European Reference Networks

European Reference Network for rare or low prevalence complex diseases

Network: Neurological Diseases (ERN-RND)

Coordinator: Universitätsklinikum Tübingen — Deutschland

European Academy of Neurology (EAN)/European Federation of Autonomic Societies (EFAS)/International Neuro-Urology Society (INUS) Guidelines for Practising Neurologists on the Assessment and Treatment of Neurogenic Urinary and Sexual Symptoms (NEUROGED Guidelines)

European Journal of Neurology, 2025; 32:e70119

https://doi.org/10.1111/ene.70119

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

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Published by ERN-RND: 28 October 2025

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Luxembourg: Publications Office of the European Union, 2019

INTRODUCTION TO THE EUROPEAN REFERENCE NETWORK FOR RARE NEUROLOGICAL DISEASES (ERN-RND)

ERN-RND is a European Reference Network established and approved by the European Union. ERN-RND is a healthcare infrastructure which focuses on rare neurological diseases (RND). The three main pillars of ERN-RND are (i) network of experts and expertise centres, (ii) generation, pooling and dissemination of RND knowledge, and (iii) implementation of e-health to allow the expertise to travel instead of patients and families.

ERN-RND unites 64 of Europe's leading expert centers as well as 4 affiliated partners in 24 member states and includes highly active patient organizations. Centers are located in Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Slovenia, Spain and Sweden.

The following disease groups are covered by ERN-RND:

- Ataxias and Hereditary Spastic Paraplegias
- Atypical Parkinsonism and Genetic Parkinson's Disease
- Dystonia, Paroxysmal Disorder and Neurodegeneration with Brain Iron Accumulation
- Frontotemporal Dementia
- Huntington's Disease and other Chorea
- Leukoencephalopathies

Specific information about the network, the expert centers and the covered diseases can be found on the network's website ***www.ern-rnd.eu****.*

Recommendation for clinical use:
The European Reference Network for Rare Neurological Diseases strongly recommends the use of the following NEUROGED guidelines as best clinical practice for the assessment and treatment of neurogenic urinary and sexual symptoms in atypical parkinsonian syndromes.

DISCLAIMER

Clinical practice guidelines, practice advisories, systematic reviews and other guidance published, endorsed or affirmed by ERN-RND are assessments of current scientific and clinical information provided as an educational service.

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METHODOLOGY

The NEUROGED guidelines were endorsed as recommendation for clinical use by the Disease Group Atypical Parkinsonism and Genetic Parkinson's Disease of ERN-RND upon unanimous consent.

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Endorsement process:

- Proposal and voting on guideline endorsement in Disease Group meeting – 02 June 2025
- Final consent to endorse document by whole disease group in terms of annual meeting group discussion: 27 October 2025
- Publication of endorsed guidelines: 28 2025

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A conclusive and introductory infographic highlighting key recommendations can be found on https://onlinelibrary.wiley.com/pb-assets/assets/14681331/infographic/EAN_NEUROGED_Infographic_V4-1746519176387.pdf

EAN NEUROGED INFOGRAPHIC (AS OF NEXT PAGE)

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NEUROGED GUIDELINES ON ASSESSING AND TREATING NEUROGENIC URINARY AND SEXUAL SYMPTOMS

Collaborative recommendations by European Academy of Neurology (EAN), European Federation of Autonomic Societies (EFAS) and International Neuro-Urology Society (INUS)

Neurological disorders often cause urinary and sexual symptoms, impacting quality of life and may contribute to unplanned hospital admissions. These evidence-based guidelines provide a comprehensive framework for neurologists to assess and treat these symptoms.

Key recommendations for assessing urinary symptoms:

Assessment	Recommendations	
History-taking and physical examination	Regularly ask about urinary symptoms and perform a targeted physical examination	☆
Urinalysis	Perform at the initial evaluation and with clinical changes, such as worsening urinary symptoms or suspected UTIs	☆
Bladder diary	Complete a three-day bladder diary as part of the initial evaluation	☆
Post void residual volume (PVR)	Measure at initial evaluation and at follow-up if new or worsening symptoms	☆
Renal function tests	Assess blood urea and serum creatinine as part of the initial evaluation	☆
Urodynamic testing	Only recommended for atypical symptoms, high risk for upper urinary tract damage, or failure of conservative treatments	☆
Red flag referrals	Refer to urologists if there is a risk of developing upper urinary tract damage, suspected urological pathology, or inadequate response to treatment	☆

☆ Good practice statement

Key recommendations for treating urinary symptoms:

Treatment	Recommendations	
Non-pharmacological management		
Fluid intake	Provide individualised advice on optimal intake and avoidance of certain beverages	☆
Bladder retraining	Offer advice when experiencing urinary urgency	↘
Pelvic floor exercises	Offer when experiencing urinary urgency and/or stress incontinence	✓
Intermittent catheterisation	Offer as first-line therapy for urinary retention when PVR consistently > 150 mL	✓
Indwelling catheterisation	Suprapubic catheter preferred over urethral catheterisation when long-term indwelling urinary bladder drainage is unavoidable	📝
Tibial nerve stimulation	May be offered when not responding well to, or cannot tolerate, other treatments	↘
Appliances (i.e. urine flasks, pads, diapers, condom catheters)	Offer appliances to alleviate the social impact of urinary incontinence	📝
Pharmacological management		
Oral medications	Offer antimuscarinic agents or beta-3 adrenoceptor agonists when reporting urinary storage (overactive bladder) symptoms	✓
Desmopressin	Desmopressin may be offered selectively for nocturia or nocturnal polyuria	📝
α_1-adrenoceptor blockers	Could be offered for voiding symptoms	↘
Antibiotic use		
Antibiotic prophylaxis	Do not use routinely in individuals who catheterise	☆
Asymptomatic bacteriuria	Do not routinely offer antibiotics to treat asymptomatic bacteriuria	✓
Treating UTIs	In individuals who use catheters, antibiotic treatment should be guided by the results of urine culture and antibiotic sensitivity	☆

☆ Good practice statement 📝 Consensus-based recommendation ✓ Strong evidence ↘ Weak evidence

Key recommendations for assessing and treating sexual symptoms:

Assessment	Recommendations	
History-taking	Regularly ask about sexual problems and explore multidimensional contributing factors	☆
Physical examination	Perform a targeted physical examination when necessary to identify physical contributors to sexual dysfunction	☆
Laboratory examinations	In the appropriate clinical context, assess vascular risk factors and testosterone level	☆
Red flag referrals	Refer individuals with complex sexual dysfunction for specialist care	☆
Lubricants	Consider for dyspareunia or vaginal dryness	📄
Vibrators	Discuss with individuals experiencing sexual problems	☆
PDE5 inhibitors	Offer as a first-line treatment to males experiencing ED	✓
Vacuum devices	May be offered as a second-line treatment to males experiencing ED May be discussed with females experiencing sexual arousal problems	↘ 📄
Intracavernous prostaglandin injections	Offer as a second-line treatment to males experiencing ED	↘
Multidimensional factors	Regularly address factors affecting sexual activity and intimacy: *Primary:* Direct neurological damage (e.g., genital numbness) *Secondary*: Associated physical symptoms (e.g., spasticity, incontinence) *Tertiary:* Social and emotional aspects (e.g., body image, relationships)	☆

☆ Good practice statement 📄 Consensus-based recommendation ✓ Strong evidence ↘ Weak evidence

ED: erectile dysfunction; PDE5: phosphodiesterase-5.
UTI: urinary tract infection
PVR: post void residual

Critical success factor:

Collaboration between neurologists, urologists, and allied specialists.

Why these guidelines matter:

- Comprehensive urogenital care minimizes complications such as urinary incontinence, UTIs, and renal damage.
- Optimal care enhances quality of life by addressing physical, psychological, and relational impacts for patients with neurological diseases.

For the full NEUROGED guidelines, visit: onlinelibrary.wiley.com/doi/full/10.1111/ene.70119 or scan this QR code.

The NEUROGED guidelines were developed by a task force of 38 experts in collaboration with EAN, EFAS, and INUS. The process followed the ADAPTE methodology, endorsed by the Guidelines International Network, to adapt existing high-quality guidelines while addressing areas with limited evidence. Guidelines were assessed using the AGREE II instrument and recommendations developed by adapting or adopting content from top-ranked guidelines. When evidence was lacking, de novo recommendations were created through expert consensus. Recommendations underwent patient review and were refined at a steering committee meeting. A modified Delphi process was used to achieve ≥80% consensus on wording and strength, applying an Evidence to Decision (EtD) framework adapted from GRADE. The NEUROGED guidelines include evidence-based recommendations, good practice statements and consensus-based recommendations.

