recruited consecutively.

2.3 | Endpoints and assessments

2.3.1 | Primary endpoint

The primary endpoint was to describe the demographic and clinical characteristics of patients with LUTS caused by BPH in primary care and urological clinics at study visit. Patients were assessed both as a whole population (ie patients from primary care and urology clinics together) and as two separate groups (primary care vs urology).

2.3.2 | Assessments

To describe demographic characteristics, the following variables were collected at the study visit: age; weight; height; body mass index (BMI); working situation; interference of LUTS with work activity and personal antecedents (hypertension, diabetes mellitus and heart failure).

To describe the clinical characteristics, the following were collected at diagnosis: date of BPH diagnosis and physician responsible for diagnosis (primary care or urologist).

At the patient's last available follow-up visit, the following variables were assessed: prostate volume, PSA value, progression criteria and treatment; in addition, diagnostic tests were performed (Figure 1). These data were used for the analyses performed at the study visit time point.

At the study visit, LUTS severity was assessed using the total score of IPSS items: mild (1-7), moderate (8-19) and severe (20-35).

Impact on QoL was based on item 8 of the IPSS, from 0 (delighted) to 6 (very bad).

Prostate volume, as assessed by echography and/or DRE, was categorised according to four qualitative groups (defined according to routine practice): volume I (≤30 cc); II (31-50 cc); III (51-75 cc) and IV (>75 cc).[1] The PSA value was used to define the clinical profile of disease progression and categorised as follows: PSA < 1.5 ng/mL and PSA ≥ 1.5 ng/mL. Progression criteria were defined using 2 criteria (moderate to severe LUTS and PSA ≥ 1.5 ng/mL) or 3 criteria (moderate to severe LUTS, prostate volume >30 cc and PSA ≥ 1.5 ng/mL).[30]

2.3.3 | Secondary endpoints

Secondary endpoints were assessed in the total population and as separate data sets for patients recruited in primary care and urology in order to describe potential differences in the profiles of patients with BPH in different healthcare settings. Endpoints assessed at diagnosis and study visit were as follows: LUTS severity according to assessment criteria (ie clinical criteria or IPSS); proportion of patients with worsening LUTS since diagnosis; proportion of patients developing progression criteria since diagnosis and diagnostic tests used to assess LUTS caused by BPH (ie those used by the investigators in their routine clinical practice, excluding the IPSS).

The therapeutic management of LUTS caused by BPH and its relationship with patient characteristics (age, time since diagnosis, prostate volume, severity of LUTS and progression criteria) was also assessed, and will be presented in a subsequent publication.

2.4 | Data analysis

Assuming the real-world population prevalence of BPH in men >50 years old was 50%[2,31] and estimating a proportion using an asymptomatic normal 95% bilateral confidence interval (CI) with a maximum imprecision rate of 4%, it was considered necessary to analyse 601 patients. To achieve this, 675 patients needed to be recruited, assuming a drop-out/missing rate of approximately 10%. As a larger proportion of patients with BPH are followed-up in primary care than in urology, the distribution of the sample 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 9.2 (SAS Institute, Inc, Cary, NC, USA).[32]

Continuous variables were described using the number of non-missing observations, number of missing observations, standard measures of central tendency and dispersion (mean and standard deviation [SD] when data were normally distributed; mean, SD, median quartiles, minimum, maximum and 95% CI when data were non-normally distributed) and eventually truncated means and percentiles. All categorical, binary and ordinal variables were summarised using number of non-missing observations, number of missing observations, count and percentage (of non-missing observations) of each category.

Statistical tests were used depending on whether response variables were discrete (chi-square test, McNemar's test or Fisher's exact test) continuous (Student's *t* test or analysis of variance test, Wilcoxon sign-rank test or Kruskal-Wallis test) or ordinal (trend chi-square test). A statistical significance level of 0.05 was used in all tests.

3 | RESULTS

3.1 | Study population

Of 155 physicians contacted, 109 met the feasibility criteria and 88 agreed to participate in the study (primary care, n = 52; urology, n = 36). Of 675 patients enrolled, a total of 670 met eligibility criteria and were included in the study (primary care, n = 435; urology, n = 235) (Figure 2).

