

Pang, K. H., Campi, R., Arlandis, S., Bø, K., Chapple, C. R., Costantini, E., Farag, F., Groen, J., Karavitakis, M., Lapitan, M. C., Manso, M., Arteaga, S. M., Nambiar, A. K., Nic An Ríogh, A., O'Connor, E., Osman, N. I., Peyronnet, B., Phé, V., Sakalis, V. I., Sihra, N., Tzelves, L., van der Vaart, H., Yuan, Y., Omar, M. I., Harding, C. (2021). Diagnostic Tests for Female Bladder Outlet Obstruction: A Systematic Review from the European Association of Urology Non-neurogenic Female LUTS Guidelines Panel. *European Urology Focus*.
<http://dx.doi.org/10.1016/j.euf.2021.09.003>

Dette er siste tekst-versjon av artikkelen, og den kan inneholde små forskjeller fra forlagets pdf-versjon. Forlagets pdf-versjon finner du her:
<http://dx.doi.org/10.1016/j.euf.2021.09.003>

This is the final text version of the article, and it may contain minor differences from the journal's pdf version. The original publication is available here:
<http://dx.doi.org/10.1016/j.euf.2021.09.003>

Diagnostic Tests for Female Bladder Outlet Obstruction: A Systematic Review from the European Association of Urology Non-neurogenic Female LUTS Guidelines Panel

Authorship by line:

1. Karl H. Pang (*) Academic Urology Unit, University of Sheffield, Sheffield, United Kingdom
2. Riccardo Campi (*) 1. Unit of Urological Robotic Surgery and Renal Transplantation, University of Florence, Careggi Hospital, Florence, Italy; 2. Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy.
3. Salvador Arlandis. Urology Department, La Fe University and Polytechnic Hospital, Valencia, Spain
4. Kari Bo. Norwegian School of Sport Sciences, Department of Sports Medicine, Oslo, Norway.
5. Christopher R. Chapple. Section of Functional and Reconstructive Urology, Department of Urology, Royal Hallamshire Hospital, Sheffield, UK, University of Sheffield
6. Elisabetta Costantini. Department of Medicine and Surgery, University of Perugia, Italy
7. Fawzy Farag. 1. Department of Urology, Sohag University Hospital, Egypt; 2. Department of Urology, East Suffolk and North Essex NHS Foundation Trust, UK
8. Jan Groen. Department of Urology, Erasmus MC, Rotterdam, The Netherlands.
9. Markos Karavitakis. Department of Urology, University General Hospital of Heraklion, University of Crete, Medical School, Heraklion, Crete, Greece
10. Marie Carmela Lapitan. College of Medicine / Philippine General Hospital / National institutes of Health, University of the Philippines Manila, Philippines
11. Margarida Manso. 1. Department of Urology, São João University Hospital Center, Porto, Portugal; 2. Faculty of Medicine of Porto, Porto, Portugal
12. Serenella Monagas Arteaga. Department of Urology, University Hospital of San Agustín, Avilés, Spain
13. Arjun K. Nambiar. Department of Urology, Freeman Hospital, Newcastle-upon-Tyne, UK
14. Aisling U. Nic An Ríogh. Department of Urology, Cork University Hospital, Cork, Ireland
15. Eabhann M. O'Connor. Department of Urology, Beaumont Hospital, Dublin, Ireland
16. Nadir I. Osman. Section of Functional and Reconstructive Urology, Department of Urology, Royal Hallamshire Hospital, Sheffield, UK, University of Sheffield
17. Benoit Peyronnet. University of Rennes, Rennes, France
18. Véronique Phé. Sorbonne University, Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Academic Hospital, Department of Urology, Paris, France
19. Vasileios I. Sakalis. Department of Urology, Agios Pavlos General Hospital of Thessaloniki, Greece
20. Néha Sihra. Guy's and St Thomas' NHS Foundation Trust, London, UK
21. Lazaros Tzelves. Second Department of Urology, National and Kapodistrian University of Athens, Sismanogleio General Hospital, Athens, Greece
22. Huub van der vaart. 1. University Medical Center Utrecht, division Woman & Baby; 2. Bergman Clinics Women's Health, The Netherlands
23. Yuhong Yuan. Division of Gastroenterology, Department of Medicine, McMaster University, Hamilton, ON, Canada
24. Muhammad Imran Omar (**), 1. University of Aberdeen, United Kingdom; 2. European Association of Urology, The Netherlands
25. Christopher K. Harding (**), Department of Urology, Freeman Hospital, Newcastle-upon-Tyne, UK

* Pang KH and Campi R should be considered joint first author; ** Omar MI and Harding CK should be considered joint senior author.

Contact Author:**Muhammad Imran Omar**

Vice-Chair Methods Committee, EAU

Member Non-Neurogenic Female LUTS Panel, EAU

Guidelines Office Methodology Supervisor, EAU

Research Fellow, Academic Urology Unit,

Health Sciences Building (second floor),

University of Aberdeen, Foresterhill,

Aberdeen

AB25 2ZD

United Kingdom

Tel: 44-1224-438126

Email: m.i.omar@abdn.ac.uk & m.i.omar@uroweb.org

Keywords:

Accuracy; Bladder Outlet Obstruction; Diagnosis; Female; Lower Urinary Tract Symptoms; Test; Urodynamics

Word Count of the abstract: 298/300

Word Count of the text: 3751/3700

Take home message: 15/40

References: 39/60

Tables: 2

Figures: 3

Appendix: 1

Supplementary Tables: 1

Funding: None

Abstract

Context: Female bladder outlet obstruction (fBOO) is a relatively uncommon condition compared to its male counterpart. Several criteria have been proposed to define fBOO, but the comparative diagnostic accuracy of these remains uncertain.

Objective: To identify and compare different tests to diagnose fBOO through a systematic review process.

Evidence Acquisition: A systematic review of the literature was performed according to the Cochrane Handbook and PRISMA checklist. The EMBASE/MEDLINE/Cochrane databases were searched up to August 4th 2020. Studies on women ≥ 18 years with suspected BOO involving diagnostic tests were included. Pressure-flow studies or fluoroscopy was used as the reference standard where possible. Two reviewers independently screened all articles, searched reference lists of retrieved articles and performed data extraction. The risk of bias was assessed using QUADAS-2.

Evidence Synthesis: Overall, 28 non-randomised studies involving 10,248 patients were included in the qualitative analysis. There was significant heterogeneity regarding the characteristics of women included in BOO cohorts (i.e., mixed cohorts including both anatomical and functional BOO). Pressure-flow studies +/- fluoroscopy were evaluated in 25 studies. Transperineal doppler ultrasound was used to evaluate bladder neck dynamics in two studies. One study tested the efficacy of transvaginal ultrasound. The urodynamic definition of fBOO also varied amongst studies with different parameters and thresholds used, which precluded meta-analysis. Three studies derived nomograms using maximum flow rate (Q_{max}) and voiding detrusor pressure at Q_{max} . The sensitivity, specificity and overall accuracy range was 54.6-92.5%, 64.6-93.9%, and 64.1-92.2% respectively.

Conclusion: The available evidence on diagnostic tests for fBOO is limited and heterogeneous. Pressure-flow studies +/- fluoroscopy remains the current standard for diagnosing fBOO.

Patient Summary: Evidence on tests used to diagnose female bladder outlet obstruction was reviewed. The most common test used was pressure-flow studies +/- fluoroscopy, which remains the current standard for diagnosing bladder outlet obstruction in women.

1. Introduction

Female bladder outlet obstruction (fBOO) is an uncommon condition that can be caused by anatomical or functional abnormalities (1). The estimated prevalence is 2–23% depending on diagnostic criteria (2). The International Continence Society (ICS) defines fBOO as “*the generic term for obstruction during voiding, characterised by a reduced urine flow rate (FR) and/or presence of a raised post-void residual (PVR) and an increased detrusor pressure (P_{det})*” (3). Female patients typically present with lower urinary tract symptoms (LUTS) which are rarely isolated voiding symptoms (4). The urodynamics criteria and diagnostic cut-off values for fBOO are not defined, and vary in the literature. This is in stark contrast to BOO in males which is well-defined and has a greater evidence base (5). The objective of the current systematic review (SR) was to identify and compare different diagnostic tests, which have been proposed for the diagnosis of fBOO.

2. Evidence Acquisition

2.1. Review protocol and search strategy

The review followed the methods detailed in the Cochrane Handbook and followed the PRISMA checklist (**Supplementary Table 1**), guided by European Association of Urology (EAU) Guidelines Office Methods Committee (6–8).

Medline, Embase, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials databases were searched without language or other restrictions for all relevant publications up to August 4th 2020. The search strategy is detailed in **Appendix 1**. Reference lists of the included studies were screened and included for full-text screening and data extraction if they fulfilled our *a priori* inclusion criteria.

Two review authors (KHP and RC) screened all abstracts and full-text articles independently. Any disagreement was discussed and resolved by the senior authors (MIO, CKH). Standardised data extraction was performed by the same two review authors who performed screening. The flow-chart depicting the overall review process according to the PRISMA statement is shown in **Figure 1**.

2.2. Eligibility criteria

Eligibility criteria of this systematic review are the following:

- *Study design*: All types of studies including at least 10 participants assessing diagnostic accuracy of tests for fBOO.
- *Participants*: Adult female (≥ 18 years) patients with non-neurogenic LUTS suspected of BOO with no established aetiology;
- *Index tests*: Any test used to diagnose BOO (including, but not limited to, uroflowmetry, standard urodynamics (UDS), video-urodynamics (VUDS), voiding fluoroscopy, electromyography, urethral pressure profilometry, doppler ultrasound, infrared spectroscopy or endoscopy);
- *Comparator tests*: Any of the above-mentioned diagnostic tests or no control group;
- *Test accuracy measures*: Any metric pertaining to diagnostic accuracy for BOO, including sensitivity, specificity, negative/positive predictive value (NPV/PPV), and overall accuracy.
- Secondary outcomes included the criteria for defining female BOO.

2.3. Assessment of Risk of bias in individual studies

Risk of bias (RoB) assessment within the included studies was performed independently by two authors (KHP and RC) according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (9) (**Figures 2-3**). This tool provides a measure for RoB and applicability over four domains of interest (patient selection, index test, reference standard, and timing of the index test and of the reference standard). A list of the most important potential confounders for outcomes was developed *a priori* with clinical content experts (EAU Non-neurogenic Female LUTS Guidelines Panel). Confounder assessment included whether each prognostic confounder was considered and whether, if necessary, it was controlled for in the analysis. Potential confounding factors assessed were: 1) whether indices for UDS were determined automatically or manually; 2) whether the UDS adhered to contemporaneous quality standards (ICS standards for studies from 2002 onwards; for studies before 2002, judgment was made by reviewers). Disagreement was solved by a third review author (MIO).

2.4. Data analysis

Due to the expected heterogeneity in definitions and thresholds of the index tests for diagnosing fBOO, a quantitative analysis and meta-analysis was not feasible and therefore a qualitative (narrative) synthesis of all included studies was performed. Where elements of diagnostic accuracy were not reported by study authors, we calculated these by using a two-by-two contingency table consisting of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) rates based on data reported by study authors. True positive cases were those diagnosed by VUDS used as reference standard. Measures of test performance included sensitivity, specificity, PPV, NPV and overall accuracy.