ORIGINAL PUBLICATION (AS OF NEXT PAGE)

European Journal of Neurology

european journal of neurology
the official journal of the european academy of neurology

GUIDELINES OPEN ACCESS

European Academy of Neurology (EAN)/European Federation of Autonomic Societies (EFAS)/International Neuro-Urology Society (INUS) Guidelines for Practising Neurologists on the Assessment and Treatment of Neurogenic Urinary and Sexual Symptoms (NEUROGED Guidelines)

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Received: 30 January 2025 | **Revised:** 27 February 2025 | **Accepted:** 28 February 2025

Funding: The project was funded by the EAN, EFAS, and INUS, and task force members received no remuneration for their work. The NEUROGED guidelines have been endorsed by the European Research Network for Rare Neurological Disorders. The American Academy of Neurology affirms the value of the EAN/EFAS/INUS guidelines for practising neurologists on the assessment and treatment of neurogenic urinary and sexual symptoms (NEUROGED guidelines) as an educational tool for neurologists.

Keywords: guideline | neurogenic | sexual dysfunction | treatment | urinary dysfunction | urogenital

ABSTRACT

Background: Urinary and sexual symptoms are common following neurological disease, and we aimed to develop multidisciplinary inter-society evidence-based management guidelines.

Methods: The ADAPTE framework was used, and a systematic search of guidelines published in different languages was performed. Guidelines, consensus statements, and systematic reviews were included, and guideline quality was appraised using AGREE II. Patient representatives reviewed the relevance and suitability of recommendations. A modified Delphi process integrating the Evidence to Decision framework adapted from GRADE and the Oxford Centre for Evidence Based Medicine system was used to reach consensus on recommendation wording and strength.

Results: Recommendations were drafted, using guidelines/consensus statements (59 urinary, 50 sexual), systematic reviews (8 urinary, 2 sexual) and others (7 urinary,13 sexual), and wordings/strengths achieved at least 80% consensus through 2 Delphi

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Jalesh N Panicker, Alessandra Fanciulli, Mario Habek were co-chairs of the NEUROGED Task Force.

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For affiliations refer to page 22.

rounds. Eleven evidence-based recommendations, 19 good practice statements, and 8 consensus-based recommendations were made. Individuals with neurological diseases should be asked about urogenital symptoms and undergo targeted physical examination when appropriate. Urinary symptom assessments include urinalysis, bladder diary completion, and post-void residual volume measurement. Treatments include fluid intake optimization, pelvic physiotherapy, tibial nerve stimulation, and oral medications. Urinary retention is managed by intermittent catheterization. Antibiotics should not be recommended to treat asymptomatic bacteriuria. Suprapubic catheterization is preferred for long-term catheterization. A comprehensive sexual history should be taken, focusing on multidimensional factors affecting sexual health. Treatments include lubricants, vibrators, and phosphodiesterase-5 inhibitors. Red flag symptoms warrant a shared-care approach with specialist colleagues.
Conclusions: The 38 NEUROGED recommendations will guide neurologists to comprehensively manage urogenital symptoms reported by individuals with neurological diseases.

1 | Introduction

Lower urinary tract (bladder and urethra) and sexual symptoms are commonly reported by individuals with neurological disorders. The relationship between neurological disease, urogenital dysfunction, and quality of life has been well researched, and urinary tract-related complications are one of the commonest causes for unplanned hospital admissions in multiple sclerosis (MS) [1], Parkinson's disease (PD) [2] and spinal cord injury (SCI) [3]. Sexual health is a significant component of overall well-being and quality of life, and neurogenic sexual dysfunction significantly impacts mental health and relationships [4, 5]. Urinary dysfunction and symptoms differ according to the topographic distribution of neurological lesions: suprapontine disorders such as stroke, PD, and traumatic brain injury present predominantly with urinary storage symptoms due to detrusor overactivity (DO) and normal voiding, whereas suprasacral spinal cord disorders such as transverse myelitis, SCI, and MS present with urinary storage and voiding symptoms due to DO and detrusor-external sphincter dyssynergia (DSD). In contrast, lesions affecting the sacral spinal cord (conus medullaris) or more caudally such as the sacral nerve roots (cauda equina) or peripheral nerves, typically resulting from conditions such as disc prolapse, pelvic surgery, or peripheral neuropathy primarily present with urinary voiding symptoms due to detrusor underactivity, although storage symptoms can also occur. Comorbid urological and medical conditions such as benign prostate enlargement and pelvic organ prolapse can additionally contribute to urinary symptoms [6].

There has been a greater understanding of the factors that can place individuals with neurological disease at greater risk for future damage to the upper urinary tract (kidneys and ureters) and potentially life-threatening complications such as urosepsis. A risk stratification system has recently been introduced, emphasizing the topographic distribution of neurological lesions and the pattern of lower urinary tract dysfunction in determining the risk for renal impairment [7]. Individuals classified as low risk typically have neurological lesions that are either suprapontine (e.g., stroke, PD) or infrasacral, are able to spontaneously void with low post-void residual (PVR) volumes and do not require a catheter to empty the bladder, have stable urinary symptoms, no history of recurrent urinary tract infections (UTIs), normal renal function, and, if investigations have been undertaken, normal upper urinary tract in ultrasound imaging and coordinated functioning of the detrusor and external urethral sphincter during voiding in urodynamic testing [7]. Individuals deemed to be at low risk can be appropriately managed by their neurologist, whereas shared care with a urologist is indispensable for those at a greater risk for future damage to the upper urinary tract or where co-morbid primary urological conditions are suspected.

Disparities in the availability of healthcare services for the management of autonomic nervous system disorders have been highlighted in a recently published survey [8], and access to specialist neuro-urology care is likewise limited. Neurologists have taken an interest in the assessment and treatment of urogenital symptoms in recent years, and guidelines have already been published by different urological societies. Developing guidelines specifically addressed to neurologists would help to establish a framework that best supports the integration of neurogenic urinary and sexual dysfunction management into neurology practice, and identify when care needs to be shared with other specialists. This would ultimately lead to an improvement in the quality of care provided to individuals living with neurological disorders. A global collaborative project was therefore initiated by the European Academy of Neurology (EAN), European Federation of Autonomic Societies (EFAS) and International Neuro-Urology Society (INUS) with the aim of developing evidence-based guidelines intended for practising NEurologists on neurogenic UROGEnital Dysfunction management (NEUROGED).

2 | Methods

A task force of 38 experts was formed in consultation with the EAN, EFAS, and INUS (see Appendix S1 for Task Force members). This group included 24 neurologists, 8 urologists, 1 physiatrist, 2 methodologists, 1 librarian, 1 data organiser, and 1 patient representative. From this task force, a steering committee of 15 members was established to lead the process. Figure 1 illustrates the adopted methodology. As several high-quality guidelines have already been published by reputable professional societies and organisations and the evidence base for several of the recommendations is low, the NEUROGED guidelines were developed based on an assessment and adaptation of existing guidelines. We developed the recommendations using the systematic approach ADAPTE, endorsed by the Guidelines International Network [9]. Clinical questions were drafted in a PICO (Patient-Intervention-Comparison-Outcome) format, and the search of literature published in the last 25 years in English and other languages was performed in 11 databases using MeSH and free-text terms derived from the clinical questions (Appendix S2-Literature search and PICO questions) and duplicates were removed. The