3.2 | Primary endpoint

3.2.1 | Demographic characteristics

At study visit, the mean (SD) age of patients included in the study was 69.1 (8.6) years; this was higher in primary care than urology ($P = .009$). Of 166/670 (24.8%) patients who worked, 42/166 (25.3%) experienced interference with working activity as a result of LUTS (Table S1).

Most patients (428/670 [63.9%]) had clinical personal antecedents; the proportion was higher in primary care than urology (primary care: 300/435 [69.0%]; urology: 128/235 [54.5%]; $P < .001$) (Table S1). A higher proportion of patients had hypertension and diabetes in primary care than urology (hypertension: primary care 270/435 [62.1%] vs urology 115/235 [48.9%], $P = .001$; diabetes: primary care 121/435 [27.8%] vs urology 48/235 [20.4%], $P = .036$); however, no difference was observed for heart failure (primary care: 29/435 [6.7%] vs urology: 16/235 [6.8%], $P = .944$) (Table S1). Almost half (310/670 [48.4%]) of patients were overweight and 178/670 (27.8%) were obese, with no difference between healthcare settings across BMI categories ($P = .078$).

3.2.2 | Clinical characteristics

In total, 371/670 (55.4%) patients were diagnosed in primary care and 299/670 (44.6%) were diagnosed in urology. Most (77.0%) patients diagnosed in primary care continued attending primary care and most (84.7%) patients diagnosed in urology were followed-up by urologists.

The mean (SD) time since diagnosis and time since last follow-up visit was longer for patients monitored in primary care than urology