3. Evidence Synthesis

3.1. Study selection

The search identified 6,344 citations. After duplicate report removal, 4076 were screened by abstract and 79 were assessed for full-text eligibility. Overall, 28 studies fulfilled the inclusion criteria set for this review and 10,248 patients were included in the qualitative analysis (4,10–32) (**Figure 1**).

3.2. Characteristics of the included studies

The characteristics of the 28 included studies are detailed in **Table 1** and **Supplementary Table 2**. Of these, 25 evaluated the use of UDS+/- fluoroscopy (4,10–22,26–36), two of which evaluated pre-existing nomograms (35,36); one evaluated the use of transvaginal ultrasound scan (TVUS) and voiding urodynamics (23); and two studies looked at transperineal doppler USS (TPUS) (24,25). Five studies defined cut-offs for UDS parameters (17,26,29,31,32), one study described fluoroscopic characteristics for fBOO (20), one study evaluated area under the curve (AUC) of detrusor pressure (18), and three studies derived a nomogram to diagnose fBOO (10,14,19).

3.3. Risk of bias assessment

QUADAS-2 tool was used to assess RoB within studies. Results are graphically illustrated in **Figures 2-3**. The proportion of studies with low risk of bias in the “patient selection”, “index test”, “reference standard” and “flow and timing” domains was 75%,

82.1%, 42.9% and 78.6%, respectively. The domain showing the highest proportion of studies with an “unclear” risk of bias was the “reference standard” domain (57.1%). Overall, there were low levels of concern about the applicability of the studies’ findings to the review question regarding the “patient selection” and “index test” domains, while there was a high level of concern regarding the “reference standard” domain in more than half of included studies (54%).

3.4. Results of individual studies: a narrative synthesis

The UDS parameter cut-offs, nomogram and diagnostic details for each study are summarised in **Table 2**. The overall range of diagnostic performance across all tests was sensitivity, 54.6-92.5%; specificity 64.6-93.9%; PPV 50-95.5%; NPV 33.3-97.1%; overall accuracy 64.1-92.2%.

3.4.1 Defining UDS cut-off values

Massey and Abrams defined cut-offs of $Q_{\max} < 12$ mL/s, $P_{\det.Q_{\max}} > 50$ cmH₂O and urethral resistance > 0.2 to diagnose fBOO (32). In 5,948 consecutive patients presenting with LUTS, 163 (2.74%) were found to have fBOO based on these criteria. Lemack and Zimmern performed receiver-operator characteristics (ROC) analyses from urodynamics on female patients with voiding LUTS. All patients had prior voiding cystourethrography and cut-off values of $Q_{\max} \leq 11$ mL/s and $P_{\det.Q_{\max}} \geq 21$ cmH₂O optimized the diagnostic accuracy for fBOO. These cut-offs provided a sensitivity, specificity and overall accuracy of 91.5%, 73.6% and 81%, respectively (31). Defreitas found in women with a range of LUTS that the $P_{\det.Q_{\max}}$ value with high specificity and the greatest sensitivity for detecting fBOO was 25 cmH₂O, and the Q_{\max} value resulting in equal sensitivity, specificity and accuracy (68%) was close to 12 mL/s (29). Kuo analysed VUDS data from 580 patients with a range of LUTS and proposed thresholds of $Q_{\max} \leq 15$ mL/s and $P_{\det.Q_{\max}} \geq 35$ cmH₂O improving sensitivity, specificity and overall accuracy for fBOO to 81.6%, 93.9% and 92.2% respectively (17). Gravina found that $Q_{\max} \leq 15$ mL/s was associated with a sensitivity of 78.9% and specificity of 85.9% in a cohort of women with a range of LUTS. A $P_{\det.Q_{\max}} \geq 28$ cmH₂O resulted in a poor sensitivity of 64.2% and specificity of 64.6%. However, when using a BOO index ($P_{\det.Q_{\max}} - 2Q_{\max}$) of > -8 , the sensitivity and specificity increased to 80.8% and 86.1% respectively (26). Cormier used the previously defined Q_{\max} of < 12 mL/s, but evaluated additional UDS parameters: 1) area under the curve of P_{\det} during voiding (AUCdet)

and, 2) AUC of P_{det} during voiding adjusted for voided volume (AUC_{det/Vol}), in a cohort of women with a clinical diagnosis of dysfunctional voiding. Dysfunctional voiding is defined by the ICS as “*an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the peri-urethral striated or levator muscles during voiding in neurologically normal women*” (3). Using linear discriminant analysis, AUC_{det/Vol} was confirmed as a relevant parameter to classify patients into obstructed, equivocal and non-obstructed groups. A cut-off value of 5.83 cmH₂O/s/mL separated obstructed from equivocal cases and 2.56 cmH₂O/s/mL distinguished equivocal from unobstructed cases (18).

3.4.2 Fluoroscopy

Nitti proposed VUDS criteria, based mainly on fluoroscopic appearance, for diagnosing fBOO. In a study of 261 women with “non-neurogenic voiding dysfunction”, BOO was defined as radiographic evidence of obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction of any magnitude, which was usually associated with reduced urinary flow rate. Bladder neck obstruction (BNO) was diagnosed when the bladder neck was closed/narrowed during attempted voiding. Radiographic obstruction of the urethra was diagnosed as a discrete area of narrowing with proximal dilatation. Strict pressure-flow criteria were not used to classify cases as obstructed or unobstructed in their study. Overall, 76 (29.1%) met the fluoroscopic criteria for obstruction but diagnostic performance statistics in comparison to pressure-flow thresholds were not reported (20).

3.4.3 Urodynamics and fluoroscopy

The ranges of diagnostic values for all VUDS studies included were sensitivity, 54.6-91.5%; specificity 64.6-93.9%; PPV 50-95.5%; NPV 33.3-97.1%; overall accuracy 64.1-92.2%. Several studies have used predefined UDS cut-offs to evaluate their cohorts.

Groutz used $Q_{max} \leq 15$ mL/s and $P_{det.Q_{max}} > 20$ cmH₂O (Chassagne criteria (37)) to diagnose BOO in 6.5% of 587 women presenting with voiding symptoms (4). Klijer used a Q_{max} of < 15 mL/s and a $P_{det.Q_{max}}$ of > 40 cmH₂O, and diagnosed BOO in 18.9% of 53 women with “chronic bladder symptoms” (30). Choi analysed 792 women with a range of LUTS and diagnosed BOO in 11.2%, using $Q_{max} < 15$ mL/s and $P_{det.Q_{max}} > 20$

cmH₂O (11). Rosenblum evaluated voiding dysfunction in 57 nulliparous women with a range of LUTS and fBNO was diagnosed in 3.5% using Nitti's radiological criteria (28).

Yenilmez examined a urodynamic database of 412 women with various LUTS and analysed 122 with complete data. Testing different Q_{max} and P_{det.Qmax} cut-offs, a Q_{max} ≤15 mL/s and P_{det.Qmax} >20 cmH₂O gave a sensitivity and specificity of 84.6% and 84.3% respectively (33).

Ha conducted UDS on 320 women with LUTS and diagnosed 39 (12.2%) with BOO using cut-offs of Q_{max} ≤12 mL/s and P_{det.Qmax} >25 cmH₂O. They found that using a Q_{max} ≤15 mL/s resulted in sensitivity and specificity of 83% and 72% respectively.

Six studies from the same group used VUDS to evaluate females with LUTS (15), voiding dysfunction (13,16,21), dysfunctional voiding (22) and signs and symptoms of BOO (12). Nitti's criteria was used for the radiological definition of BOO (20) and the Q_{max} (<15 mL/s) and P_{det.Qmax} (>35 cmH₂O) cut-offs were used as pressure-flow thresholds (17). In another study VUDS findings from 1914 women with suspected voiding dysfunction were examined and BOO was diagnosed in 42.3%. Using diagnostic thresholds of P_{det.Qmax} >30 cmH₂O for fBOO a sensitivity, specificity and overall accuracy of 54.6%, 91.8% and 76% were obtained. Using an Abrams-Griffiths BOO index cut-off of 30 for differentiating anatomic BOO from functional BOO yielded a sensitivity of 46.9%, and specificity of 76.5% (21). Ong identified bladder neck dysfunction (BND) in 12.3% of 810 women with voiding dysfunction. They further classified BND into high pressure (P_{det.Qmax} ≥35 cmH₂O) or low pressure (<35 cmH₂O) (13).

Akikwala compared five UDS definitions and determined their correlation in women with clinical suspicion of fBOO (27):

- 1) Nitti's radiological definitions (20);
- 2) Q_{max} ≤15 mL/s and P_{det.Qmax} ≥20 cmH₂O (Chassagne) (37);
- 3) Q_{max} ≤11 mL/s and P_{det.Qmax} ≥21 cmH₂O (Lemack) (31);
- 4) Q_{max} ≤12 mL/s and P_{det.Qmax} ≥25 cmH₂O (Defreitas) (29);
- 5) Blaivas-Groutz nomogram (19).

A total of 91 women were evaluated and 40 (44%) had fBOO by at least one criterion. Overall, 38 (42%) were diagnosed with fBOO using the Blaivas-Groutz nomogram, 28 (31%) using Chassagne's criteria, 26 (29%) using Nitti's criteria, 18 (20%) using Lemack and Zimmern's criteria and 13 (14%) using Defreitas' proposed thresholds. The study concluded that Nitti's radiological criteria and Chassagne's pressure-flow criteria have the highest concordance, the Blaivas-Groutz nomogram overestimated fBOO, whereas Defreitas' cut-offs tended to underestimate it (27).

3.4.4 Nomograms to define fBOO

Nomograms are commonly-used for the diagnosis of male BOO and most show good concordance (5). However, there is greater disparity in diagnostic methods for fBOO. The Blaivas-Groutz nomogram used free Q_{max} and $P_{det,max}$ to define four groups: severe, moderate, mild and no obstruction. Using this nomogram 50 obstructed patients ($Q_{max} \leq 12$ mL/s and $P_{det,Qmax} \geq 20$ cmH₂O) were re-classified into severe (n=4, 8%), moderate (n=12, 24%) and mild (34, 68%) BOO. Of the 50 unobstructed controls, 40 (80%) women were classified as no obstruction by the nomogram, six (12%) as between no obstruction and mild obstruction, and the remaining four (8%) as mildly obstructed (19). Viseda categorised 52 women with LUTS according to the Blaivas-Groutz nomogram and compared the results with VUDS findings. Using the nomogram, the sensitivity for BOO was 100%, but its specificity was 67.5% (36). In addition, Viseda (35) also used the Liverpool uroflowmetry nomogram (38) to categorise women with Q_{max} percentile ≥ 50 or ≤ 10 , and using UDS, found that the urethral resistance average was the only significant UDS parameter to diagnose voiding dysfunction in women (35).

Dybowski proposed a new nomogram following the observation that when Q_{max} and $P_{det,Qmax}$ of individual patients were plotted on a pressure-flow graph, a distinctive distribution of patients with clinical signs and symptoms of BOO was noted, enabling a straight line to be drawn. The straight line separating obstructed from the rest (described by the equation $P_{det,Qmax} = 1.5 \times Q_{max} + 10$) was tested on 67 women and the sensitivity, specificity, PPV, NPV and overall accuracy were 90.5%, 65.2%, 54.3%, 94% and 73.1% respectively (14).