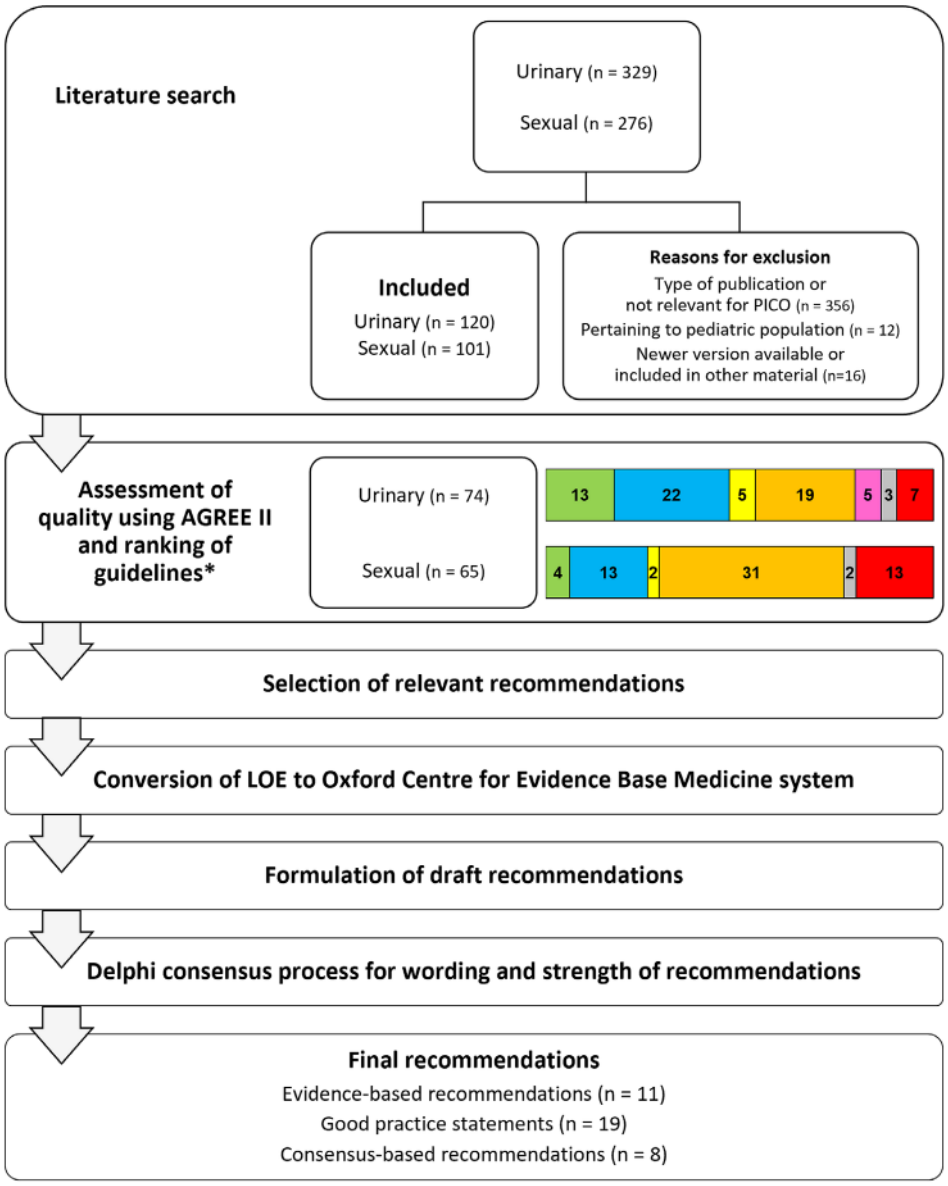

FIGURE 1 | Flowchart outlining steps of guideline development. *Guidelines selected based on overall quality and practicality of recommendations. Guidelines and consensus statements were ranked according to quality (AGREE II domain 3 score of rigour of development), currency, and relevance to individuals with neurological disease: *Green*: High-quality guidelines, pertaining to neurological patients; *Blue*: Moderate-quality guidelines, pertaining to neurological patients + high-quality guidelines, not pertaining to neurological patients; *Yellow*: Low-quality guidelines, pertaining to neurological patients; *Orange*: Moderate/low-quality guidelines, not pertaining to neurological patients; *Pink*: Systematic Reviews, pertaining to neurological patients; *Grey*: Systematic Reviews, not pertaining to neurological patients; *Red*: Other literature. LOE, level of evidence; PICO, population intervention comparison outcome.

steering committee also included relevant papers published during the period that the guidelines were being prepared. Abstracts were screened for format, currency, and relevance to the PICOs, and only guidelines, consensus statements, and systematic reviews that met the search definition were included. We assessed the quality of the selected guidelines using the AGREE II (Appraisal of Guidelines, Research and Evaluation) instrument [10]. Each guideline was appraised independently by two steering committee members to derive a common score, and the guidelines were ranked according to quality, using the Domain 3 score of rigour of development in AGREE II (high ($\geq 70\%$), moderate (40%–69%) and low quality ($< 40\%$)), currency, and relevance to the neurological population (Appendix S3-Ranking documents based on quality). For each PICO, guidelines were reviewed for relevant recommendations in order of ranking, and a minimum of the top five guidelines were used primarily; however, recommendations from guidelines ranked further down were also reviewed. We presented levels of evidence (LOE) from the original guidelines, and the Oxford Centre for Evidence-Based Medicine system (2011) [11] was used to determine the level of evidence of the NEUROGED guideline recommendations; a conversion was performed for guidelines that used a different grading system, apart from those using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) framework (Appendix S4-LOE conversion). We

developed the recommendations for the NEUROGED guidelines by adapting or adopting recommendations from existing guidelines, and they were prepared de novo using consensus if not available in the included guidelines or could be answered using additional evidence. Nine individuals with neurological disease reviewed the draft recommendations during an online meeting to assess relevance and suitability. The wording of proposed recommendations underwent a review during a hybrid meeting of the steering committee that was attended by the patient representative and was accepted only after reaching 80% consensus amongst the committee members. The levels of evidence for the recommendations varied, leading to evidence-based recommendations, good practice statements, and consensus-based recommendations (see Appendix S3-Definitions of recommendation types). The strength of the evidence-based recommendations was determined using an Evidence to Decision (EtD) framework adapted from GRADE [12] (Appendix S3-Determining the strength of recommendations). We integrated this into a modified Delphi process to achieve consensus on the wording and strength of the recommendations. Task force members were presented with summaries of the desirable and undesirable effects and the screened guidelines for each clinical question (Appendix S3-Delphi survey). Recommendations wordings and strengths that did not achieve 80% consensus were then revised based on feedback and went through a second Delphi round.

3 | Results

Two rounds of Delphi voting were conducted with 100% participation from the task force, and all the recommendation wordings and strengths ultimately achieved at least 80% consensus. Eleven clinical questions had sufficient evidence to make evidence-based recommendations, and the strength of six met the criteria for being strong. Nineteen good practice statements and eight consensus-based recommendations were made for the remaining clinical questions. Results of the literature search, data synthesis, and Delphi voting are provided as Supporting Information (Appendices S5–S8). Tables 1–4 summarise the evidence supporting recommendations for the assessment and treatment of urinary and sexual symptoms. Based on the recommendations, algorithms that illustrate the assessment and treatment of urinary and sexual symptoms were developed (Figures 1 and 2). Enlarged versions of these algorithms suitable for use in clinic are also available (Appendices S9 and S10). Table 5 presents a practical checklist of urogenital symptoms that should be covered during history taking.

3.1 | Section 1: Assessment of Urinary Symptoms

Table 1 and Appendix S5 present the evidence supporting the recommendations for assessing urinary symptoms. Figure 2 illustrates the assessment and treatment algorithm for urinary symptoms based on these recommendations.

Clinical Question 1. Should neurologists obtain a history of a patient's urinary symptoms versus not asking about urinary symptoms?

History taking forms the cornerstone of the assessment of urinary symptoms, and this is summarised as a checklist in Table 5.

Recommendation: Neurologists should actively ask about urinary symptoms in individuals with neurological diseases on a regular basis. (Good practice statement; Consensus: 100%).

Clinical Question 2. Should individuals with neurological disease reporting urinary symptoms undergo a focused physical examination versus not undergoing a physical examination?

Individuals reporting urinary symptoms should undergo a targeted physical examination at initial evaluation, which is repeated annually in moderate or high-risk individuals [7]. The examination helps to plan investigations and treatments and screen for complications.

Recommendation: Neurologists should perform a targeted physical examination in individuals with neurological diseases and urinary symptoms. (Good practice statement; Consensus: 94%).

Clinical Question 3. Should individuals with neurological disease reporting urinary symptoms undergo a urinalysis versus not undergoing a urinalysis?

Screening urinalysis, which includes physical, chemical (dipstick testing) and/or microscopic evaluation of urine, should be a part of the initial evaluation when an individual reports urinary symptoms [7, 13, 20]. The urine should be tested at follow-up in case of significant changes in urinary symptoms [14]. Urinalysis is more useful to exclude UTIs, and when a UTI is suspected, the urine should be sent for culture. Urinalysis should not be routinely performed to screen for UTIs in individuals who are using a catheter, given the high prevalence of asymptomatic bacteriuria and leukocyturia [7, 13, 15]. Urine dipstick testing can also screen for glucosuria, proteinuria, and microscopic haematuria, prompting further investigations if persistent and unexplained.

Recommendation: Urinalysis should be performed at initial evaluation and when clinically indicated at follow-up visits for individuals with neurological diseases and urinary symptoms. (Good practice statement; Consensus: 94%).

Clinical Question 4. Should urine cultures versus no testing be offered for individuals with neurological disease and urinary symptoms?

Quantitative urine culture is used to diagnose a UTI by testing for the type of organisms and antibiotic sensitivity, and should be performed only in patients with symptoms such as dysuria, cloudy and/or malodorous urine, lower abdominal pain, and fever.

Recommendation: A urine culture should be performed for individuals with neurological diseases reporting urinary symptoms only if there is a suspicion of a UTI. (Good practice statement; Consensus: 91%).