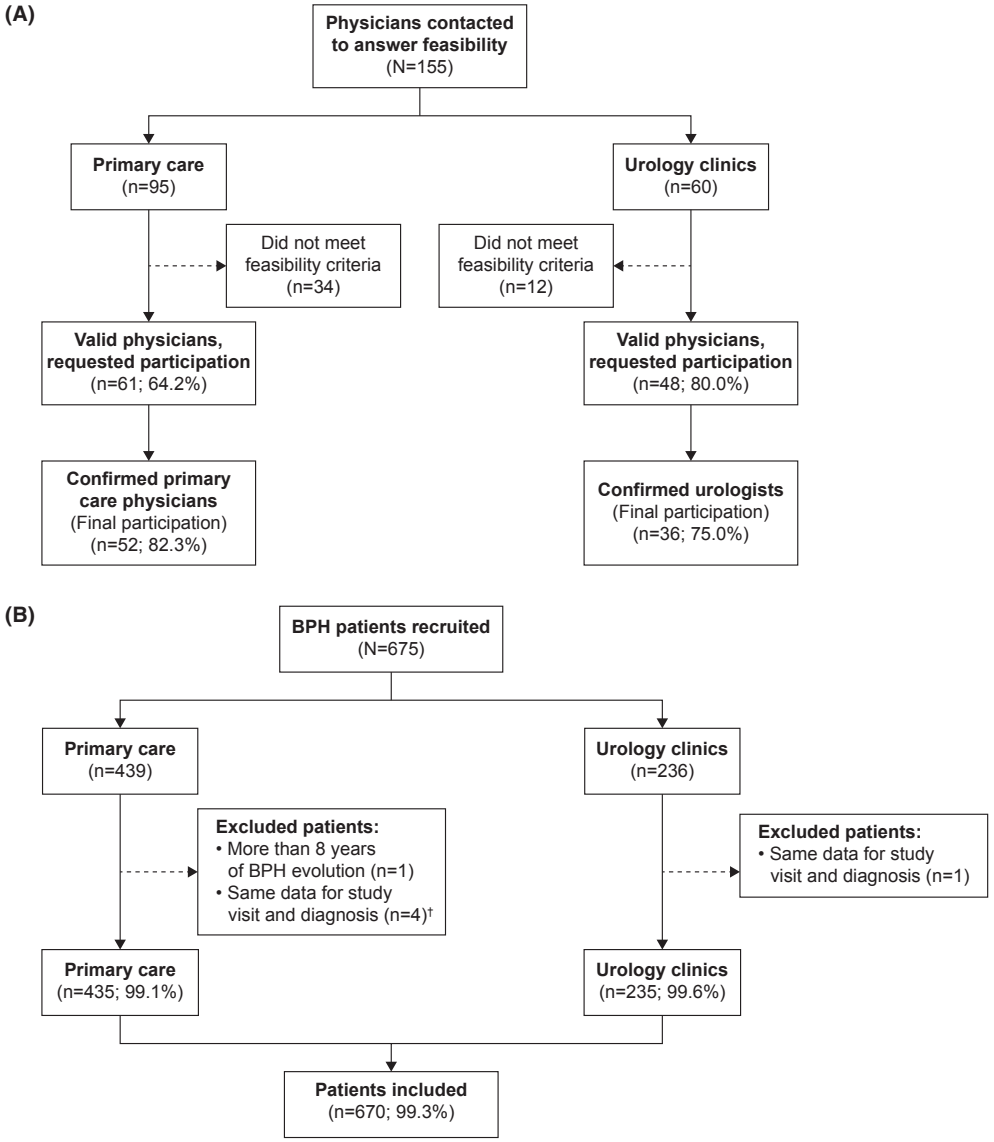

FIGURE 2 Physician (A) and patient (B) population flow diagram. †One patient had both >8 y of BPH evolution and the same data for study visit and diagnosis. BPH, benign prostatic hyperplasia

(time since diagnosis: primary care 3.73 [2.39] years, urology: 2.99 [2.29] years [$P < .001$]; time since last follow-up visit: primary care 5.17 [9.10] months, urology 3.99 [9.19] months [$P < .001$]) (Table S2). Time since last follow-up was >12 months in a small proportion of patients (81/670 [12.1%]), with no difference between healthcare settings ($P = .693$).

The mean (SD) IPSS at the study visit was 12.6 (6.9); most patients (500/670 [74.6%]) had moderate to severe LUTS (primary care 316/435 [72.6%] vs urology 184/235 [78.3%]). There was no difference between healthcare settings in the proportion of patients with mild, moderate, and severe LUTS ($P = .080$) (Table 1).

The BPH symptoms that caused the most disturbance (category: "almost always") were weak stream (90/670 [13.4%]) and frequency (58/670 [8.7%]). Nocturia (frequency 1-2 times/night) was reported by most (408/670 [60.9%]) patients.

On IPSS item 8 (QoL), most patients (525/670 [78.4%]) reported feeling "delighted" to "mixed" and 145/670 (21.6%) patients felt "mostly dissatisfied" to "terrible", with no significant difference between healthcare settings ($P = .305$) (Table 1).

Prostate volume was similar between healthcare settings at study visit, regardless of the diagnostic procedure, and most patients had a prostate volume >30 cc (global measure) at study visit (358/438 [81.7%]) (Table 2). Of patients with a prostate volume ≤30 cc, the proportion determined by DRE was higher than echography (DRE: 51/231 [22.1%]; echography: 43/281 [15.3%]) (Table 2); however, no statistical tests were performed.

Mean (SD) PSA was higher in primary care than urology ($P < .001$) at study visit (primary care: study visit 6.8 [13.3] ng/mL; urology: study visit 2.8 [2.2] ng/mL) (Table 3). Most patients had a PSA ≥ 1.5 ng/mL at study visit (primary care: 324/435 [74.5%], and

TABLE 1 IPSS score and LUTS severity and QoL according to IPSS per healthcare setting

	Primary care (n = 435)	Urology clinics (n = 235)	Total (N = 670)	*P*-value[a]
IPSS at study visit, mean (SD)	12.1 (6.8)	13.4 (7.0)	12.6 (6.9)	.024
LUTS severity, n (%)				.080
Mild (IPSS 0-7)	119 (27.4)	51 (21.7)	170 (25.4)	
Moderate (IPSS 8-19)	251 (57.7)	135 (57.4)	386 (57.6)	
Severe (IPSS 20-35)	65 (14.9)	49 (20.9)	114 (17.0)	
IPSS item 8 at study visit, mean (SD)	2.5 (1.4)	2.5 (1.5)	2.5 (1.4)	.974
IPSS item 8 caused by LUTS, n (%)				.305
Delighted	18 (4.1)	16 (6.8)	34 (5.1)	
Pleased	89 (20.5)	49 (20.9)	138 (20.6)	
Mostly satisfied	135 (31.0)	58 (24.7)	193 (28.8)	
Mixed	99 (22.8)	61 (26.0)	160 (23.9)	
Mostly dissatisfied	58 (13.3)	25 (10.6)	83 (12.4)	
Unhappy	24 (5.5)	18 (7.7)	42 (6.3)	
Terrible	12 (2.8)	8 (3.4)	20 (3.0)	

Abbreviations: IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; QoL, quality of life; SD, standard deviation.