The Solomon-Greenwell nomogram used Q_{\max} and $P_{\det.Q_{\max}}$ based on radiographic evidence of increased urethral resistance and a Bayesian approach rather than suggesting discrete pressure-flow thresholds. In a cohort of 535 women with various LUTS the sensitivity, specificity, PPV, NPV and overall accuracy was 86%, 93%, 78.8%, 95.7% and 91.4% respectively. The authors proposed a female BOO index (BOOIf) calculated using the formula $BOOIf = P_{\det.Q_{\max}} - 2.2 \times Q_{\max}$. The percentage of fBOO was <10%, 50%, and >90% if the BOOIf was <0, >5 and >18 respectively (10). This nomogram was tested for correlation with symptoms in 1014 women with LUTS and the most common symptom in the 19% diagnosed with fBOO was increased daytime urinary frequency (37). Treatment-validation was also examined in a study of 21 women treated at the authors' own institution (38). Sensitivity-to-change was demonstrated with consistent reductions in indices and probability of fBOO post-treatment.

3.4.5 Transvaginal USS

Galica investigated the role of TVUS in women with LUTS suggestive of BOO and $Q_{\max} < 12$ mL/s and $P_{\det.Q_{\max}} > 20$ cmH₂O. A mean distance of 1.3 cm from the BN to the vaginal wall was found in women with bladder neck obstruction (fBNO). The authors concluded that VUDS remains the principal diagnostic method and did not propose a diagnostic method based on ultrasonographic indices (23).

3.4.6 Transperineal doppler USS (TPUS)

Two separate studies in women with a range of LUTS, evaluated TPUS in diagnosing fBNO. In one study, transperineal sonography and Virtual Touch tissue quantification were used. BOO was defined as $Q_{\max} < 12$ mL/s and $P_{\det.Q_{\max}} > 20$ cmH₂O. The thickness and shear wave velocity (SWV) of the BN were higher in the fBNO group. For the anterior and posterior lip of the BN, an SWV of 2.11 m/s (AUC 0.78; sensitivity, 69.4%; specificity, 81.5%) and 2.06 m/s (AUC 0.83; sensitivity, 66.7%; specificity, 85.2%) were the best thresholds for diagnosing fBNO (24). In another study, fBNO was diagnosed with cystoscopy and/or UDS and the diagnostic efficacy of shear wave elastography (SWE) and acoustic radiation force impulse imaging (ARFI) was compared. Using both in combination was better than using either ARFI or SWE alone. This provided a sensitivity, specificity, PPV, NPV and overall accuracy of 92.5%, 87.5%, 89.3%, 91.3% and 90.2% respectively (25).

3.4.7 Excluded studies

A couple of earlier studies were not included in the current SR because the inclusion criteria were not met. Axelrod and Blaivas in a study of three patients defined fBNO as $Q_{\max} < 12$ mL/s, sustained detrusor contraction ≥ 20 cmH₂O and radiological evidence of obstruction at the vesical neck (39). Chassagne in a study which was not included as a proportion of patients had stress urinary incontinence, used thresholds of $Q_{\max} \leq 15$ mL/s and $P_{\det.Q_{\max}} > 20$ cmH₂O to diagnose fBOO, and reported a sensitivity and specificity of 74.3% and 91.1% respectively (37). These cut-off values were also used in a number of studies included in this SR.

4. Discussion

4.1 Principal findings

This is the first SR to summarise evidence from 28 studies involving 10,248 patients comparing the diagnostic measures of different tests used to diagnose fBOO. It is evident that studies within this topic-area are difficult to compare for a number of reasons. Firstly, the included studies show considerable variation in inclusion criteria. Some studies have looked at a general population of women with LUTS whereas others have concentrated on those with predominant voiding symptoms, and some have investigated groups with a poorly defined range of clinical diagnoses such as “voiding dysfunction” or “chronic bladder symptoms”. This results in a wide range of prevalence rates and consequently the true incidence of fBOO is difficult to define.

Further heterogeneity is encountered due to lack of consensus and consistency regarding reference urodynamic criteria used to diagnose fBOO. This variation has ultimately precluded any meta-analysis of these data. Nitti's radiological definition of fBOO and the urodynamic thresholds of $Q_{\max} < 12$ mL/s and $P_{\det.Q_{\max}} > 20$ cmH₂O appear to be the most widely used diagnostic cut-offs indicating that VUDS is the current standard investigation for fBOO which is reflected in recommendations of contemporary guidelines (1).

Novel diagnostic measurements and parameters have not enjoyed widespread uptake. The area under the curve/volume method proposed by Cormier has not been replicated

in larger studies (18). Similarly the BOO index cut-off of ≥ -8 to diagnose fBOO, proposed by Gravina is derived from the work in males by Abrams and Griffiths and may not be applicable in women (26). Urethral pressure profile studies and surface electromyography are not widely utilised in contemporary clinical practice and considered optional, perhaps due to poor correlation between results from different centres and continuing scepticism regarding the additional value provided by these tests (1,40).

Three nomograms (Blaivas-Groutz, Dybowski, Solomon-Greenwell) were identified in this SR, and were based on Q_{\max} and $P_{\det\max}$ or $P_{\det.Q\max}$ (10,14,19). However, there have been no head-to-head studies and hence strong recommendations cannot be made regarding their comparative utility.

4.2 Implications for clinical practice

At present there are no standardised urodynamic parameters and hence no widely-accepted definition for fBOO. Clinical history, pelvic USS and flow rates provide guidance to decide on more invasive investigations such as endoscopy or (V)JDS. TPUS is as an alternative non-invasive method in diagnosing fBNO (24,25), and the use of TVUS to assess the BN (20), may be more appropriate as adjuncts rather than primary diagnostic modalities.

4.3 How the review compares to previous reviews/guidelines

We have highlighted the difficulties in establishing appropriate and accepted criteria to define fBOO. The complexity of the diagnosis of fBOO was highlighted in a meeting of experts which concluded that the diagnosis should be multifactorial and include a detailed history, neurological and uro-gynaecological examination, and pressure-flow studies, voiding phase fluoroscopy, urethral pressure profile, ultrasound and cystoscopy (2).

4.4 Strengths and Limitations

A major strength of this review is the systematic approach taken to examine the evidence base, including the use of Cochrane methodology, RoB assessment using QUADAS-2 tool, and adherence to the PRISMA checklist.

There are limitations at a review-level. Firstly, we included only studies with a minimum sample size (including ≥ 10 patients), potentially limiting the inclusion of promising studies on other diagnostic techniques. However, such smaller series are deemed unlikely to influence practice due to lack of power and potential for selection bias. Secondly, we intentionally excluded from the final qualitative analysis those studies including female patients with LUTS for whom a clear etiological diagnosis was established *before* undergoing any diagnostic test for suspected BOO. While following this criterion has allowed us to homogenize the final qualitative analysis by focusing only on studies including women with *suspected* BOO of (predominantly) unknown cause, this choice might have led us to exclude potentially relevant papers describing useful diagnostic tests for fBOO. Thus, our findings should be carefully interpreted in light of the specific research question framework defined for this review.

There are limitations at a study-level including the heterogeneity amongst studies with regard to both definitions and the use of index tests and reference standards, as shown by our RoB assessment (**Figures 2-3**).

We assumed, based on current guidelines (1) and consensus publications (2) that pressure-flow studies with fluoroscopy was the definitive diagnostic test and reference standard. However, a lot of studies omitted this or the criteria for index UDS, such as Q_{\max} and $P_{\det.Q_{\max}}$ varied. Therefore, for over half of the studies included, test accuracy was either not reported or not possible to calculate. A second key limitation was the heterogeneity across included studies regarding the study design and the patient inclusion/exclusion criteria (**Supplementary Table 2**), which partly limit the generalizability of this review's findings. Finally, the extent to which the different time period in which the included studies were performed might have contributed to differences in the diagnostic criteria for fBOO (in light of the changing paradigms to evaluate female patients with LUTS over time) is unknown.

4.5 Future research

Larger studies with more stringent methodological standards are urgently required. Future researchers in this topic area are encouraged to study better defined cohorts and as a minimum separate fBOO into its anatomical and functional entities. The evaluation of diagnostic methods should include precise detail of diagnostic

parameters, conventional measures of accuracy, an assessment of prediction of treatment outcome and sensitivity-to-change following treatment. In addition, future research/guidelines should focus on a standardized reporting system for fBOO that may enable meta-analysis of individual trials, which was not possible in this review.

5. Conclusions

The available evidence on diagnostic tests and definition criteria for fBOO is limited and heterogeneous. Nomograms using pressure-flow measurements have also been proposed but variation exists between them. Clearly in contemporary practice the appropriate management of patients and the diagnosis of fBOO should be based on a careful history, clinical examination, and video-urodynamics remains the recommended standard evaluation as it provides objective functional and anatomical data but agreement regarding diagnostic criteria is urgently needed.

Take Home Message

The available evidence on diagnostic tests for female bladder outlet obstruction is limited and heterogeneous. The most common test used was video-urodynamics, which remains the current standard for diagnosing bladder outlet obstruction in women.

References

1. Harding C., Lapitan M., Arlandis S, Bo K, Costantini E, Groen J, et al. EAU Guidelines on Management of Non-neurogenic Female Lower Urinary Tract Symptoms. EAU Guidel. 2021.
2. Panicker JN, Anding R, Arlandis S, Blok B, Dorrepaal C, Harding C, et al. Do we understand voiding dysfunction in women? Current understanding and future perspectives: ICI-RS 2017. *Neurourol Urodyn*. 2018 Jun 1;37(S4):S75–85.
3. Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J*. 2010 Jan 25;21(1):5–26.
4. Groutz A, Blaivas JG, Chaikin DC. Bladder outlet obstruction in women: Definition and characteristics. *Neurourol Urodyn*. 2000 Jan 1;19(3):213–20.
5. Malde S, Nambiar AK, Umbach R, Lam TB, Bach T, Bachmann A, et al. Systematic Review of the Performance of Noninvasive Tests in Diagnosing Bladder Outlet Obstruction in Men with Lower Urinary Tract Symptoms. *Eur Urol*. 2017;71(3):391–402.
6. Knoll T, Omar MI, Maclennan S, Hernández V, Canfield S, Yuan Y, et al. Key Steps in Conducting Systematic Reviews for Underpinning Clinical Practice Guidelines: Methodology of the European Association of Urology. *Eur Urol*. 2018;73(2):290–300.
7. McInnes MDF, Moher D, Thoms BD, McGrath TA, Bossuyt PM, and the PRISMA-DTA Group C, et al. Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. *JAMA*. 2018;319(4):388–96.
8. Cochrane. Handbook for DTA Reviews. Cochrane Methods Screen. Diagnostic Tests. 2021.
9. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011 Oct 18;155(8):529–36.
10. Solomon E, Yasmin H, Duffy M, Rashid T, Akinluyi E, Greenwell TJ. Developing and validating a new nomogram for diagnosing bladder outlet