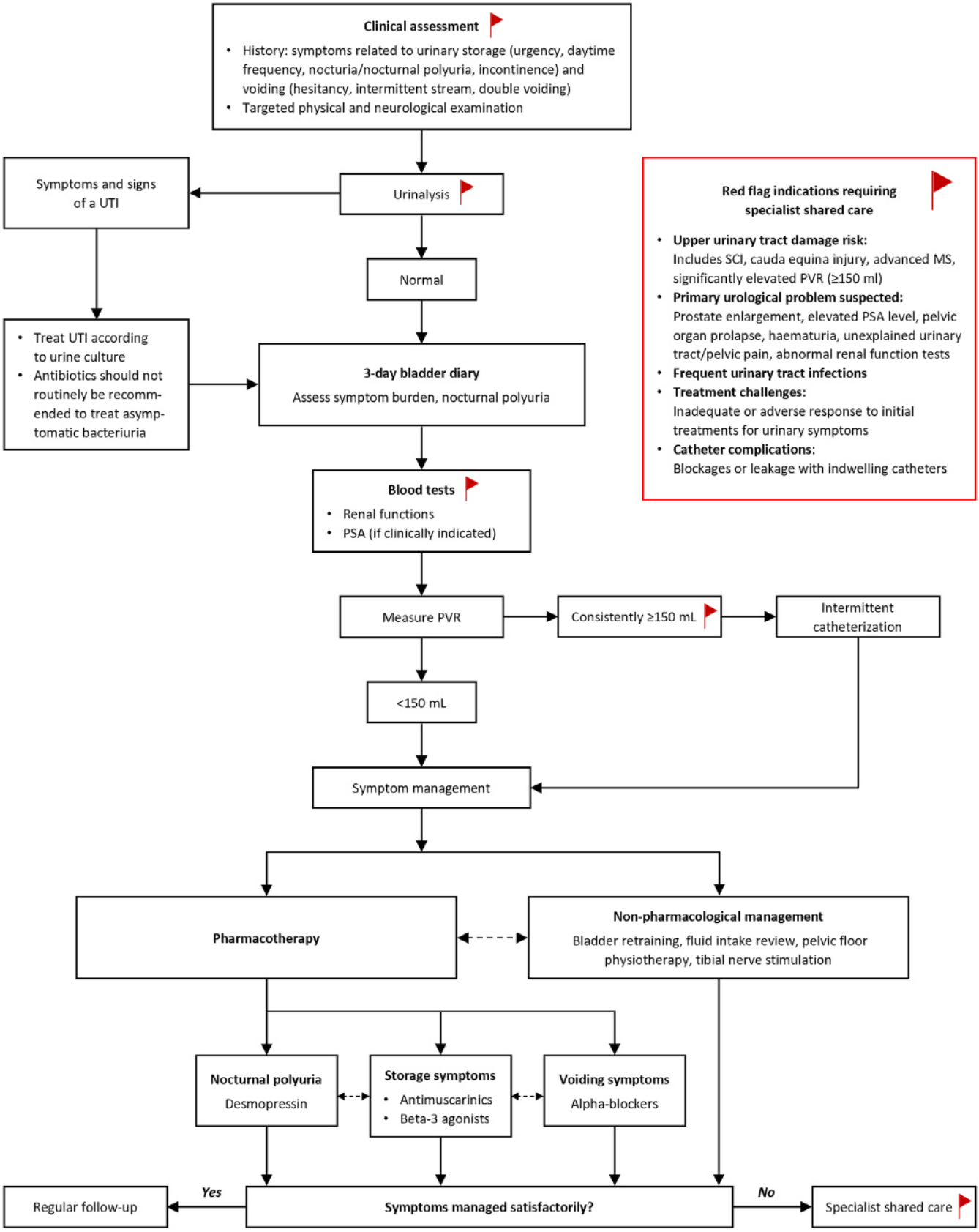

FIGURE 2 | Algorithm illustrating the assessment and treatment of urinary symptoms*. *Derived from NEUROGED recommendations, which are based on different levels of evidence. Refer to the manuscript for further details. MS, multiple sclerosis; PSA, prostate-specific antigen; PVR, post-void residual volume; SCI, spinal cord injury; UTI, urinary tract infection.

Clinical Question 5. Should individuals with neurological diseases reporting urinary symptoms complete a bladder diary versus not complete a bladder diary?

Recording fluid intake, ideally together with urine output, helps to corroborate the history, recognize beverages and drinking habits detrimental to urinary symptoms, and provide an assessment of the functional bladder capacity. Nocturnal polyuria and polydipsia can be diagnosed only by using a bladder diary.

Recommendation: A three-day bladder diary should be completed by individuals with neurological diseases having urinary problems at initial evaluation and at follow-up visits when clinically indicated to provide an objective assessment of urinary symptoms. (Good practice statement; Consensus: 94%).

Clinical Question 6. Should individuals with neurological disease reporting urinary symptoms have their post-void residual measured vs. not have their post-void residual measured?

Post-void residual volume is defined as the volume of urine left in the urinary bladder at the end of micturition and is a valuable indicator of bladder emptying [13].

Recommendation: The PVR should be measured for individuals with neurological diseases having urinary symptoms who void spontaneously, preferably using non-invasive methods, during the initial evaluation and during follow-up visits as deemed clinically appropriate. (Good practice statement; Consensus: 94%).

Clinical Question 7. Should individuals with neurological disease reporting urinary symptoms undergo blood tests (e.g., renal function test) versus not undergo blood tests?

Measuring serum creatinine and blood urea levels has utility in identifying renal disease, and no additional patient preparation is required when collecting samples.

Recommendation: Assessment of renal function, including blood urea and serum creatinine, is recommended for individuals with neurological diseases and urinary symptoms as part of their initial evaluation and repeated during follow-up if clinically indicated. For those with stable urinary symptoms but at risk of upper urinary tract damage, renal function should be tested annually. (Good practice statement; Consensus: 88%).

Clinical Question 8. Should male individuals with neurological disease reporting urinary symptoms undergo PSA testing versus not undergoing this test?

Prostate-specific antigen (PSA) is produced by the prostate and, in healthy males, levels in the blood are low. Measuring blood PSA levels is a validated screening test for prostate cancer.

Recommendation: Prostate cancer screening by measuring the PSA level may be offered to male individuals who have neurological diseases and urinary symptoms, particularly in men between the ages of 50 and 70. However, the decision to test should be shared with the patient after a discussion about possible benefits and harms. (Consensus-based recommendation; Consensus: 88%).

Clinical Question 9. Should individuals with neurological disease reporting urinary symptoms undergo urodynamics testing versus not undergo urodynamics testing?

Urodynamics testing is useful for evaluating the cause of lower urinary tract dysfunction and should be performed selectively.

Recommendation: Invasive urodynamic testing is not recommended as part of the initial evaluation for individuals with neurological diseases and urinary symptoms. However, if individuals exhibit atypical urinary symptoms, are at a high risk of upper urinary tract damage, or have not experienced improvement with conservative treatment options, it is recommended that they be referred for urodynamic testing. (Good practice statement; Consensus: 91%).

Clinical Question 10. Should there be red flags that initiate a urological referral for individuals with neurological disease reporting urinary symptoms versus place a urological referral for all individuals versus not to refer to urology services?

Individuals at low risk for developing upper urinary tract damage can generally be managed by a neurologist [7]. This would include those with a neurological lesion that is either supraspontine (e.g., stroke, Parkinson's disease (PD) or infrasacral), who are able to spontaneously void with low PVR volumes and do not require a catheter to empty the bladder, have stable urinary symptoms, no history of recurrent UTIs, normal renal functions, and, if the individual has undergone tests, synergistic voiding in urodynamics testing and normal upper tract imaging [7]. Following an acute neurological event, risk should be stratified only once the neurological condition has stabilized [7]. The management of individuals with greater risk for developing upper urinary tract damage (such as spinal cord injury, elevated PVR volumes, requiring catheterisation) or urinary symptoms refractory to first-line treatment should be shared between neurologists and urologists.

Recommendation: Individuals with neurological diseases reporting urinary symptoms should be referred to urologists if there is a risk of developing upper urinary tract damage, suspected urological pathology, or poor response or significant side effects to first-line treatments. (Good practice statement; Consensus: 100%).

3.2 | Section 2: Treatment of Urinary Symptoms

Table 2 and Appendix S6 present the evidence supporting recommendations made for the treatment of urinary symptoms, and Figure 2 illustrates the assessment and treatment algorithm of urinary symptoms based on the recommendations.

Clinical Question 11. Should advice for fluid intake versus no advice be offered for individuals with neurological disease and urinary symptoms?

The volume and type of fluids consumed can affect urinary symptoms, and optimizing fluid management can help in the management of storage symptoms, reduce the risk of complications, and improve quality of life.

Recommendation: Advice on adequate fluid intake should be offered to individuals with neurological diseases and urinary symptoms. The benefits and potential risks/burdens should be discussed. (Good practice statement; Consensus: 94%).

Clinical Question 12. Should advice for bladder retraining versus no advice be offered to individuals with neurological disease and urinary symptoms?

Behavioural conservative measures that could help with managing urinary urgency include bladder retraining, timed voiding, prompted voiding, and habit retraining [41]. Bladder retraining involves scheduling a bladder routine with progressively increasing intervals between voids and could be offered to individuals at low risk for developing upper urinary tract damage, experiencing urinary urgency, and who can spontaneously void [13, 15].

Recommendation: Advice for bladder retraining could be offered to individuals with neurological diseases who experience urinary urgency and can spontaneously void. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: weak; LoE III; Consensus: 82% for recommendation wording and 85% for recommendation strength).