[a]Primary care versus urology clinics.

urology: 159/235 [67.7%]); with no difference between healthcare settings (study visit: $P = .060$) (Table 3).

The proportion of patients fulfilling progression criteria was 48.4% at study visit (primary care 216/435 [49.7%]; urology 108/235 [46.0%]); proportions were similar in both healthcare settings (study visit: $P = .361$) (Table 4).

3.3 | Secondary endpoints

3.3.1 | LUTS severity according to assessment criteria at diagnosis and study visit

Overall, clinical criteria were used more often than IPSS to determine the severity of LUTS at diagnosis (primary care: clinical criteria 317/434 [73.0%], IPSS 117/435 [26.9%]; urology: clinical criteria 179/234 [76.5%], IPSS 55/235 [23.4%]). Patient distribution across LUTS severity differed depending on the method of assessment used; the proportion of patients with mild LUTS at diagnosis was higher with clinical criteria than IPSS (primary care: clinical criteria 168/317 [53.0%], IPSS 20/117 [17.1%]; urology: clinical criteria 81/179 [45.3%], IPSS 6/55 [10.9%]) and the proportion with moderate to severe LUTS was lower (primary care: clinical criteria 149/317 [47.0%], IPSS 97/117 [82.9%]; urology: clinical criteria 98/179 [54.7%], IPSS 49/55 [89.1%]) (Table 5). When using clinical criteria at diagnosis, there was a difference in severity of LUTS between diagnosis and study visit, with a larger proportion of patients with severe symptoms at study visit regardless of healthcare setting ($P < .001$). The observed difference in severity of LUTS at diagnosis and study visit was lower when IPSS was used to assess LUTS severity at diagnosis (Table 5).

3.3.2 | Proportion of patients with worsening LUTS from diagnosis to study visit according to assessment criteria

Less than half of patients in both healthcare settings experienced a worsening of LUTS severity from diagnosis to study visit (primary care: 158/434 [36.4%]; urology: 77/234 [32.9%]), with no difference between healthcare settings ($P = .366$) (Table S3). The proportion of patients with worsening LUTS was higher in patients diagnosed using clinical criteria than IPSS (203/496 [40.9%] and 17/172 [9.9%]; $P < .001$) (Table 6).

The proportion of patients who transitioned from mild LUTS at diagnosis to moderate or severe LUTS at the study visit was higher when assessed by clinical criteria compared with IPSS (clinical criteria: 161/249 [64.7%]; IPSS: 7/26 [26.9%]); this was also true for patients transitioning from moderate to severe LUTS (clinical criteria: 42/227 [18.5%]; IPSS: 10/99 [10.1%]) (Table S4).

3.3.3 | Proportion of patients developing progression criteria from diagnosis to study visit

The proportion of patients fulfilling 3 progression criteria was similar in both healthcare settings at diagnosis (primary care: 77/184 [41.8%]; urology 100/223 [44.8%]; $P = .544$) and study visit (primary care: 117/231 [50.6%]; urology: 92/207 [44.4%]; $P = .194$) (Table 4).

At diagnosis, the proportion of patients without progression criteria was similar between healthcare settings (primary care: 244/399 (61.2%);