- obstruction in women. *Neurourol Urodyn*. 2018 Jan 30;37(1):368–78.
11. Choi YS, Kim JC, Lee KS, Seo JT, Kim H-J, Yoo TK, et al. Analysis of female voiding dysfunction: a prospective, multi-center study. *Int Urol Nephrol*. 2013 Aug 31;45(4):989–94.
 12. Kuo H-C. Videourodynamic characteristics and lower urinary tract symptoms of female bladder outlet obstruction. *Urology*. 2005 Nov 1;66(5):1005–9.
 13. Ong HL, Lee C, Kuo H. Female bladder neck dysfunction- A video-urodynamic diagnosis among women with voiding dysfunction. *LUTS Low Urin Tract Symptoms*. 2020 Sep 8;12(3):278–84.
 14. Dybowski B, Bres-Niewada E, Radziszewski P. Pressure-flow nomogram for women with lower urinary tract symptoms. *Arch Med Sci*. 2014 Aug 29;10(4):752–6.
 15. Kuo H-C. Clinical symptoms are not reliable in the diagnosis of lower urinary tract dysfunction in women. *J Formos Med Assoc*. 2012 Jul;111(7):386–91.
 16. Chuang F-C, Kuo H-C. Videourodynamic differential diagnosis of voiding dysfunction in Taiwanese women. *Tzu Chi Med J*. 2012 Jun 1;24(2):51–5.
 17. Kuo H-C. Urodynamic parameters for the diagnosis of bladder outlet obstruction in women. *Urol Int*. 2004;72(1):46–51.
 18. Cormier L, Ferchaud J, Galas J-M, Guillemin F, Mangin P. Diagnosis of Female Bladder Outlet Obstruction and Relevance of the Parameter Area Under the Curve of Detrusor Pressure During Voiding: Preliminary Results. *J Urol*. 2002 May;167(5):2083–7.
 19. Blaivas JG, Groutz A. Bladder outlet obstruction nomogram for women with lower urinary tract symptomatology. *Neurourol Urodyn*. 2000 Jan 1;19(5):553–64.
 20. Nitti VW, Tu LM, Gitlin J. Diagnosing bladder outlet obstruction in women. *J Urol*. 1999 May;161(5):1535–40.
 21. Hsiao S-M, Lin H-H, Kuo H-C. Videourodynamic Studies of Women with Voiding Dysfunction. *Sci Rep*. 2017 Dec 28;7(1):6845.
 22. Chen Y-C, Kuo H-C. Clinical and video urodynamic characteristics of adult women with dysfunctional voiding. *J Formos Med Assoc*. 2014 Mar;113(3):161–5.
 23. Galica V, Toska E, Saldutto P, Galatioto GP, Vicentini C. Use of transvaginal ultrasound in females with primary bladder neck obstruction. A preliminary

- study. *Arch Ital Urol Androl.* 2015 Jul 7;87(2):158–60.
24. Qian M, Su C, Jiang D, Yu G. Application of Acoustic Radiation Force Impulse Imaging for Diagnosis of Female Bladder Neck Obstruction. *J Ultrasound Med.* 2016 Jun 1;35(6):1233–9.
 25. Qian M, Jiang D, Su C, Wang X, Zhao X, Yang S. Value of Real-Time Shear Wave Elastography Versus Acoustic Radiation Force Impulse Imaging in the Diagnosis of Female Bladder Neck Obstruction. *J Ultrasound Med.* 2019 Sep 1;38(9):2427–35.
 26. Gravina GL, Costa AM, Ronchi P, Paradiso Galatioto G, Gualà L, Vicentini C. Bladder outlet obstruction index and maximal flow rate during urodynamic study as powerful predictors for the detection of urodynamic obstruction in women. *Neurourol Urodyn.* 2007 Mar 1;26(2):247–53.
 27. Akikwala T V., Fleischman N, Nitti VW. Comparison of Diagnostic Criteria for Female Bladder Outlet Obstruction. *J Urol.* 2006 Nov;176(5):2093–7.
 28. Rosenblum N, Scarpero HM, Nitti VW. Voiding dysfunction in young, nulliparous women: symptoms and urodynamic findings. *Int Urogynecol J Pelvic Floor Dysfunct.* 2004;15(6):373–7; discussion 377.
 29. Defreitas GA, Zimmern PE, Lemack GE, Shariat SF. Refining diagnosis of anatomic female bladder outlet obstruction: comparison of pressure-flow study parameters in clinically obstructed women with those of normal controls. *Urology.* 2004 Oct 1;64(4):675–9.
 30. Klijer R, Bar K, Bialek W. Bladder Outlet Obstruction in Women: Difficulties in the Diagnosis. *Urol Int.* 2004;73(1):6–10.
 31. Lemack GE, Zimmern PE. Pressure flow analysis may aid in identifying women with outflow obstruction. *J Urol.* 2000 Jun;163(6):1823–8.
 32. Massey JA, Abrams PH. Obstructed voiding in the female. *Br J Urol.* 1988 Jan;61(1):36–9.
 33. Yenilmez A, Turgut M, Colak E, Erkul A. Cut-off values of pressure-flow study for the design of bladder outlet obstruction in women. *Turk J Urol.* 2005;31:405–10.
 34. Ha SB, Kim SS, Lee ST, Min KE, Jeong SJ, Hong SK, et al. Predictive Factors for Female Bladder Outlet Obstruction Defined by Pressure-Flow Study. *Korean J Urol.* 2009 Sep 1;50(9):848.
 35. Vírveda Chamorro M, Salinas Casado J, Aristizábal Agudelo JA, Fernández

- Ajubita H, Resel Estévez L. [Urodynamic models in the analysis of pressure-flow studies in the adult male]. *Arch Esp Urol*. 1998 Dec;51(10):1011–20.
36. Vírveda Chamorro M, Salinas Casado J, Adot Zurbano JM, Martín García C. [May the Blaivas and Groutz nomogram substitute videourodynamic studies in the diagnosis of female lower urinary tract obstruction?]. *Arch Esp Urol*. 2006;59(6):601–6.
37. Chassagne S, Bernier PA, Haab F, Roehrborn CG, Reisch JS, Zimmern PE. Proposed cutoff values to define bladder outlet obstruction in women. *Urology*. 1998 Mar;51(3):408–11.
38. Haylen BT, Parys BT, Anyaegbunam WI, Ashby D, West CR. Urine flow rates in male and female urodynamic patients compared with the Liverpool nomograms. *Br J Urol*. 1990 May;65(5):483–7.
39. Axelrod SL, Blaivas JG. Bladder neck obstruction in women. *J Urol*. 1987 Mar;137(3):497–9.
40. Abrams P, Andersson K-E, Apostolidis A, Birder L, Bliss D, Brubaker L, et al. 6th International Consultation on Incontinence. Recommendations of the International Scientific Committee: EVALUATION AND TREATMENT OF URINARY INCONTINENCE, PELVIC ORGAN PROLAPSE AND FAECAL INCONTINENCE. *Neurourol Urodyn*. 2018;37(7):2271–2.

Table and Figures Legends

Table 1. Overview of the design, patient population and diagnostic criteria for bladder outlet obstruction (BOO) among the studies included in the review.

BND, bladder neck dysfunction; BNO, bladder neck obstruction; BOO, bladder outlet obstruction; BOOI, BOO index; BOOIf, BOOI female; DSD, detrusor sphincter dyssynergia; DV, dysfunctional voiding; EMG, electromyography; FR, flow rate; LUTS, lower urinary tract symptoms; P_{det} , detrusor pressure; $P_{detQ_{max}}$, detrusor pressure at Q_{max} ; PF, pelvic floor; PRPF, poor relaxation of pelvic floor; PVR, postvoid residual; Q_{max} , maximum flow rate; ROC, receiver operating characteristic curve; SWV, shear wave velocity; TPUS, transperineal 2D doppler ultrasound; TVUS, transvaginal ultrasound; UP, urethral profiling; USS, ultrasound scan; VD, voiding dysfunction; VCMG, video cystometrogram; VCUG, voiding cysto-urethrography; VP, vesical pressure; VUDS, video urodynamics.

NR, not reported.

Table 2. Overview of the accuracy metrics (including sensitivity, specificity, negative predictive value [NPV], positive predictive value [PPV] and overall accuracy) of different tests used to diagnose bladder outlet obstruction (BOO) among the studies included in the review.

ARFI, acoustic radiation force impulse; AUC, area under the curve; BND, bladder neck dysfunction; BOO, bladder outlet obstruction; BOOIf, BOOI female; DV, dysfunctional voiding; NPV, negative predictive value; $P_{detQ_{max}}$, detrusor pressure at Q_{max} ; PPV, positive predictive value; Q_{max} , maximum flow rate; SWE, shear wave elastography; SWV, shear wave velocity; TPUS, transperineal 2D doppler ultrasound; TVUS, transvaginal ultrasound; USS, ultrasound scan.

* Defined Q_{max} and $P_{detQ_{max}}$ cut-offs.

NA, not applicable; NR, not reported or necessary information required to calculate this test accuracy measure was not reported.

Figure 1. Flow-chart showing the main steps of the review process according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement recommendations.

Figure 2. Risk of bias and applicability concerns summary.

The figure shows the reviewers' judgements on each domain for each included study according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 2 tool.

Figure 3. Risk of bias and applicability concerns graph.

The figure shows the reviewers' judgements on each domain presented as percentages across included studies according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 2 tool.

Supplementary Material

Appendix 1. Details on the systematic review process and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist.

Supplementary Table 1. PRISMA for Diagnostic Test Accuracy checklist.

Supplementary Table 2. Overview of the main characteristics of the studies included in the review with regard to the patient inclusion/exclusion criteria and the criteria used by the authors to define bladder outlet obstruction (BOO) cases and controls among the studies included in the review.

BND, bladder neck dysfunction; BOD, bladder outlet dysfunction; BOO, bladder outlet obstruction; BPS, bladder pain syndrome; CBC, cystometric bladder capacity; DO, detrusor overactivity; DUA, detrusor under-activity; DV, dysfunctional voiding ; IC, interstitial cystitis; LUTS, lower urinary tract symptoms; POP, pelvic organ prolapse; PFS, pressure-flow study; PVR, post-void residual; SUI, stress urinary incontinence; UDS, urodynamics; UTI, urinary tract infections; VCMG, video cystometrogram; VD, voiding dysfunction; VUUDS, video urodynamics.

NR, not reported.

Acknowledgements

Jae Hung Jung, Murat Gul, Ege Can Serefoglu (translation of foreign language articles) and Karin Plass for administrative support.

Funding

None

Take Home Message

The available evidence on diagnostic tests for female bladder outlet obstruction is limited and heterogeneous. The most common test used was video-urodynamics, which remains the current standard for diagnosing bladder outlet obstruction in women.

Appendix

Databases: EBM Reviews - Cochrane Central Register of Controlled Trials, EBM Reviews - Cochrane Database of Systematic Reviews, Embase, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)

Search platform: via Ovid.