Clinical Question 13. Should advice for performing pelvic floor exercises versus no advice be offered to individuals with neurological disease and urinary symptoms?

Pelvic floor muscle training has been shown to be effective for managing stress urinary incontinence and lower urinary tract dysfunction due to MS, stroke, or other neurological conditions where the potential to voluntarily contract the pelvic floor is preserved [15].

Recommendation: Advice on pelvic floor exercises should be offered to individuals with neurological diseases who experience urinary urgency and/or stress incontinence. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: strong; LoE: II; Consensus: 97% for recommendation wording and 88% for recommendation strength).

Clinical Question 14. Should advice for intermittent catheterization versus no advice be offered for individuals with neurological disease and urinary symptoms?

Intermittent catheterisation (IC) enables the bladder to be emptied in individuals with urinary retention [7, 13, 14, 20, 29, 30, 33, 34, 36, 37, 49–51, 55, 56, 58, 59, 107, 108] and is preferred over an indwelling catheter because of fewer complications [55]. A PVR volume consistently above 150 mL is considered a cut-off for commencing IC; however, this decision should take into account individual preferences and the prognosis of the underlying neurological disease. Neurological abilities such as cognition, vision, dexterity, truncal balance, and sensations impact the ability to perform self-catheterisation, and the suitability of carers to perform catheterisation may need to be considered in these situations [14, 33, 55].

Recommendation: Intermittent catheterisation should be offered as first-line therapy in individuals with neurological disease with an elevated postvoid residual urine (>150 mL) or urinary retention (an inability to void) after considering the associated risks, benefits, and resulting burden. (Evidence-based recommendation; Strength: strong; LoE: III; Consensus: 97% for recommendation wording and 97% for recommendation strength in Delphi round 2).

Clinical Question 15. Should advice for indwelling catheterization versus no advice be offered for individuals with neurological disease and urinary symptoms?

Indwelling catheterisation may need to be considered for emptying the bladder when IC is not feasible or for managing urinary incontinence. A suprapubic catheter is preferred over urethral in view of less risk for complications such as urethral injury (false passages, strictures, sphincter injury and stretch, tears, traumatic hypospadias) and ease of catheter management when sitting or when engaging sexually. However, this requires shared decision-making, and complication risks should be discussed with the individual and, if appropriate, their family [13, 14, 20, 29, 33, 41, 50, 51, 55, 57].

Recommendation: When long-term indwelling urinary bladder drainage is unavoidable, individuals with neurological diseases should be advised that suprapubic catheter drainage is preferred over urethral catheterization. (Consensus-based recommendation; Consensus: 100%).

Clinical Question 16. Should prophylactic antibiotic therapy versus no advice be offered for individuals with neurological disease and urinary symptoms using a catheter?

Recurrent urinary tract infections should prompt an assessment for an underlying urological cause (e.g., bladder stones) or suboptimal catheterization technique if performing IC [13–15, 54, 57, 58]. Antibiotic prophylaxis should not be routinely used; however, if no modifiable causes are identified, low-dose antibiotic prophylaxis may need to be considered on an individual basis [13–15, 20, 33, 36, 41, 50, 54, 55, 57–59].

Recommendation: Antibiotic prophylaxis should not be routinely used in individuals with neurological diseases who catheterize. The benefits and potential risks/burdens should be discussed. (Good practice statement; Consensus: 100%).

Clinical Question 17. Should advice for antibiotic therapy versus no advice be offered for individuals with neurological disease and urinary symptoms having asymptomatic bacteriuria?

Asymptomatic bacteriuria should be treated with antibiotics only in exceptional circumstances [13, 20, 26, 29, 50, 54, 57–59]. The choice of antibiotics should take into account urine culture and sensitivity results, previous antibiotic use, and recommendations in local antibiotic formularies as part of antimicrobial stewardship.

Recommendation: Antibiotics should not be routinely recommended to treat asymptomatic bacteriuria in individuals with neurological diseases having urinary problems*. The benefits and potential risks/burdens should be discussed. *Exceptions where antibiotic treatment for asymptomatic bacteriuria may be considered are pregnancy, planned urological procedures, or immunomodulatory treatments. (Evidence-based recommendation; Strength: strong; LoE: I; Consensus: 100% for recommendation wording and 97% for recommendation strength).

Clinical Question 18. Should antibiotic treatment be guided by urine culture sensitivity versus given empirically for individuals with neurological disease and urinary symptoms who use catheters having UTI?

Antibiotics should be prescribed for individuals using catheters reporting symptoms of a UTI ideally only once the results of urine culture and sensitivity tests are available, and the choice of antibiotics should take into account recommendations in local antibiotic formularies as part of antimicrobial stewardship. However, in certain instances, antibiotics may need to be started empirically beforehand depending upon the severity of symptoms and the risk for developing complications if antibiotics are delayed.

Recommendation: Antibiotic treatment of urinary tract infections in individuals with neurological diseases who use catheters should be guided by the results of urine culture and antibiotic sensitivity. (Good practice statement; Consensus: 100%).

Clinical Question 19. Should advice for tibial nerve stimulation versus no advice be offered to individuals with neurological disease and urinary symptoms?

Tibial nerve stimulation is a safe and effective treatment for managing urinary storage symptoms in individuals with neurological disease [13, 50]. Both the percutaneous (PTNS) and the transcutaneous techniques (TTNS) can be considered.

Recommendation: Tibial nerve stimulation may be offered to individuals with neurological diseases having urinary symptoms who do not respond well to or cannot tolerate other treatments. Patient preference should be considered. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: weak; LoE: II; Consensus: 82% for recommendation wording and 88% for recommendation strength).

Clinical question 20. Should advice for appliances versus no advice be offered to individuals with neurological disease and urinary symptoms?

Appliances can be used for urinary containment (absorbent products (continence pads, pants) and draining aids (condom catheter)) or to facilitate bladder emptying (flasks or jugs).

Recommendation: Appliances (i.e., urine flasks, pads, diapers, condom catheters) should be offered to alleviate the social impact of urinary incontinence in selected individuals with neurological diseases having urinary symptoms. The benefits and potential risks/burdens should be discussed. (Consensus-based recommendation; Consensus: 97%).

Clinical question 21. What is the clinical effectiveness of antimuscarinic agents versus placebo or non-pharmacological measures, or comparison with different pharmacological interventions or no treatment for individuals with neurological disease and urinary symptoms?

Antimuscarinic agents improve clinical symptoms such as urinary urgency, voided volumes, and urinary incontinence, as well as urodynamic parameters during filling cystometry, including maximum cystometric capacity (volume when voiding can no longer be delayed) and bladder compliance (measure for the distensibility of the bladder) [13, 50]. Their adverse effects should be considered before prescribing, including potential impact on neurological symptoms.

Recommendation: Antimuscarinic drugs should be offered to individuals with neurological diseases and urinary storage (overactive bladder) symptoms. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: strong; LoE: I, Consensus: 100% for recommendation wording and 94% for recommendation strength).

Clinical question 22. What is the clinical effectiveness of beta-3 adrenoceptor agonists versus placebo or non-pharmacological measures, or comparison with different pharmacological interventions or no treatment for individuals with neurological disease and neurogenic urinary symptoms?

Beta-3 adrenoceptor agonists offer comparable patient-reported outcomes and a superior safety profile to antimuscarinic agents [13, 20, 29, 50].

Recommendation: Beta-3 adrenoceptor agonists should be offered to individuals with neurological diseases and urinary storage (overactive bladder) symptoms. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: strong; LoE: II; Consensus: 94% for recommendation wording and 88% for recommendation strength).

Clinical question 23. What is the clinical effectiveness of cholinergic drugs versus placebo or non-pharmacological measures, or comparison with different pharmacological interventions or no treatment be offered for individuals with neurological disease and neurogenic urinary symptoms?

Cholinergic drugs are expected to improve voiding function in individuals with detrusor underactivity by activating muscarinic receptors. However, the evidence supporting their use is limited due to the low quality of studies [13, 29, 37].

Recommendation: There is insufficient evidence to recommend the use of cholinergic drugs to promote bladder emptying in individuals with neurological diseases having urinary retention due to detrusor underactivity. (Consensus-based recommendation; Consensus: 94%).

Clinical question 24. What is the clinical effectiveness of desmopressin versus placebo or non-pharmacological measures, or comparison with different pharmacological interventions or no treatment for individuals with neurological disease and neurogenic urinary symptoms?