TABLE 2 Prostate volume at diagnosis and study visit per healthcare setting

Measurement method	Primary care (n = 435)		Urology clinics (n = 235)		Total (N = 670)		*P*-value[a]	
	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit
DRE, n (%)							.893	.192
Total	178 (100)	110 (100)	139 (100)	121 (100)	317 (100)	231 (100)		
I (≤30 cc)	45 (25.3)	20 (18.2)	37 (26.6)	31 (25.6)	82 (25.9)	51 (22.1)		
II (31-50 cc)	89 (50.0)	54 (49.1)	69 (49.6)	59 (48.8)	158 (49.8)	113 (48.9)		
III (51-75 cc)	30 (16.9)	23 (20.9)	25 (18.0)	25 (20.7)	55 (17.4)	48 (20.8)		
IV (>75 cc)	14 (7.9)	13 (11.8)	8 (5.8)	6 (5.0)	22 (6.9)	19 (8.2)		
Missing, n	257	0	96	0	353	0		
Echography							.609	.533
Total, n (%)	257	156	96	125	353	281		
Mean (SD)	56.17 (44.19)	55.41 (30.11)	54.34 (36.48)	60.11 (38.59)	55.35 (40.85)	57.50 (34.16)		
Median (P25, P75)	48.0 (31.0, 65.0)	47.0 (35.0, 72.5)	45.0 (30.0, 70.0)	50.0 (35.0, 70.0)	46.0 (31.0, 65.0)	49.0 (35.0, 72.0)		
Min, max	14.0, 456.0	12.0, 214.0	12.0, 282.0	14.0, 282.0	12.0, 456.0	12.0, 282.0		
95% CI		50.6, 60.2		53.3 66.9		53.5, 61.5		
Missing, n	279	0	108	0	387	0		
Echography category, n (%)							.910	.696
Total	156 (100)	156 (100)	127 (100)	125 (100)	283 (100)	281 (100)		
I (≤30 cc)	30 (19.2)	23 (14.7)	26 (20.5)	20 (16.0)	56 (19.8)	43 (15.3)		
II (31-50 cc)	50 (32.1)	60 (38.5)	44 (34.6)	40 (32.0)	94 (33.2)	100 (35.6)		
III (51-75 cc)	45 (28.8)	39 (25.0)	32 (25.2)	37 (29.6)	77 (27.2)	76 (27.0)		
IV (>75 cc)	31 (19.9)	34 (21.8)	25 (19.7)	28 (22.4)	56 (19.8)	62 (22.1)		
Missing, n	279	0	108	0	387	0		
Global measure, n (%)[b]							.925	.699
Total	244 (100)	231 (100)	185 (100)	207 (100)	429 (100)	438 (100)		
I (≤30 cc)	55 (22.5)	38 (16.5)	43 (23.2)	42 (20.3)	98 (22.8)	80 (18.3)		
II (31-50 cc)	94 (38.5)	102 (44.2)	71 (38.4)	84 (40.6)	165 (38.5)	186 (42.5)		
III (51-75 cc)	61 (25.0)	53 (22.9)	42 (22.7)	50 (24.2)	103 (24.0)	103 (23.5)		
IV (>75 cc)	34 (13.9)	38 (16.5)	29 (15.7)	31 (15.0)	63 (14.7)	69 (15.8)		
Missing, n	191	204	50	28	241	232		

Abbreviations: CI, confidence interval; DRE, digital rectal examination; P25, percentile 25; P75 percentile 75; SD, standard deviation.

[a]Primary care versus urology clinics.

[b]Global measure is the prostate volume obtained by echography or, if not available, by rectal examination.

urology: 121/205 [59.0%]; *P* = .613). Of those without progression criteria at diagnosis, the proportion going on to develop progression criteria at the study visit was higher in primary care than urology (primary care: 85/244 [34.8%]; urology: 26/121 ([21.5%]; *P* = .009) (Table S5).

3.3.4 | Diagnostic tests used to assess LUTS caused by BPH

In both healthcare settings, diagnostic tests used in >50% patients were general and urological clinical history PSA determination, physical examination and renal function (Figure S1). The following diagnostic tests were used more commonly in urology than in primary care: clinical history, DRE, abdominal echography and urine flow. The proportion of patients with a PSA determination at diagnosis was higher in primary care than urology. In both healthcare settings, IPSS was used in less than a third of patients at diagnosis (Figure S1).

4 | DISCUSSION

This observational study described the real-world demographic and clinical characteristics of patients with LUTS caused by BPH in Spain in primary care and urology clinic settings. Most patients were diagnosed