Search Strategy:

1. exp Urinary Bladder Neck Obstruction/ or exp bladder obstruction/
2. exp bladder neck stenosis/
3. (Bladder adj5 (outlet or neck or outflow) adj5 obstruct*).tw,kw.
4. (bladder obstruction or BOO).tw,kw.
5. (Bladder adj5 (outlet or neck) adj5 (sclerosis or strangulation or stenosis or stenoses or scleroses or contracture or stricture* or narrow*)).tw,kw.
6. (voiding adj2 dysfunction).tw,kw.
7. Pelvic prolapse*.tw,kw.
8. (bladder emptying adj (dysfunction* or incomplete or incompetent)).tw,kw.
9. (Urethral adj2 (sclerosis or strangulation or stenosis or stenoses or scleroses or contracture or stricture* or narrow*)).tw,kw.
10. urethral diverticulum.tw,kw.
11. extrinsic urethral compression.tw,kw.
12. Anterior vaginal wall mass.tw,kw.
13. Fowler* Syndrome.tw,kw.
14. or/1-13
15. female/ or (female* or women or woman).af.
16. 14 and 15
17. (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or adolescen* or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)
18. 16 not 17
19. (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1 or basic research or cell lines or in vitro or animal model or canine).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)
20. 18 not 19
21. case report/ or case reports/ or case report.ti.
22. (note or editorial or letter or Comment or news).pt.
23. note/ or editorial/ or letter/ or Comment/ or news/
24. conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt.
25. or/21-24
26. 20 not 25
27. ((neurogenic or neurological) not (non or "not" or without or excluding or other than)).ti.

28. 26 not 27
29. 28 use ppez, oemezd
30. 18 use coch,cctr
31. 29 or 30
32. remove duplicates from 31

Figure 1

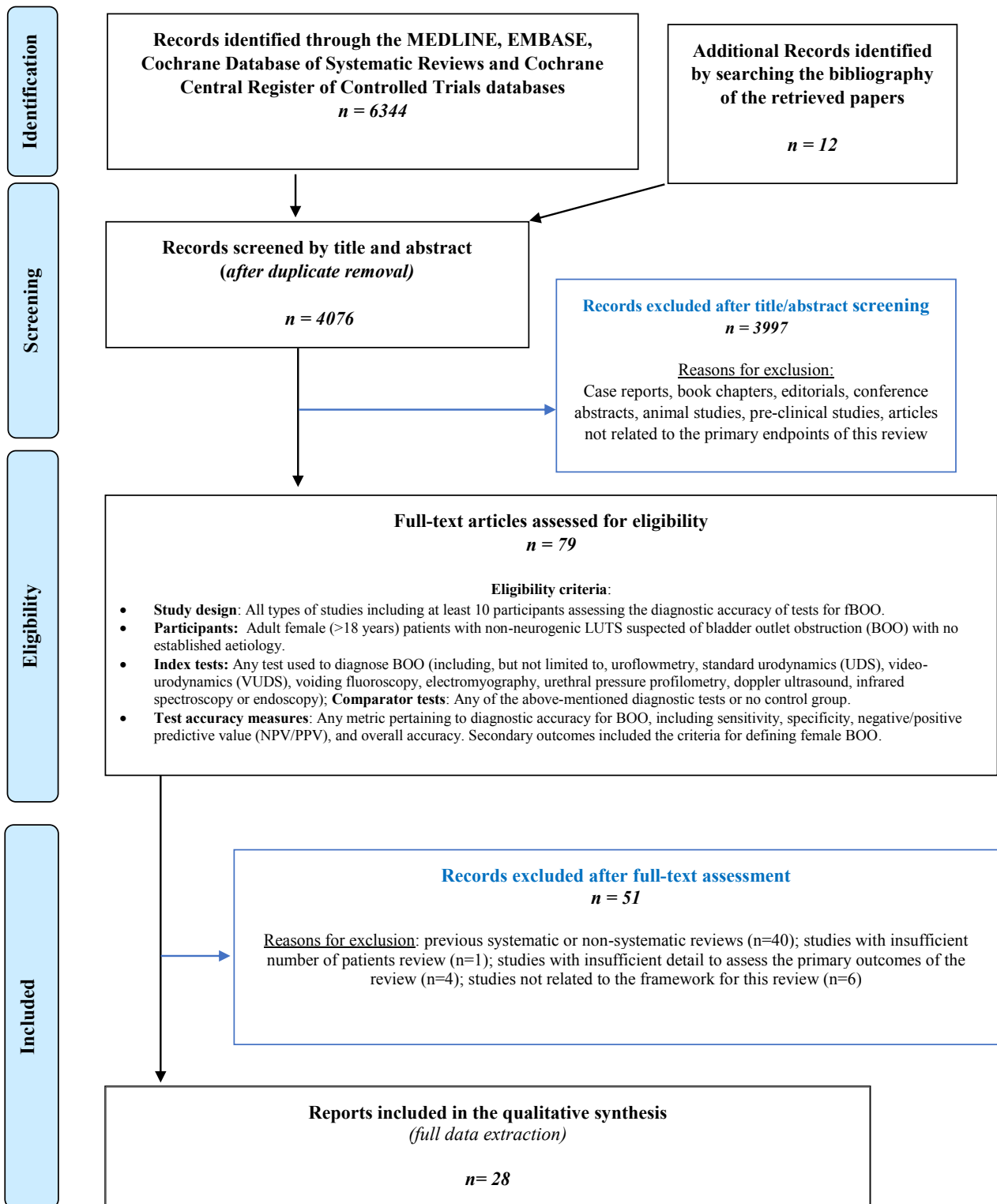


Figure 1. Flow-chart showing the main steps of the review process according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement recommendations.

Figure 2,3

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Akikwala 2006	+	+	?	+	+	+	●
Blaivas 2000	+	+	+	?	+	+	+
Chamorro 1998	?	+	+	+	?	+	+
Chamorro 2006	?	+	+	+	?	+	+
Chen 2014	+	+	?	+	+	●	●
Choi 2013	+	+	?	+	+	+	●
Chuang 2012	+	+	?	+	+	+	●
Cormier 2002	+	+	?	+	+	+	●
Defreitas 2004	+	+	+	+	+	●	+
Dybowski 2014	●	+	?	+	+	+	●
Galica 2015	+	?	+	+	+	●	+
Gravina 2007	+	+	?	?	+	+	●
Groutz 2000	+	+	?	+	+	+	●
Ha 2009	?	●	?	+	+	+	+
Hsiao 2017	+	+	+	+	+	+	+
Klijer 2004	+	+	?	+	+	+	●
Kuo 2004	+	+	+	+	+	+	+
Kuo 2005	+	+	+	+	+	+	+
Kuo 2012	+	+	?	+	+	+	●
Lemack 2000	+	+	?	+	+	+	●
Massey 1988	+	+	?	?	+	+	●
Nitti 1999	+	+	+	+	+	+	+
Ong 2020	+	+	?	?	+	+	●
Qjan 2016	●	?	+	+	+	●	+
Qjan 2019	+	?	+	+	+	●	+
Rosenblum 2004	●	+	?	+	●	+	●
Solomon 2017	+	+	+	?	+	+	+
Yenilmez 2005	●	?	?	●	+	?	?

● High ? Unclear + Low

Figure 2. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study.

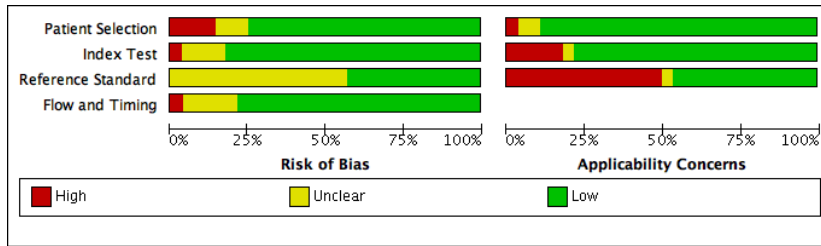


Figure 3. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies.



PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	4
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4,5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	4, Suppl material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	4,5,6
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	5
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	6
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	6



PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	6, Figure 1
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	Table 1, 2 and Suppl table 1
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	6, 7
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	8-11, Table 2
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	8-11, Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	12, 13
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	13, 14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	15
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	22

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

For more information, visit: www.prisma-statement.org.

First Author/year	Recruitment period	P (Participants) - Inclusion criteria	P (Participants) - Exclusion criteria	Criteria to define cases	Criteria to define controls
Aikwala / 2006 [27]	NR	Women who underwent VUDS for various LUTS.	1. Women with a history of neurological disease; 2. Those who were unable to generate a detrusor contraction or who voided uncharacteristically during urodynamics (defined as voiding by abdominal straining, which they stated was not normal, or when a patient had an unsustained detrusor contraction)	Clinical obstruction was suspected in cases in which history, physical examination, symptoms and basic testing, e.g. increased PVR or abnormal uroflowmetry, raised suspicion. If noninvasive uroflowmetry was uncharacteristic, e.g. low volume or voiding without urge, it was repeated.	No controls
Blaivas / 2000 [19]	NR	UDS for LUTS	NR	As per BOO criteria	UDS showing no obstruction +/- sphincteric-incontinence
Chen / 2014 [22]	1997-2010	VUDS for LUTS that could not be eradicated after medical treatment or physiotherapy for >3 months	POP, genuine SUI, previous genitourinary surgery, history of genitourinary tract cancer, neurogenic voiding dysfunction, interstitial cystitis/painful bladder syndrome, or active UTI	LUTS: storage symptoms (including frequency, urgency, urgency incontinence, and nocturia), voiding symptoms (including hesitancy, difficult urination, slow stream, intermittency, terminal dribbling, and urine retention), pain symptoms (including painful sensation in the bladder, urethra, or perineum) and post-micturition symptoms	Normal UDS

Choi / 2013 [11]	October 1, 2005, to December 31, 2005	Female patients who visited urology departments.	NR	Clinical assessment with past medical history and International Prostate Symptom Score (IPSS). Classification of patients in: 1. Patients with voiding difficulties; 2. Patients with LUTS	No controls
Chuang / 2012 [16]	Aug 1996- July 2010	1st time VUDS for LUTS (storage, voiding, pain symptoms)	Chronic UTI, urodynamic SUI, POP, frank neurogenic VD, previous lower urinary tract surgery, previous anti incontinence surgery, interstitial cystitis/painful bladder syndrome, previous genito-urinary tract malignancy	Difficult urination was classified as the main symptom if reported as the chief complaint. If complained of difficult urination in association with other main symptoms, then it was classified as an associated symptom. Voiding detrusor pressure (VP) >35 cmH2O = High ; 10-35 cm H2O= normal; <10 cm H2O = Low. High/normal VP and Low VP with normal flow rate = Normal detrusor contractility; Low VP with Low flow rate and/or large (PV/R) >150 ml = Low detrusor contractility.	Sensory: bladder oversensitivity (strong desire to void at CBC <350ml and no DO); IC/PBS: bladder pain during filling and positive potassium chloride; no sensation at CBC >500ml: reduced bladder sensation. DO: detrusor contraction during filling; DO with incomplete emptying with PV/R >100ml: detrusor hyperactivity and impaired contractility (DHC); IDO: DO without BOO or DHC; DUA: detrusor contractility ≤10cmH2O and needing to void with abdominal straining OR unable to void
Cormier / 2002 [18]	Jan 1996- Dec 1999	Voiding disorders	Bacteriuria >100,000 bacteria and/or leukocyturia >10,000/ml., neurologic bladder, noninsulin or insulin dependent diabetes, post-radiation cystitis, renal and/or bladder tuberculosis, or urinary Schistosomiasis, history of a surgical procedure to modify bladder compliance or capacity, interstitial cystitis, a pelvic surgical procedure less than 3 months earlier, acute urinary retention less than 3 months in duration, urothelial tumor or gynaecologic pathology.	As per BOO criteria	equivocal or non-obstructed