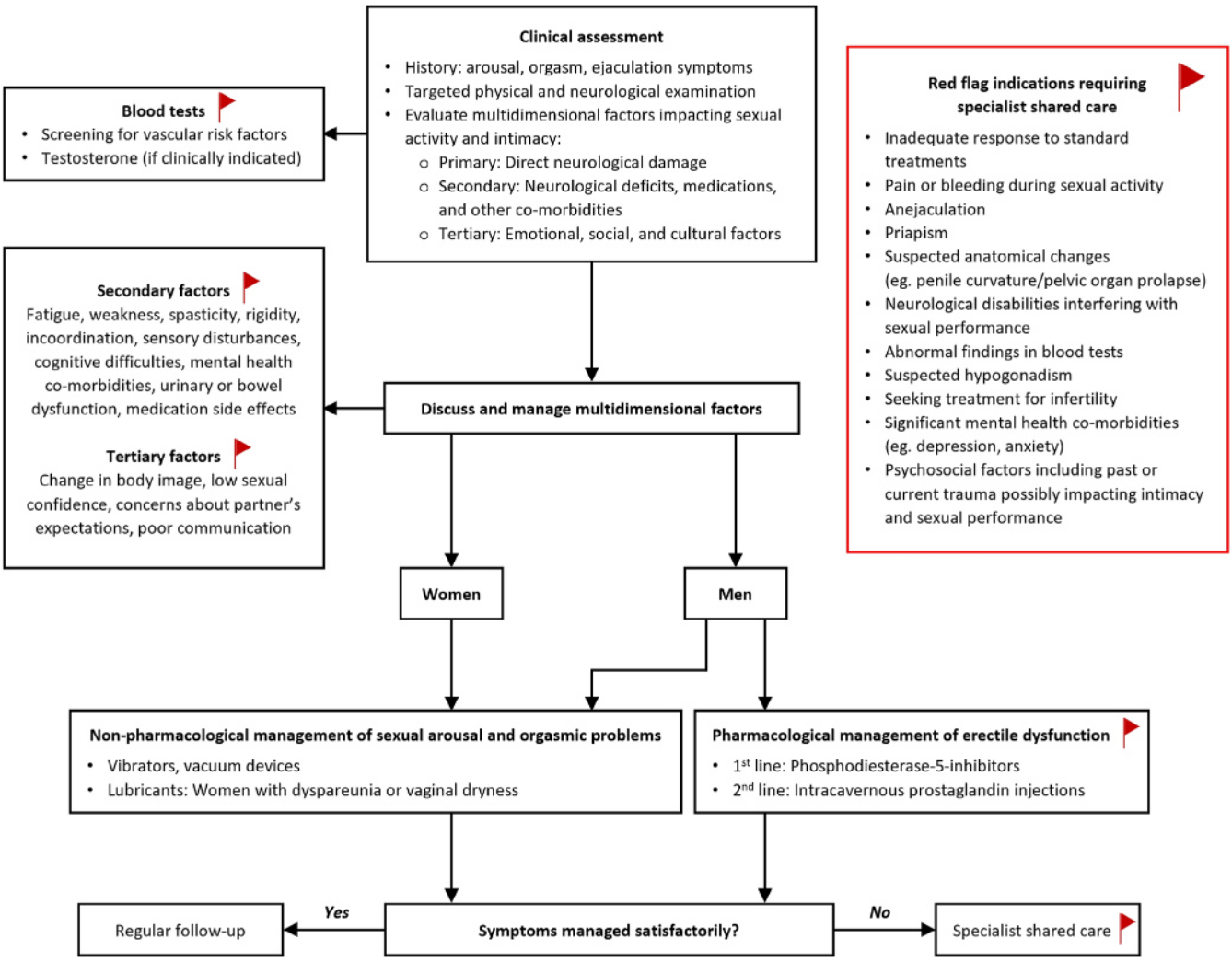

FIGURE 3 | Algorithm illustrating the assessment and treatment of sexual symptoms*. *Derived from NEUROGED recommendations, which are based on different levels of evidence. Refer to the manuscript for further details.

Desmopressin, a synthetic arginine-vasopressin analogue, reduces urine volume by promoting water reabsorption in the renal collecting ducts and the ascending limb of the loop of Henle. Taken at bedtime, desmopressin has been shown to reduce nocturnal urine production and nocturia.

Recommendation: Desmopressin may be offered to selected individuals with neurological diseases who experience nocturia or nocturnal polyuria that affects their quality of life. The benefits and potential risks/burdens should be discussed. (Consensus-based recommendation; Consensus: 91%).

Clinical question 25. What is the clinical effectiveness of α_1-adrenoceptor blockers versus placebo or non-pharmacological measures, or comparison with different pharmacological interventions or no treatment for individuals with neurological disease and neurogenic urinary symptoms?

α_1-adrenoceptor blockers reduce bladder outlet resistance by decreasing urethral resistance and are recommended for use in individuals with neurological disease [13, 50]. They have been shown to improve urinary storage symptoms and emptying in individuals with SCI, PD, and MS.

Recommendation: α_1-adrenoceptor blockers could be offered to select individuals with neurological diseases who experience voiding symptoms. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: weak; LoE III; Consensus: 100% recommendation for wording and 82% for recommendation strength in Delphi round 2).

3.3 | Section 3: Assessment of Sexual Symptoms

Table 3 and Appendix S7 present the evidence supporting recommendations made for the assessment of sexual symptoms, and Figure 3 illustrates the assessment and treatment algorithm of sexual symptoms based on the recommendations.

Clinical question 26. Should neurologists obtain a history of a patient's sexual symptoms versus not asking about sexual symptoms? Should there be a multidimensional assessment about primary, secondary, and tertiary factors versus no multidimensional assessment?

History taking forms the cornerstone of the assessment, and this is summarised as a checklist in Table 5. High-quality guidelines

TABLE 1 | Summary of evidence supporting recommendations for the assessment of urinary symptoms.

Clinical question 1. History taking

History taking should include [7, 13–19] (checklist presented in Table 5):

- Urinary symptoms:
  - Storage symptoms (urgency, daytime frequency, nocturia, urinary incontinence), bladder sensations; whether incontinence is associated with urgency (urgency urinary incontinence) or effort/exertion (stress urinary incontinence), continuous (e.g., incontinence from chronic urinary retention), related to neurological disability (impaired cognition and/or mobility) or sexual arousal
  - Voiding symptoms (how voiding is initiated, posture adopted during voiding, hesitancy, quality of stream (e.g., strength, whether interrupted), dysuria, abdominal straining when voiding, voided volumes, terminal dribble)
  - Post-micturition symptoms (sensation of incomplete bladder emptying after voiding, double voiding, post-micturition incontinence)
- Onset and course of symptoms in relation to the neurological disease; extent of neurological disabilities
- Current and past treatment for urinary symptoms- treatment outcomes and any adverse reactions, use of continence products and appliances (e.g., pads or diapers, sheaths, catheters). If using a catheter, whether intermittent (frequency of catheterisation) or indwelling (urethral or suprapubic catheter)
- Any complications: (recurrent) urinary tract infections, haematuria, pain from the urinary tract, catheter blockages or bypassing
- Lifestyle factors: fluid intake and timing, type of fluid intake (e.g., alcohol, caffeine, fizzy drinks), smoking, alcohol and recreational drug use
- Sexual and bowel symptoms
- Medical, psychological and surgical co-morbidities both past and current- co-existent genitourinary conditions eg. prostate enlargement, stones or surgery; obstetric history.
- Impact of urinary symptoms on quality of life (patient and carer).
- Support at home; expectations of patient and carers from symptom management in the context of the neurological condition.
- Periodic review for new or changing urinary symptoms. In case of a recent deterioration, enquire about symptoms of a UTI, change in bowel movements, recent change in neurological symptoms or in medications

Clinical question 2. Targeted physical examination

Targeted physical neuro-urological examination should include [7, 13, 15, 17, 20–22]:

- Assessment of vital signs, including blood pressure and pulse rate in supine and standing positions, to detect conditions like orthostatic hypotension and bradycardia that could impact urinary symptom management (e.g., contraindications to alpha-blockers, antimuscarinic agents)
- Neurological assessment of cognitive, motor, and sensory functions including evaluating the sacral innervation (sensory changes in the sacral dermatomes (S2-5)), sacral cord mediated reflexes (anal, bulbocavernosus). Assess ability to undergo investigations or treatments (e.g., ability to perform self-catheterisation)
- External genitalia, if appropriate, to identify contributors to urogenital dysfunction; screen for local complications (e.g., atrophy, skin infection)
- Specialist referral when prostate pathology, pelvic organ prolapse or abnormal pelvic floor muscle function are suspected

Clinical question 3. Urinalysis

- Chemical assessment of the urine using urine dipsticks detect pyuria, glucosuria, proteinuria, and haematuria, prompting further investigations if persistent and unexplained. Interpret results in the context of the patient's underlying condition [7, 15, 20]
- Positive leukocytes and nitrites have reported sensitivity (78%) and specificity (65%) to detect significant bacteriuria ($\geq 10^5$ CFU/mL) in MS [23, 24]
- Urine dipsticks have a 50% positive predictive value and 98% negative predictive value for UTIs [24, 25] and are more useful to exclude UTIs. Formal urinalysis (microscopic assessment) and urine cultures are preferred for UTI diagnosis [7, 13–15]
- Significant leukocyturia is defined as ≥ 10 leukocytes per microscopic field in centrifuged urine samples [13]
- Collection methods include clean-catch midstream, freshly inserted sterile catheter, or catheter sampling port [7, 15]; avoid leg bags [15]