TABLE 3 PSA at diagnosis and study visit

	Primary care (n = 435)		Urology clinics (n = 235) [a]		Total (n = 670)		*P*-value	
	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit
PSA							<.001	<.001
Mean (SD)	6.5 (10.9)	6.8 (13.3)	3.3 (3.3)	2.8 (2.2)	5.1 (8.6)	5.4 (10.9)		
Median (P25, P75)	3.3 (1.6, 6.1)	2.9 (1.5, 5.2)	2.5 (1.3, 4.3)	2.4 (1.2, 3.7)	3.0 (1.5, 5.0)	2.7 (1.4, 4.6)		
Min, max	0.1, 97.0	0.1, 96.7	0.1, 33.5	0.0, 15.6	0.1, 97.0	0.0, 96.7		
95% CI	5.3, 7.7	5.6, 8.1	2.9, 3.7	2.5, 3.1	4.4, 5.8	4.6, 6.2		
PSA by category, n (%)							.149	.060
PSA < 1.5 ng/mL	80 (23.8)	111 (25.5)	78 (29.0)	76 (32.3)	158 (26.1)	187 (27.9)		
PSA ≥ 1.5 ng/mL	256 (76.2)	324 (74.5)	191 (71.0)	159 (67.7)	447 (73.9)	483 (72.1)		
Missing, n	35	0	30	0	65	0		

Abbreviations: CI, confidence interval; P25, percentile 25; P75 percentile 75; PSA, prostate-specific antigen; SD, standard deviation.
[a]Primary care versus urology clinics.

TABLE 4 Progression criteria at diagnosis and study visit

	Primary care (n = 435)		Urology clinics (n = 235)		Total (N = 670)		*P*-value[a]	
	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit	Diagnosis	Study visit
Progression, n (%)							.744	.361
Total	336 (100)	435 (100)	268 (100)	235 (100)	604 (100)	670 (100)		
No progression	205 (61.0)	219 (50.3)	160 (59.7)	127 (54.0)	365 (60.4)	346 (51.6)		
Progression	131 (39.0)	216 (49.7)	108 (40.3)	108 (46.0)	239 (39.6)	324 (48.4)		
Missing, n	35	0	31	0	66	0		
Number of criteria, n (%)							<.001	<.001
Total	371 (100)	435 (100)	299 (100)	235 (100)	670 (100)	670 (100)		
Not available	35 (9.4)	0	31 (10.4)	0	66 (9.9)	0		
2 criteria	152 (41.0)	204 (46.9)	45 (15.1)	28 (11.9)	197 (29.4)	232 (34.6)		
3 criteria	184 (49.6)	231 (53.1)	223 (74.6)	207 (88.1)	407 (60.7)	438 (65.4)		
Progression criteria (3 determinants), n (%)							.544	.194
Total	184 (100)	231 (100)	223 (100)	207 (100)	407 (100)	438 (100)		
No	107 (58.2)	114 (49.4)	123 (55.2)	115 (55.6)	230 (56.5)	229 (52.3)		
Yes	77 (41.8)	117 (50.6)	100 (44.8)	92 (44.4)	177 (43.5)	209 (47.7)		
Progression criteria (2 determinants), n (%)								
Total	152 (100)	204 (100)	45 (100)	28 (100)	197 (100)	232 (100)	.024	.393
No	98 (64.5)	105 (51.5)	37 (82.2)	12 (42.9)	135 (68.5)	117 (50.4)		
Yes	54 (35.5)	99 (48.5)	8 (17.8)	16 (57.1)	62 (31.5)	115 (49.6)		

Note: Progression criteria (3 determinants): LUTS severity, PSA and PV available data.
Progression criteria (2 determinants): LUTS severity and PSA available data, PV data not available.
Abbreviations: LUTS, lower urinary tract symptoms; PSA, prostate-specific antigen; PV, prostate volume.
[a]Primary care versus urology clinics.

and followed-up in primary care, partly because of the study design (recruitment in primary care vs urology was 2:1). In addition, the low proportion of patients in primary care with severe LUTS (14.9%) or rating their QoL caused by LUTS as "unhappy or terrible" (8.3%) may have limited the number of referrals to urology. In accordance with the cost-effective approach to managing chronic conditions, it is recommended that the majority of BPH management takes place in primary care, with referral to urology services reserved for more specialised

TABLE 5 LUTS severity at diagnosis and study visit with diagnosis according to IPSS and clinical criteria in primary care and urology clinics