			bladder or ureteral pelvic lithiasis		
Defreitas / 2004 [29]	March 2000 to February 2003	Cases were women with clinically diagnosed obstruction who were seen in the urology clinic for LUTS and who had undergone multichannel UDS. Controls were patients with SU1 and 20 healthy female volunteers.	BOO Group --> 1. Women with a neurologic condition that could affect bladder function, 2. Women who had a bladder capacity of less than 100 mL, 3. Women who voided with abdominal straining greater than 10 cmH2O, 4. Women who failed to relax the pelvic floor or urethral sphincter during voiding as determined by patch electrode electromyographic testing, 5. Women who were unable to void for the PFS, SU1 Group --> 1. A history of anti-incontinence surgery; 2. Obstructive voiding symptoms; 3. Cystocele; 4. Urethral pathologic findings on physical examination or standing lateral voiding cystourethrography.	All women had BOO as determined by the presence of obstructive and/or irritative LUTS; a history of urethral or bladder neck surgery; a pelvic examination revealing urethral hyper-elevation or Stage 3 or 4 anterior vaginal wall prolapse; standing voiding cystourethrography showing deviation of the urethra or urethrovesical angle from its normal course (urethral kinking) or a narrow-caliber distal urethra with proximal widening or distension (urethral narrowing) on lateral voiding films; and/or endorectal coil magnetic resonance imaging demonstrating perirethral fibrosis and/or an obstructing urethral diverticulum	The volunteers were recruited from the community and none of them had LUTS or a history of bladder or urethral surgery. The SU1 cohort consisted of women who presented to the clinic with incontinence as their primary complaint and who underwent a UDS identical to that of the BOO and control groups.

Dybowski / 2014 [14]	1997-2002	suspected BOO. PFS Qmax ≤12ml/s	Diseases of the central and peripheral nervous system (except for vertebral disc disease and diabetes mellitus without pronounced neurological deficits), stroke, pregnancy, locally advanced/disseminated neoplastic processes, severe heart /pulmonary failure, with severe insufficiency of any other organ or system. women after anti-incontinence procedures, POP grade >2, urethral strictures/diverticula, other anatomical forms of obstruction.	Qmax ≤12ml/s	NR
Gallica / 2015 [23]	2012-2015	BOO symptoms	POP, UTI,	Qmax <12ml/s, PdetQmax >20cmH2O, No images for urethral stricture at fluoroscopy, silent EMG. No stricture on urethroscopy	No BOO on VUDS (Qmax, PdetQmax)
Gravina / 2007 [26]	January 2004 to February 2005	All women seen in the centre's urology unit who were assessed with urodynamics.	BOO Group --> women with: 1. Any form of urinary incontinence; 2. Urinary tract infection; 3. Bladder stone; 4. Bladder tumour; 5. Medications that could affect the lower urinary tract function; 6. History of neurological disease. Previous anti-incontinence surgery, urethral stricture, or stage 3 or 4 cystocele (POP-Q system) were	Patients referring symptoms suggestive of voiding disorders and a non-intubated uroflowmetry (NIF) with a Qmax <15 ml/sec and a post-void residual urine volume greater than 50 ml with a minimum total bladder volume of 150 ml before voiding (volume voided + residual) were included in the BOO group.	Women sent to the urology department and evaluated for urinary symptoms. These women were enrolled only if a normal non-intubated uroflowmetry (NIF) was present, symptoms suggestive of voiding disorders occurred less than occasionally. (A normal NIF was defined as a bell-shaped curve in presence of a Qmax >15 ml/sec and a post-void residual urine volume of less than 50 ml with a minimum total bladder volume of 150 ml before

			considered inclusion criteria only in presence of symptoms suggestive of voiding disorders. Control Group --> 1. No previous anti-incontinence surgery; 2. No prior urethral stricture; 3. No vaginal wall prolapse of any degree		voiding (volume voided + residual); The NIF curve was also considered normal if they had one or two small spikes with no other abnormal parameters).
Groutz / 2000 [4]	NR	UDS for Voiding symptoms	NR	Voiding symptoms classified as obstructive (hesitancy, weak or intermittent stream, incomplete emptying, straining to void) or irritative symptoms (frequency, urgency, nocturia, and incontinence).	NR
Ha / 2009 [34]	Jan 2004- Dec 2007	Women who did not have anatomical BOO in whom urodynamic study was conducted for LUTS.	Women with an underlying neurological disorder, anatomical causes of BOO such as POP, urethral stricture, urethral diverticulum, or prior surgical history of urinary incontinence or POP	BOO was defined when the PFS maximal flow rate (Qmax) was ≤ 12 ml/s and Pdet Qmax was ≥ 25 cmH ₂ O.	Controls were women who were not diagnosed as BOO.
Hsiao / 2017 [21]	October 1997 to January 2015	Women with complaints of voiding dysfunction who underwent VUDS. Only moderate and severe voiding symptoms were included in this retrospective analysis.	Patients with: 1. A history of genitourinary tract cancer; 2. Overt neurogenic bladder dysfunction; 3. High grade cystocele or prolapse; 4. Prior surgery for stress urinary incontinence; 5. An established diagnosis of interstitial cystitis/painful bladder syndrome; 6. Chronic or active urinary tract infection	Anatomic and functional BOO. Anatomical BOO included urethral stricture and cystocele. Functional BOO was categorized into three types: bladder neck dysfunction, dysfunctional voiding and poor relaxation of the external sphincter. Women were classified as anatomically obstructed if there was radiographic evidence of obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction. The final	Patients with voiding dysfunction symptoms but normal tracing at VUDS and patients with bladder dysfunction (Acontractile detrusor, Detrusor underactivity, Detrusor hyperactivity with impaired contractility, Detrusor overactivity, Bladder oversensitivity) at VUDS

				diagnosis of functional obstruction was made based on the main VUDS findings and electromyography. Cystoscopy was used in conjunction with the VUDS findings for differential diagnosis of the aetiology of BOO.	
Klijer R / 2004 [30]	NR	Women with chronic bladder symptoms	Women with neurological or organic diseases	Women with chronic bladder symptoms	No controls
Kuo / 2004 [17]	NR	VUDS for LUTS	Not interpretable traces, neuropathy, UDS DUA	LUTS: frequency, urgency, nocturia, dysuria, intermittency, residual urine sensation	mono-symptomatic SU1, asymptomatic volunteers
Kuo / 2005 [12]	1997 to 2004	Women with both clinical signs and symptoms and urodynamic diagnosis of BOO.	1. Patients with neurologic disease; 2. Patients who could not urinate with the catheter in place	Women with both clinical signs and symptoms and urodynamic diagnosis of BOO.	No controls

Kuo / 2012 [15]	Aug 1996- July 2010	1st time VUDS for LUTS (storage, voiding, pain symptoms)	Chronic urinary retention, chronic UTI, urodynamic SUI, POP, frank neurogenic voiding dysfunction (NVD), previous lower urinary tract surgery, interstitial cystitis/painful bladder syndrome, GU tract malignancy	Bladder outlet conditions: BND, DV, urethral stricture, PPRF. Voiding detrusor pressure (VP) >35 cmH2O = HIGH; 10-35 cm H2O= normal; <10 cm H2O= LOW. HIGH/ normal VP AND LOW VP with normal flow rate = NORMAL detrusor contractility; LOW VP with LOW flow rate and/or large (PVR) >150 ml = LOW detrusor contractility.	Sensory: bladder oversensitivity (strong desire to void at CBC <350ml and no DO); IC/PBS: bladder pain during filling and positive KCL; no sensation at bladder volume >500ml: reduced bladder sensation. DO: detrusor contraction during filling. DO with incomplete emptying with PVR >100ml: detrusor hyperactivity and impaired contractility (DHC); IDO: DO without BOO or DHC; DUA: detrusor pressure ≤10cmH2O
Lemack / 2000 [31]	NR	Women with obstructive voiding complaints and, as controls, women with a primary complaint of SUI.	BOO GROUP --> 1. Women with underlying neurological condition. (Those with a history of anti-incontinence surgery or a large cystocele were only included in the study if they also had symptoms suggestive of obstruction) CONTROL GROUP --> 1. No previous incontinence surgery; 2. No obstructive voiding symptoms; 3. No cystocele; 4. No urethral pathology on physical examination and standing lateral cystography. ALL PARTICIPANTS --> 1. Patients requiring abdominal straining greater than 10 cmH2O to void; 2. Those with any abnormal sphincteric activity at voiding, such as dyssynergia or dysfunctional voiding; 3. Patients with bladder capacity less than 100mL.	Clinical obstruction: women with obstructive voiding complaints, such as straining, squatting or bending forward to void, sensation of incomplete emptying, significant hesitancy, prolonged flow or need to reduce associated prolapse manually to void.	Patients not clinically obstructed. These patients were also evaluated by voiding cystourethrography and all had a normal appearing urethra without proximal ballooning.

Massey / 1988 [32]	October 1975 to October 1986	All women referred to the Urology unit	Patients with : 1. Detrusor/sphincter dyssynergia; 2. Overt neuropathy; 3. Acontractile bladder	Clinical assessment with previous medical history	No controls
Nitti / 1999 [20]	NR	VUDS for non-neurogenic VD	NR	As per BOO criteria	NR
Ong / 2020 [13]	Aug 1996 - Jan 2014	Women, Age \geq 18yo. At least one voiding symptom, with or without storage symptoms. BND-bladder neck dysfunction; BOD-bladder outlet dysfunction; DV-dysfunctional voiding.	UTI, neurogenic; IC/BPS, SUI, previous genito-urinary surgery, malignancy	High voiding pressure: \geq 35cmH ₂ O, Low voiding pressure: <10cm H ₂ O.	Normal VUDS tracing
Qian / 2016 [24]	Apr 2011-May 2014	1) All had polyuria, urgency, frequency, nocturia, dysuria; 2) BN enlarged on USS, PVR >50ml; 3) cystoscopy-resistance on insertion thickened, apophysis on anterior or posterior lip; 4) BOO low flow <12ml/s on repeated noninvasive flow	Urethral caruncle, urethral stricture, urinary mucosal prolapse, urethral tumour	None had prior pharmacologic treatment, had spontaneous improvement in LUTS or underwent previous urinary tract surgery. None had small pelvis, neurologic deficit or diabetes.	Healthy, no LUTS, normal cystoscopic and uroflow results, no previous urinary tract surgery.