(Continues)

TABLE 1 | (Continued)

Clinical question 4. Urine culture

- Urine culture should not routinely be sent unless there are symptoms suggestive of a UTI, exceptions being: pregnancy, planned invasive urological procedures [13–15, 20, 26] and before the administration of immunomodulatory agents in individuals with MS and hypogammaglobulinemia reporting recurrent UTIs [26]
- Due to impaired sensations, not all individuals may report typical UTI symptoms. UTIs can present as worsening neurological (e.g., autonomic dysreflexia, motor symptoms, delirium) or urological (e.g., urinary frequency, urinary urge or urge incontinence) symptoms [7]
- Urinary bacterial colonisation is common when using a catheter, however the risk of progression to symptomatic UTI is low [7]
- Collection of urine samples should follow the clean-catch midstream technique. If catheterized, sample to be taken from a freshly inserted sterile catheter or from the sampling port of a catheter bag; avoid leg bags [7, 15]
- Significant growth in urine culture: $>10^4$ cfu/mL in clean-void specimens, $>10^2$ cfu/mL in samples from IC, any detectable growth in suprapubic aspirates [13]
- Routinely sending urine for culture in the absence of UTI symptoms can lead to unnecessary antibiotic treatment and consequent risk of side effects and antibiotic resistance

Clinical question 5. Bladder diary

- A diary spanning three consecutive days is considered optimal, though there is limited normative data from the neurological population [7]
- Record voiding times and voided volumes using a jug, sleep and wake times, timing and type of fluid intake and volume, severity of urgency incontinence episodes and timing of medications, eg. diuretics [15, 17, 27]
- The link https://iciq.net/iciq-bladder-diary provides an example of a bladder diary

Clinical question 6. Post-void residual volume

- The PVR is most commonly expressed as an absolute value. Percentage of bladder emptying (voiding efficiency) can also be calculated as a percentage and is particularly relevant when the bladder is overdistended or has a small capacity [7]
- The PVR should be measured during the initial evaluation [7, 13–15, 20, 28, 29] of individuals who can void spontaneously, and rechecked at follow up if there is an unexplained change in urinary symptoms [7]
- PVR is preferably measured by ultrasonography, however in-out catheterisation can also be used [7]
- An elevated PVR suggests voiding dysfunction. Urodynamics testing is needed to assess the cause ie. from detrusor underactivity, anatomical or functional bladder outlet obstruction, or both [7]

Clinical question 7. Renal function tests

- Assessing renal functions by measuring blood urea and serum creatinine levels, or more accurately estimating the GFR (eGFR), is recommended as routine during the initial evaluation, particularly for high-risk individuals [7, 20]
- Frequency of follow-up testing is individualised based on risk profile [7, 13]
- Measuring serum creatinine alone may underestimate renal dysfunction in individuals with significant sarcopenia, and in these situations 24 h creatinine clearance or cystatin-C based estimates of GFR would need to be considered for assessing renal functions

Clinical question 8. PSA testing

- Men experiencing urinary symptoms should be given information and time to decide on undergoing PSA testing, especially if their symptoms suggest bladder outlet obstruction due to benign prostate enlargement, abnormalities are found on digital rectal examination performed by the attending urologist or they are concerned about prostate cancer [30, 31]
- Shared decision-making is essential, considering the benefits of reducing metastatic prostate cancer and preventing prostate cancer-related deaths against potential screening and treatment harms. Men should be offered a PSA test every 2 to 4 years between the ages of 50 to 70 years, though this may begin at age 40 to 45 years for individuals at greater risk for developing prostate cancer, namely black ancestry, germline mutations, strong family history of prostate cancer. The decision to continue screening is based on patient preference, age, PSA, prostate cancer risk and life expectancy [30–32]
- PSA levels may be elevated in men with urethral indwelling catheters or prostatitis, and alternative assessments will be needed if prostate cancer is suspected

(Continues)

TABLE 1 | (Continued)

Clinical question 9. Urodynamics testing

- The need for urodynamics testing is determined by stratification of risk for developing upper urinary tract damage [7, 20, 33]
- With suprapontine lesions, urodynamics testing is omitted as a first-line examination as PVR and bladder pressures are typically low [7]
- Urodynamics can help identify specialised management options if first line treatments fail
- Urodynamics is a first-line examination for moderate/high risk individuals with neurological disease eg. suprasacral spinal cord lesions, spina bifida
- Follow-up urodynamics testing should be individualised based on risk profile [7, 13]
- Individuals with neurological disease should be referred to a urology service for undergoing urodynamics testing

Clinical question 10. Red-flags for specialist referral

Shared care with specialist urology input is recommended in the following situations:

- Neurological disorders associated with a greater risk of upper urinary tract damage, such as spinal cord injury, spinal dysraphism, transverse myelitis, or advanced MS [7, 13]
- Recurrent UTIs, particularly with fever [13, 15, 17, 21, 34]
- Haematuria without an apparent cause [15]
- Loin pain is suspected to originate from the urinary tract [15, 34]
- Abnormal findings on ultrasonography, including hydroureteronephrosis, renal or bladder stones, bladder diverticulum, renal scarring, or renal parenchymal loss [7, 15, 21, 34]
- PVR volume > 100–150 mL [7, 17, 35]
- Renal impairment [7, 15]
- When urological lesions are suspected, such as urinary symptoms secondary to prostate enlargement in men or pelvic organ prolapse in women [34]

Abbreviations: CFU, colony forming units; GFR, glomerular filtration rate; IC, intermittent catheterisation; MS, multiple sclerosis; PSA, prostate specific antigen; PVR, post-void residual volume; UTI, urinary tract infection.

for individuals with neurological disease highlight the importance of a comprehensive medical and sexual history in evaluating sexual dysfunction, emphasising primary, secondary, and tertiary sexual dysfunctions. A detailed history should explore sexual dysfunction's nature, onset, and impact, including specific challenges faced by those with SCI or post-stroke, considering both physical and psychosocial factors. Sexual orientation, relationship history, emotional well-being, substance use, and previous treatments should also be assessed [13, 85–90, 95, 109].

Recommendation: Neurologists should actively ask individuals with neurological diseases about sexual problems regularly and explore multidimensional contributing factors. (Good practice statement; Consensus: 97%).

Clinical Question 27. Should Individuals With Neurological Disease Reporting Sexual Problems Undergo a Focused Physical Assessment Versus no Physical Assessment?

Identifying the physical contributors to sexual dysfunction in individuals with neurological disorders is crucial for effective management and treatment planning. These individuals should undergo a targeted physical examination when necessary.

Recommendation: Neurologists should perform a targeted physical examination when appropriate in individuals with neurological diseases who experience sexual problems. (Good practice statement; Consensus: 85%).

Clinical Question 28. Should Individuals With Neurological Disease Reporting Sexual Dysfunction Undergo Further Laboratory Diagnostic Evaluations (Vascular Risk Factors) Versus no Diagnostic Evaluation?

Evidence suggests that men with erectile dysfunction (ED) should undergo vascular risk screening, including fasting glucose, HbA1c, and lipid profiles, based on guidelines not aimed at individuals with neurological disease. ED is now seen as a standalone risk for cardiovascular disease and a potential early sign of diabetes, necessitating baseline measurements of serum lipids and glucose. If no recent tests are available, a comprehensive lipid and glucose profile is recommended. Although not all tests will diagnose ED directly, they offer a chance to uncover important co-morbidities. Serum testosterone should be measured in those showing signs of hypogonadism, with morning blood samples being preferred for accuracy [85, 87, 89, 90, 93, 95–98]. Screening for urogenital cancers and sexually transmitted infections (STI) may be required on an individualized basis.

Recommendation: Individuals with neurological diseases who have sexual problems should undergo screening laboratory testing for additional contributing factors in the appropriate clinical context. (Good practice statement; Consensus: 97% in Delphi round 2).

Clinical Question 29. Should Individuals With Neurological Disease Reporting Sexual Problems Undergo Further Instrumental Diagnostic Evaluations (Ex: MRI, Neurophysiology) Versus no Diagnostic Evaluation?

Routine instrumental diagnostic tests, such as pelvic neurophysiology and MRI, are not typically necessary for individuals with neurological diseases experiencing sexual dysfunction, as these tests often do not provide additional information beyond a thorough history and examination. These tests include the assessment of pelvic somatic sensory and motor functions, reflexes, and autonomic innervation, and may be useful in specific situations such as the assessment of unexplained urogenital

TABLE 2 | Summary of evidence supporting recommendations for the treatment of urinary symptoms.