Method	Severity	Primary care (n = 435)	Urology clinics (n = 235)	Total (N = 670)	*P*-value[a]
Diagnosis by IPSS	Diagnosis, n (%)				.329
	Total	117 (100)	55 (100)	172 (100)	
	Mild (0-7 points)	20 (17.1)	6 (10.9)	26 (15.1)	
	Moderate (8-19 points)	63 (53.8)	36 (65.5)	99 (57.6)	
	Severe (20-35 points)	34 (29.1)	13 (23.6)	47 (27.3)	
	Study visit, n (%)				.945
	Total	117 (100)	55 (100)	172 (100)	
	Mild (0-7 points)	24 (20.5)	12 (21.8)	36 (20.9)	
	Moderate (8-19 points)	67 (57.3)	30 (54.5)	97 (56.4)	
	Severe (20-35 points)	26 (22.2)	13 (23.6)	39 (22.7)	
	P-value[b]	.0678	.1796	.0162	
Diagnosis by clinical criteria	Diagnosis, (%)				.084
	Total	317 (100)	179 (100)	496 (100)	
	Mild (0-7 points)	168 (53.0)	81 (45.3)	249 (50.2)	
	Moderate (8-19 points)	140 (44.2)	87 (48.6)	227 (45.8)	
	Severe (20-35 points)	9 (2.8)	11 (6.1)	20 (4.0)	
	Missing, n	1	1	2	
	Study visit, n (%)				.024
	Total	318 (100)	180 (100)	498 (100)	
	Mild (0-7 points)	95 (29.9)	39 (21.7)	134 (26.9)	
	Moderate (8-19 points)	184 (57.9)	105 (58.3)	289 (58.0)	
	Severe (20-35 points)	39 (12.3)	36 (20.0)	75 (15.1)	
	P-value[b]	<.001	<.001	<.001	

Abbreviations: IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms.

[a]Primary care versus urology clinics.

[b]Diagnosis versus study visit.

TABLE 6 Change in disease severity according to different methods of assessing disease severity at diagnosis

	IPSS	Clinical criteria	Total	*P*-value[a]
Severity change, n (%)				<.001
Total	172 (100)	496 (100)	668 (100)	
1—Improvement	32 (18.6)	51 (10.3)	83 (12.4)	
2—Maintain	123 (71.5)	242 (48.8)	365 (54.6)	
3—Worsening	17 (9.9)	203 (40.9)	220 (32.9)	
Missing, n	0	2	2	

Abbreviation: IPSS, international prostate symptom score.

[a]IPSS versus clinical criteria.

care (eg invasive treatment) that expands beyond diagnostic assessments.[13,22] Our findings showed that, although the demographic and clinical characteristics of patients with BPH were generally consistent across healthcare settings, patients attending primary care tended to be slightly older (although this was not statistically supported), with more pre-existing comorbidities, possibly reflecting a more chronic BPH profile than those attending urology clinics. Additionally, the time elapsed since last follow-up was far greater in primary care compared with urology, which may reflect a tendency towards more complex BPH management in urology compared with primary care,[13,22] or the lack of institutional protocols for BPH management in primary care, which are present in urology clinics. A strength of this study is that patient demographics and clinics are similar to other previous studies including patients with BPH[63839]; therefore, the patient population is likely representative of the wider population and results are generalisable to other countries.

Furthermore, our findings showed that patients attending urology settings had, in general, more severe symptomatic BPH disease compared with patients attending primary care, although this difference was not statistically significant. An unexpected finding was that clinical criteria would be more commonly used than the validated IPSS questionnaire to evaluate LUTS severity at diagnosis in both primary care and urology. LUTS severity was generally assessed as lower, and the proportion of patients with worsening LUTS showed to be higher when LUTS severity was assessed at diagnosis using clinical criteria compared with IPSS. Additionally, differences between LUTS severity at diagnosis and follow-up were

more pronounced when LUTS severity evaluation at diagnosis was performed with clinical criteria compared with IPSS. Given these findings, it is possible that clinical criteria underestimate LUTS severity at diagnosis. Therefore, this study suggests that the way LUTS severity is determined using either IPSS or clinical criteria could have a direct impact on therapeutic decisions, which ultimately may affect clinical progression during follow-up.

The IPSS is a widely used, validated method of assessing the severity of LUTS in patients with BPH[33] and is recommended by clinical guidelines.[7,9] However, our findings revealed that it is not commonly used in the evaluation of LUTS severity in either primary care or urology clinics. This may be partly because of limitations of the IPSS, including reproducibility of responses, which is affected by the level of patient education.[34] Clinical guidelines recommend the use of tools that allow an objective evaluation of symptoms rather than subjective perception.[7,9] Therefore, increasing the use of IPSS could be valuable in facilitating the appropriate diagnosis and follow-up management of BPH.