		studies with high PdetQmax >20cmH2O on pressure-flow studies			
Qian / 2019 [25]	Apr 2016- Mar 2018	BNO by cystoscopy and/or urodynamic. All had storage, voiding or combination of symptoms ranging from 3-5 years. 3 had urinary retention. None had previous urinary tract surgery or pharmacologic treatment. None had neurologic deficit or diabetes	Urethral stricture, urinary mucosa prolapse, urethral tumour	Prostatic Symptom Assessment to check for BNO symptoms, with scores ranging between 16 and 34 (average, 28), and the quality-of-life score ranged from 3 to 6 points (average, 5)	Healthy adults
Rosenblum / 2004 [28]	NR	Premenopausal, nulliparous women who underwent VUDS evaluation for LUTS. None of the patients had a history of prior incontinence or lower urinary tract reconstructive surgery or a medical condition that could be primarily responsible for LUTS. In addition, none of the patients had POP beyond stage 1.	1. Patients with a history of pre-existing neurological disease or suspicion of neurological disease based on history and/or physical examination; 2. Women with a chief complaint of SUI	Clinical assessment: The women were divided into six groups depending on their presenting symptoms (Frequency and urgency alone; Frequency, urgency, and pain; Frequency, urgency, and urge incontinence; Obstructive or voiding symptoms; Unaware incontinence; Pain only)	No controls

Solomon / 2017 [10]	September, 2009 to August, 2011 (development cohort); January, 2007 to August, 2009 (validation cohort)	Women having VCMG for investigation of treatment refractory LUTS	1. Patients with an underlying neurological diagnosis or those who were unable to generate a detrusor voiding contraction. 2. Traces that did not demonstrate good subtraction before and after the void were excluded from consideration	Cases were defined as patients with radiographic evidence of obstruction and were then classified according to the aetiology of BOO: functional (group 1); intrinsic anatomical—urethral/paraurethral pathology; that is, urethral diverticulum and paraurethral cyst (group 2); extrinsic anatomical—secondary to anti-incontinence surgery (group 3) and positional anatomical—obstructive POP (group 4).	Controls were identified as: women with LUTS and anterior POP with no radiological evidence of obstruction (group 5), women with a history of refractory SUJ in whom incontinence was not demonstrated during the VCMG despite use of all precipitating manoeuvres (group 6) and women in whom it was (group 7).
Viseda / 1998 [35]	NR	Consecutive women who underwent UDS	NR	Qmax percentile in noninvasive uroflowmetry less than or equal to 10 (according to Haylen nomogram)	Qmax percentile in noninvasive uroflowmetry greater than or equal to 50 and no PVR (according to Haylen nomogram)
Viseda / 2006 [36]	NR	Women with LUTS referred to undergo VUDS	NR	All women with LUTS referred to undergo VUDS. Categories: No obstruction, Bladder neck obstruction and urethral obstruction	No controls
Yenilmez / 2005 [33]	2000-2005	Women who were suspected for BOO with a history of forced urination (stranguria), feeling of inability to void, prolonged urine flow, pause in urination, or manual pushing of prolapse to be able to urinate, or urethral	Neurogenic bladder, bladder cancer, bladder stone, bladder infection and who did not urinate after UDS.	LUTS	Women with SUJ without BOO symptoms (not clear how they defined this group)

		caruncle and urethral stricture on genital examination.			
--	--	---	--	--	--

Supplementary Table 2. Overview of the main characteristics of the studies included in the review with regard to the patient inclusion/exclusion criteria and the criteria used by the authors to define bladder outlet obstruction (BOO) cases and controls among the studies included in the review.

BND, bladder neck dysfunction; BOD, bladder outlet dysfunction; BOO, bladder outlet obstruction; BPS, bladder pain syndrome; ; CBC, cystometric bladder capacity; DO, detrusor overactivity; DUA, detrusor under-activity; DV, dysfunctional voiding; IC, interstitial cystitis; LUTS, lower urinary tract symptoms; POP, pelvic organ prolapse; PFS, pressure-flow study; PVR, post-void residual; SUL, stress urinary incontinence; UDS, urodynamics; UTI, urinary tract infections; VCMG, video cystometrogram; VD, voiding dysfunction; VUDS, video urodynamics.
 NR, not reported.

First Author/year	Study design	Country	Clinical presentation	Total no. patients analysed	BOO, n (%)	Mean (SD or range) age (years)	Test evaluated	Reference test	Diagnostic criteria for BOO as reported by authors
Akikwala / 2006 [27]	Prospective – Single centre	USA	LUTS	91	40 (44.0)	62.3 (16-90)	VUUS, PF EMG	Fluoroscopy	5 criteria, including 1) Fluoroscopy, 2) Qmax <15mL/s and PdetQmax ≥20cmH ₂ O, 3) Qmax <11mL/s and PdetQmax ≥21cmH ₂ O, 4) Qmax <12mL/s and PdetQmax ≥25cmH ₂ O and 5) the Blaiwas-Groultz nomogram
Blaivas / 2000 [19]	Retrospective – Single centre	USA	LUTS	100	50 (50)	BOO: 64.4 (17.6); Unobstructed: mean 64.8 (10.7)	VUUS, EMG, endoscopy	Fluoroscopy	One or more: 1) Free Qmax <12mL/s and PdetQmax ≥20cmH ₂ O, 2) radiographic evidence BOO with sustained detrusor contraction ≥20cmH ₂ O and poor Qmax regardless of free Qmax, 3) inability to void with transurethral catheter in place despite a sustained detrusor contraction ≥20cmH ₂ O
Chen / 2014 [22]	Retrospective – Single centre	Taiwan	LUTS	440	168 (38.2)	DV: 67.8 (18.1); Control: 58.9 (18.4)	VUUS	Fluoroscopy	DV: high Pdet, intermittent or increased external sphincter EMG activity and a spinning top urethral appearance on cinefluoroscopy during voiding
Choi / 2013 [11]	Prospective – Multicentre	Korea	LUTS	792	89 (11.2)	Voiding difficulty: 61.8 (12.1); LUTS: 62.7 (10.2)	UDS	Clinical assessment	Qmax <15mL/s and PdetQmax >20cmH ₂ O
Chuang / 2012 [16]	Retrospective – Single centre	Taiwan	LUTS	781	405 (51.9)	NR	VUUS	Fluoroscopy	BND: VUUS revealing narrow BN with high/normal detrusor contractility; DV: High Pdet with open BN and narrow mid urethra during voiding; stricture: narrow distal urethra with low FR regardless high/normal VP; PRPF- could not relax their PF muscle with Low VP and intermittent flow
Cormier / 2002 [18]	Prospective – Single centre	France	VD	85	21 (24.7)	55 (18-83)	VUUS, UP	Fluoroscopy	Qmax <12mL/s and PVr >150mL
Defreitas / 2004 [29]	Prospective – Single centre	USA	LUTS	313	169 (54.0)	BOO: 60 (15); control 42 (7)	UDS	Clinical assessment	Qmax <12mL/s and PdetQmax >25cmH ₂ O
Dybowski / 2014 [14]	Retrospective – Multicentre	Poland	Voiding LUTS	67	21 (31.3)	Median 53	UDS	Clinical assessment	BOO= (PdetQmax – 1.5 ×Qmax) > 10
Galica / 2015 [23]	Retrospective – Single centre	Italy	BOO symptoms	15	3 (20)	NR	TVUS, VUUS, EMG	Fluoroscopy	Qmax <12mL/s and PdetQmax >20cmH ₂ O. No images for urethral stricture at fluoroscopy, silent EMG

Gravina / 2007 [26]	Retrospective – Single centre	Italy	LUTS	170	133 (78.2)	BOO: Median (IQR): 62 (56-69); Unobstructed: 57.5 (48.3-63.5)	UDS	Clinical assessment	1) Qmax cut-off less than 15 mL/sec; 2) A BOOI cut-off greater than -8; 3) PdetQmax \geq 28cmH ₂ O
Groutz / 2000 [4]	Retrospective – Single centre	USA	Voiding LUTS	587	38 (6.5)	63.9 (17.5)	VUDS, EMG, endoscopy	Fluoroscopy	Qmax <12mL/s and PdetQmax >20cmH ₂ O: Site of obstruction: narrowest point in the urethra during VCUG; Urethral obstruction: 1) visible signs of narrowed urethra, analogous to urethral stricture in men; 2) the urethra felt narrow because it "gripped" the cystoscope; or 3) the bladder neck and proximal urethra appeared to be compressed from without, analogous to benign prostatic hyperplasia in men
Ha / 2009 [34]	Retrospective – Multicentre	Korea	LUTS	320	39 (12.2)	BOO: 55.4 \pm 14.7 Non BOO: 55.2 \pm 12.4	UDS	Clinical assessment	Qmax \leq 12mL/s and PdetQmax \geq 25cmH ₂ O
Hsiao / 2017 [21]	Retrospective – Single centre	Taiwan	VD	1914	1858 (97.1)	Anatomic BOO: 57.8 (16.7); Functional BOO: 59.4 (13.8); Bladder dysfunction: 64.7 (16.2); Normal tracings: 54.0 (14.3)	VUDS, urethral EMG	Fluoroscopy	PdetQmax cut-off= 30 cmH ₂ O for differentiating BOO from bladder dysfunction and normal tracings. Cystoscopy was used in conjunction with the VUDS findings for differential diagnosis of the etiology of BOO
Kijler / 2004 [30]	Prospective – Single centre	Poland	Chronic bladder symptoms	53	19 (35.9)	Median (range) 37.5 (16–70)	Uroflowmetry, UDS, VCUG	Fluoroscopy	Qmax <15mL/s and PdetQmax >40cmH ₂ O: Site determined by fluoroscopy
Kuo / 2004 [17]	Retrospective – Single centre	Taiwan	LUTS	580	76 (13.1)	BOO: 50.2 (15.1); SUI: 51 (12.7); asymptomatic: 44.6 (16.4)	VUDS	Fluoroscopy	1) obstructive voiding and irritative symptoms, 2) sustained detrusor contraction during voiding phase in UDS, 3) radiological evidence of narrow BN or distal urethra during voiding phase. 4) DSD: increased sphincter EMG during voiding; PRPF: no concomitant relaxation of EMG activity during micturition

Kuo / 2005 [11]	Retrospective – Single centre	Taiwan	BOO signs and symptoms	207	194 (93.7)	57 (23)	VUUS, urethral EMG	Fluoroscopy	BOO: radiologic evidence of obstruction in the bladder outlet on voiding cystourethrography plus a voiding detrusor pressure >35 cmH ₂ O in combination with a Qmax <15mL/s. DSD: increased sphincter EMG during voiding; PRPF: no concomitant relaxation of EMG activity during micturition
Kuo / 2012 [12]	Retrospective – Single centre	Taiwan	LUTS and pain	1605	314 (19.6)	58 (18-98)	VUUS	Fluoroscopy	BND: VUUS revealing narrow BN with high/normal detrusor contractility; DV: high Pdet with open BN and narrow mid urethra during voiding; stricture: narrow distal urethra with low FR regardless high/normal VP; PRPF- could not relax their PF muscle with low VP and intermittent flow
Lemack / 2000 [31]	Prospective – Single centre	USA	Voiding LUTS	211	87 (41.2)	NR	UDS, PF EMG	Clinical assessment	Qmax ≤11mL/s and PdetQmax ≥21cmH ₂ O
Massey / 1988 [32]	Retrospective – Single centre	UK	LUTS	163	163 (100)	51.6 (8-81)	Uroflowmetry, UDS, UP, EMG	Fluoroscopy	Two or more of the following parameters: 1) Qmax <12mL/s, 2) PdetQmax >50cmH ₂ O, 3) Urethral resistance >0.2 (P/F ²), 4) "Significant" residual urine in the presence of a raised PdetQmax or urethral resistance
Nitti / 1999 [20]	Retrospective – Single centre	USA	Non-neurogenic VD	261	76 (29.1)	BOO: 57.5; Unobstructed: 55	VUUS	Fluoroscopy	BOO: radiographic evidence of obstruction between BN and distal urethra with sustained detrusor contraction of any magnitude, which was usually associated with reduced or delayed urinary flow rate; radiographic obstruction at the BN was diagnosed when BN was closed/narrow during voiding; radiographical obstruction of the urethra was diagnosed as a discrete area of narrowing with proximal dilatation.
Ong / 2020 [13]	Retrospective – Single centre	Taiwan	LUTS	530	474 (89.4)	BOO: 57.8 (16.7); BND: 63.9 (17.1); DV: 61.1 (16.5); Normal VUUS: 54.0 (14.3)	VUUS, EMG, VCUG	Fluoroscopy	High voiding pressure: PdetQmax ≥35cmH ₂ O