Consistent with existing literature, progression criteria were prevalent from diagnosis in both healthcare settings.[1] Additionally, most patients had a prostate volume >30 cc and/or PSA ≥ 1.5 ng/mL at both diagnosis and follow-up, irrespective of healthcare setting. PSA was higher in primary care than urology clinics at diagnosis; however, the median PSA values observed are less pronounced than the mean values. Together with the LUTS severity (IPSS ≥ 8), these are the defined predictors of BPH progression; the appropriate identification of BPH is important as it will facilitate optimal medical management of patients with BPH.

The use of diagnostic assessments was not fully in accordance with clinical guideline recommendations.[9,35] In both healthcare settings, the most commonly used diagnostic assessments were clinical history, PSA determination, physical examinations and renal function. Urinalysis was used in less than half of patients and IPSS in less than one third of patients in both healthcare settings at diagnosis. Additionally, although considered an important diagnostic test for BPH,[9] DRE was performed in less than half of patients in primary care. This low adherence to the recommended practice of using IPSS and DRE may be partly as a result of the high clinical load of patients in Spain. Both IPSS and DRE take longer to perform than clinical history alone; therefore, time and resource constraints may have precluded their use. Changes in usual clinical practice could improve diagnostic assessment in both primary care and urology. PSA was used more commonly in primary care than urology in the current study. A European prospective epidemiological study concluded that objective variables such as age, IPSS and PSA support the accurate diagnosis of patients with BPH in primary care.[6] Therefore, the initial evaluation of LUTS severity using simple diagnostic tools available in primary care may be an appropriate strategy to minimise delay in the management of BPH and inform the appropriate referral to urology services.[13,14]

There are some limitations to this study. Firstly, with the use of real-world clinical data, important information that may help address the study objectives could be missing; however, this limitation is common to all real-world studies based on routinely collected data (ie they are not unique to this study).[36] To mitigate this, initial feasibility tests assessed the use of IPSS and determined whether investigators had access to the required information in patient health records. An associated strength is that this study's results are applicable to the real-world patient population. Secondly, prostate volume >30 cc (a definition of disease progression in this study) was based on global judgement which is a composite of DRE and echography measurements. Finally, specific eligibility criteria, such as the requirement for ≥1 PSA determination at follow-up visit, may limit the overall generalisability of the study sample; however, there is no reason to assume that patients with a previously documented PSA value would have different characteristics from those without. To overcome the potential selection bias, investigators were required to recruit five consecutive patients who met the eligibility criteria.

5 | CONCLUSION

Real-world evidence for patients with BPH managed in Spain showed that patients who attended primary care tend to be older and with more comorbidities compared with those in urology clinics. Most patients had moderate to severe LUTS, a prostate volume >30 cc, a PSA value ≥1.5 ng/mL and progression criteria were present in almost half of patients with BPH. Overall, these results were similar between primary care and urology.

Although demographic and clinical characteristics of patients with BPH in Spain were largely similar in primary care and urology clinics, the methods used for the evaluation of LUTS severity and BPH diagnosis differed between healthcare settings and were not completely aligned with clinical guidelines recommendations. Specifically, LUTS were diagnosed as less severe, and a higher proportion of worsening LUTS was observed when the assessment method was clinical criteria compared with IPSS, suggesting that clinical criteria may underestimate LUTS severity. The use of IPSS versus clinical criteria may impact therapeutic decisions and consequently could increase the risk of clinical symptom progression. Therefore, increasing the use of validated tools (ie IPSS) and other recommended assessments (ie prostate volume determination) according to clinical guidelines may enhance an optimal management of patients with BPH. Further research and educational efforts should aim to enhance optimal diagnosis and follow-up of patients with LUTS by reconciling BPH clinical guidelines and clinical practice in primary care and urology clinics. Further analyses are needed to assess the relationship between the methods used to determine symptom severity, treatment decisions and disease progression during follow-up.

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DISCLOSURES

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; speaker's bureaus for GSK, Astellas and Pierre Fabre and has received compensation from GSK and Pierre Fabre for being a trial investigator. 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. JMP-M, DLM, AAR and RCP are employees of GSK and hold shareholder status in the company. MTM-F has received compensation from GSK for travel expenses and for being a 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.

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SUPPORTING INFORMATION

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

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