Qian / 2016 [24]	Retrospective – Single centre	China	LUTS	66	36 (54.6)	BNO: 55 (13); Control: 50 (14)	TPUS and Virtual Touch tissue quantification	UDS	1) Polyuria, urgency, frequency, nocturia, dysuria; 2) BN enlarged on USS, PVR >50mL; 3) cystoscopy: resistance on insertion, BN thickened, apophysis on anterior or posterior lip; 4) BOO: Qmax <12mL/s with PdetQmax >20cmH ₂ O
Qian / 2019 [25]	Retrospective – Single centre	China	LUTS	51	27 (52.9)	FBNO: 56 (10); Control: 47 (16)	TPUS	UDS	Best ROC cut-off for FBNO: SWV 2.38m/s
Rosenblum / 2004 [28]	Retrospective – Single centre	USA	LUTS	57	2 (3.5)	30 (19–47)	VUDS, PF EMG, CMG	Fluoroscopy	BOO: fluoroscopy; DV: increased external sphincter activity during voluntary voiding; as evidenced by EMG tracing and/or fluoroscopy, with a sustained detrusor contraction
Solomon / 2017 [10]	Retrospective – Single centre	UK	LUTS	535	125 (23.4)	Obstructed: 51.9 (12.3); Unobstructed: 49.1 (16.1)	VCMG	Fluoroscopy	BOO likely if PdetQmax > 2.2*Qmax + 5 BOOIf = PdetQmax – 2.2*Qmax; that is, BOOIf < 0, <10% probability of obstruction, BOOIf >5 likely obstructed (50%) and If BOOIf >18, obstruction almost certain (>90%)
Viseda / 1998 [35]	Retrospective - Single centre	Spain	LUTS	80	56 (70)	62.19 (13.29); range (18-84) Women with VD: 64.39 (11.62) Women without VD: 56.36 (15.76)	Standard UDS, urethral resistance	Clinical assessment	Noninvasive Qmax ≤ 10 th percentile in Haylen nomogram
Viseda / 2006 [36]	Cross sectional study	Spain	LUTS	52	25 (48.1)	48.7 (14.4); (range 20-81)	VUDS, Blaivas-Groutz nomogram	Fluoroscopy	High Pdet associated with one of the following: 1) Absence of bladder neck opening (BNO); 2) decrease in urethral diameter with proximal dilatation (urethral obstruction)
Yenilmez / 2005 [33]	Retrospective – Single centre	Turkey	LUTS	122	39 (32.0)	Group 1 Urethral stricture (n=19) 58.6 ± 10.5; Group 2 DV (n=13) 46.8 ± 15.2; Group 3 Pelvic prolapse (n=7) 56.1 ± 9.4; Controls (SUI group) (n=83) 54.1 ± 9.7	UDS, Endoscopy	Clinical assessment	Qmax ≤15mL/s and PdetQmax >20cmH ₂ O (endoscopic measures and clinical symptoms should be considered also)

Table 1. Overview of the design, patient population and diagnostic criteria for bladder outlet obstruction (BOO) among the studies included in the review.

BND, bladder neck dysfunction; BNO, bladder neck obstruction; BOO, bladder outlet obstruction; BOOI, BOO index; BOOf, bladder BOO female; DSD, detrusor sphincter dyssynergia; DV, dysfunctional voiding; EMG, electromyography; FR, flow rate; LUTS, lower urinary tract symptoms; Pdet, detrusor pressure; PdetQmax, detrusor pressure at Qmax; PF, pelvic floor; PRPF, poor relaxation of pelvic floor; PVR, postvoid residual; Qmax, maximum flow rate; ROC, receiver operating characteristic curve; SWV, shear wave velocity; TPUS, transperineal 2D doppler ultrasound; TVUS, transvaginal ultrasound; UP, urethral profiling; USS, ultrasound scan; VD, voiding dysfunction; VCMG, video cystometrogram; VCUG, voiding cysto-urethrography; VP, vesical pressure; VUDS, video urodynamics.

NR, not reported.

First Author/year	Qmax (mL/s)	PdetQmax (cmH2O)	Nomogram	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)
(Video)urodynamics								
Akikwala / 2006 [27]	≤15, ≤11, ≤12	≥20, ≥21, ≥25	NA	NR	NR	NR	NR	NR
Chen / 2014 [22]	DV = >15	>35	NA	NR	NR	NR	NR	NR
Choi / 2013 [11]	<15	>20	NA	NR	NR	NR	NR	NR
Chuang / 2012 [26]	NR	>35	NA	NR	NR	NR	NR	NR
Cormier / 2002 * [18]	<12	NR	NA	NR	NR	NR	NR	NR
Defreitas / 2004 * [29]	<12	>25	NA	Qmax: 68; PdetQmax: NA	Qmax: 68; PdetQmax: NA	Qmax: 71.4; PdetQmax: NA	Qmax: 64.5; PdetQmax: NA	Qmax: 68; PdetQmax: NA
Gravina / 2007 * [26]	≤15	≥28	NA	Qmax: 78.9; BOOI: 80.8; PdetQmax: 64.2	Qmax: 85.9; BOOI: 86.1; PdetQmax: 64.6	Qmax: 95.4; BOOI: 95.5; PdetQmax: 86.7	Qmax: 53.3; BOOI: 56.1; PdetQmax : 33.3	Qmax: 80.5; BOOI: 82.3; PdetQmax: 64.1
Groutz / 2000 [4]	<12	>20	NA	NR	NR	NR	NR	NR
Ha / 2009 [34]	≤15 Maximal voided volume ≤350mL	-	NA	Qmax: 82 Maximal voided volume: 71	Qmax: 72 Maximal voided volume: 46	Qmax: 34.4 Maximal voided volume: 28.2	Qmax: 96.5 Maximal voided volume: 91.2	Qmax: 73.1 Maximal voided volume: 49.0
Hsiao / 2017 [21]	≤15	>30	NA	54.6	91.8	82.9	73.4	76.0
Kijler / 2004 [30]	<15	>40	NA	NR	NR	NR	NR	NR
Kuo / 2004 * [17]	≤15	≥35	NA	PdetQmax ≥35cmH2O AND Qmax ≤15ml/s: 81.6	PdetQmax >35cmH2O AND Qmax <15ml/s: 93.9	66.7	97.1	92.2
Kuo / 2005 [12]	<15	>35	NA	NR	NR	NR	NR	NR
Kuo / 2012 [15]	NR	>35	NA	NR	NR	NR	NR	NR
Lemack / 2000 * [31]	≤11	≥21	NA	91.5	73.6	50.0	96.8	81

Massey / 1988 * [32]	<12	>50	NA	NR	NR	NR	NR	NR	NR
Nitti / 1999 [20]	NR	NR	NA	NR	NR	NR	NR	NR	NR
Ong / 2020 [13]	NR	≥35: high pressure BND; <35: low pressure BND	NA	NR	NR	NR	NR	NR	NR
Rosenblum / 2004 [28]	NR	NR	NA	NR	NR	NR	NR	NR	NR
Viseda / 1998 [35]	≤10 percentile	-	Used the Haylen (Liverpool) nomogram	91	45	79.6	68.7	77.5	
Viseda / 2006 [36]	≤12	≥20	Used Blaiwas-Groutz	100	67.5	71.4	100	80.8	
Yenilmez / 2005 [33]	≤15	>20	NA	84.6	84.3	76.7	92.1		
Nomograms									
			Classify into No, mild, moderate, severe obstruction. 1) Between unobstructed and minimally obstructed: a line with slope 1.0 and intercept 7cmH2O; 2) Between minimally and moderately obstructed: a horizontal line at Pdet: max 57cmH2O; 3) Between moderately and severely obstructed: a horizontal line at Pdet: max 107cmH2O	NR	NR	NR	NR	NR	NR
Blaiwas / 2000 [19]	≤12	≥20							
			PdetQmax = 1.5 x Qmax + 10; BOO = (Pdet(Qmax) - 1.5 x Qmax) > 10						
Dybowski / 2014 [14]	≤12	NR		90.5	65.2	54.3	94	73.1	
			If PdetQmax = 2.2 * Qmax + 5 or BOO If = PdetQmax - 2.2 * Qmax (<0 = <10%, >5 = 50%, >18 = >90% obstructed)						
Solomon / 2017 [10]	NR	NR		86	93	78.8	95.7	91.4	

Transvaginal USS							
Galica / 2015 [26]	<12	>20	NA	NR	NR	NR	NR
Transperineal doppler USS							
			NA				
Qian / 2016 [24]	<12	>20		Anterior lip SWV 2.11m/s; 69.4 (AUC 0.782); Posterior lip SWV 2.06m/s; 66.7 (AUC 0.831)	Anterior lip SWV 2.11m/s; 81.5 (AUC 0.782); Posterior lip SWV 2.06m/s; 85.2 (AUC 0.831)	Anterior: 80.7; Posterior: 85.7	Anterior: 68.6; Posterior: 68.4
Qian / 2019 [25]	n/a	n/a	NA	ARFI: 88.9; SWE: 81.5; combined: 92.5	ARFI: 79.2; SWE: 79.2; combined: 87.5	ARFI: 82.8; SWE: 81.5; combined: 89.3	ARFI: 86.4; SWE: 79.2; combined: 91.3
						Anterior: 74; Posterior: 80.6	ARFI: 84.3; SWE: 80.4; combined: 90.2

Table 2. Overview of the accuracy metrics (including sensitivity, specificity, negative predictive value [NPV], positive predictive value [PPV] and overall accuracy) of different tests used to diagnose bladder outlet obstruction (BOO) among the studies included in the review.

ARFI, acoustic radiation force impulse; AUC, area under the curve; BND, bladder neck dysfunction; BOO, bladder outlet obstruction; BOOF, BOO index female; DV, dysfunctional voiding; NPV, negative predictive value; PdetQmax, detrusor pressure at Qmax; PPV, positive predictive value; Qmax, maximum flow rate; SWE, shear wave elastography; SWV, shear wave velocity; TPUS, transperineal 2D doppler ultrasound; TVUS, transvaginal ultrasound; USS, ultrasound scan.

* Defined Qmax and PdetQmax cut-offs

NA, not applicable; NR, not reported or necessary information required to calculate this test accuracy measure was not reported.

Authorship Form



Click here to access/download
Authorship Form
fBOO DTA Authorship form.pdf