Clinical question 11. Fluid intake

- Maintaining an optimal daily fluid intake (1–2 L for an average adult) [14] and avoiding certain beverages (caffeinated drinks, carbonated drinks, citrus products and alcohol) can improve urinary storage symptoms [21, 36, 37], particularly when going outside the home or at night [38, 39]
- For individuals in urinary retention, the volume of fluids consumed can also affect the frequency of intermittent catheterisation
- Individuals at risk of developing constipation [40], dehydration [41], or with geriatric multi-morbidities [41] should limit their fluid intake cautiously
- Restricting fluid intake may exacerbate symptoms of orthostatic hypotension in those with autonomic failure [42] and increase the risk for recurrent UTIs or stone formation [36]

Clinical question 12. Bladder retraining

- Bladder retraining is effective in individuals with neurological disease, however a certain level of physical and cognitive abilities are required to recognise the urge to void and to be able to adopt techniques to postpone voiding [13, 15, 17, 29, 33, 37, 41, 43–47]; hence unsuitable if there is cognitive impairment
- Symptoms recur after cessation of bladder retraining [46, 48]
- Not recommended for individuals with urinary incontinence who are unable to void spontaneously, such as following SCI [29, 41]

Clinical question 13. Pelvic floor exercises

- Pelvic floor exercises should be offered only to individuals at low-risk of developing upper urinary tract damage for improving continence [13–15, 17, 27, 29, 33, 37, 49, 50]
- Pelvic floor assessment and treatment regimen should preferably be organised through a pelvic floor physiotherapist [14, 15, 41]
- For long-term benefits, exercises should be continued even after continence had been achieved [51, 52]
- Prerequisites for performing pelvic floor exercises include active patient cooperation and ability to contract pelvic floor muscles, ie. partially preserved neural control over pelvic floor muscles [14, 15, 29, 41]
- Additionally, biofeedback may improve incontinence due to external sphincter deficiency [49], and pelvic floor electrical stimulation may improve urinary urge incontinence [37] however should be considered on an individual basis [15, 51]; these techniques may not be feasible in those with impaired cognition or sensorimotor skills

Clinical question 14. Intermittent catheterisation

- Individuals with voiding dysfunction can present in chronic urinary retention. This can manifest as urinary storage symptoms such as urinary urgency, frequency and incontinence, recurrent UTIs, bladder stones, and upper urinary tract deterioration [50]
- A threshold PVR volume at which to initiate IC has not been defined [50]. A figure of 100 mL has been suggested in MS [14], whereas 300 mL was a suggested definition for non-neurogenic chronic urinary retention [53]. The task force came to a consensus of 150 mL
- Individuals require adequate support when learning IC, and teaching should be undertaken by health care professionals who are proficient with the technique, aware of locally available catheter products and understand the neurological disorder [33]
- A clean or aseptic technique should be adopted, and care should be taken to minimise trauma [33, 54]
- Complications of IC include UTIs, urethra trauma, false passages, stricture, and autonomic dysreflexia for SCI above T6 level [13, 33, 54–57]
- Hydrophilic, gel-coated, disposable catheters may lower the risk of urethral trauma and recurrent UTIs [57]
- Regular follow-up may be required to monitor complications, typically on an annual basis. However more frequent monitoring may be required if experiencing problems like recurrent UTIs [14, 20, 33, 51, 54, 55, 57]

Clinical question 15. Indwelling catheterisation

- Both urethral and suprapubic catheterisation help to reduce intravesical pressure, however long-term catheterisation can lead to complications such as biofilm formation and thereby increasing the risk of urosepsis, catheter encrustation and bladder stones
- Suprapubic catheterisation is preferable when a long term catheter is being considered, however there is a risk for developing complications such as intestinal perforation at the time of catheter insertion and wound site infection
- A urethral catheter is appropriate as a temporary measure for acute urinary retention until a management plan is formulated
- In-out catheterisation may be required in select situations, eg. individuals with delirium who forcibly remove an indwelling catheter [41]

(Continues)

TABLE 2 | (Continued)

Clinical question 16. Antibiotic prophylaxis

- Long term antibiotic use is associated with a risk for developing side effects and bacterial resistance, and therefore the need should be re-evaluated at follow-up [14, 15, 57, 58]. The choice of antibiotics should take into account urine culture and sensitivity results, previous antibiotic use and recommendations in local antibiotic formularies as part of antimicrobial stewardship

Clinical question 17. Treating asymptomatic bacteriuria

- Routinely treating asymptomatic bacteriuria can lead to antibiotic resistance without improving patient outcomes [13, 26, 29]
- In pregnant women, asymptomatic bacteriuria can pose a greater risk for developing complications such as pyelonephritis and premature delivery, and therefore antibiotic treatment is indicated [20, 26, 57–59]
- Treating asymptomatic bacteriuria prior to invasive urological procedures or immunomodulatory therapy including corticosteroids has been recommended by some guidelines to mitigate potential risks [20, 26, 57–59]

Clinical question 18. Treating UTIs

- Individuals with neurological disease with catheters reporting UTI symptoms should undergo urine culture and antibiotic sensitivity testing before starting antibiotics
- Antibiotic therapy should follow recommended dosages for at least 7 days, however duration of treatment may vary depending on clinical status and recommendations from local antibiotic formularies as part of antimicrobial stewardship [20, 57, 59]
- If antibiotic treatment is being started empirically whilst awaiting the results of the urine culture test, the choice of antibiotics should be based on previous antibiotic usage and, if available, results of earlier urine culture and sensitivity tests

Clinical question 19. Tibial nerve stimulation

- Tibial nerve stimulation has been shown to improve urinary symptoms and urodynamic parameters in neurological disorders such as MS [60–62], PD [63–65], SCI [66, 67] and stroke [68], with demonstrable durable effects lasting over 12 months [69]. There is still uncertainty regarding the type of lower urinary tract dysfunction that best responds to tibial nerve stimulation [20]
- Adverse effects are generally mild and include pain [20], inflammation and bleeding at the treatment site (for PTNS)
- Avoid this treatment in individuals with pacemakers or implantable defibrillators or if pregnant or planning pregnancy. PTNS should be avoided for those prone to excessive bleeding

Clinical question 20. Appliances

- Condom catheters are worn outside of the penis and can be used for men who can empty their bladder [14, 30, 33]. A specialist nurse should assess penile length and girth, skin health and manual dexterity and, if appropriate, caregiver support [30, 33, 36, 41, 54, 56, 59]. Complications can include skin irritation and infection; rarely penile necrosis, urethral diverticula and UTIs [20, 33, 41]. Complications can be reduced by adhering to instructions on use, maintaining hygiene, regular changes, and periodic specialist nurse reviews [33]. Silicone condom catheters are preferred [33]
- Urine flasks can be used by individuals with mobility impairment to facilitate bladder emptying [41], and reduces the risk for falls from nocturnal toilet visits
- Temporary containment products such as continence pads may be offered till a urinary symptom management plan has been formulated [30]
- External appliances should be avoided for managing overflow incontinence due to urinary retention

Clinical question 21. Antimuscarinic agents

- Efficacy between different antimuscarinic agents has been shown to be similar [70]
- Combination therapy of two antimuscarinic agents, or an antimuscarinic agent and beta-3 adrenoceptor agonist, could be considered in cases of poor treatment response [13, 33, 50]
- The PVR volume should be measured before initiating antimuscarinic treatment [14] and in cases of poor response to treatment.
- Adverse effects of antimuscarinic agents may include constipation, dry mouth and eyes, blurred vision, tachycardia, drowsiness, dyspepsia [50]. Voiding difficulties may worsen, however the risk of developing urinary retention in neurological patients is low
- Studies have evaluated the relationship between antimuscarinic agent use and cognitive changes and the risk for dementia [71]. In individuals at risk for cognitive impairment, antimuscarinic agents with favourable physicochemical and pharmacokinetic properties that make it less likely to cross the blood–brain barrier and having no demonstrated cognitive risks should be considered, such as trospium chloride or darifenacin. The decision on starting an antimuscarinic agent should be shared with the patient [50]
- Contra-indications include uncontrolled angle-closure glaucoma, gastro-intestinal obstruction, myasthenia gravis, severe ulcerative colitis, significant bladder outflow obstruction, toxic megacolon
- Use with caution if susceptibility to QT-interval prolongation (specifically for solifenacin)

(Continues)

TABLE 2 | (Continued)

Clinical question 22. Beta-3 adrenoceptor agonists

- Beta-3 adrenoceptor agonists show similar clinical efficacy to antimuscarinic agents, however less consistent improvements in urodynamic outcomes including first detrusor contraction volume and bladder capacity [13, 20, 72]
- They can be considered in cases of poor response to antimuscarinic agents, either as an alternative or in combination [72–79]
- They may be considered in place of antimuscarinic agents in cases of unacceptable side effects or contraindications [37], and are considered a first-line treatment for individuals with cognitive disorders or in the elderly [71]. They have less detrimental effects on cognition and lower incidences of dry mouth, urinary retention and constipation. Adverse effects of beta-3 adrenoceptor agonists may include a rise in blood pressure, palpitations, increased heart rate and the risk of developing atrial fibrillation. Worsening voiding dysfunction has been reported in individuals with bladder outflow obstruction due to benign prostate enlargement [80], however the risk of developing urinary retention in neurological patients is low
- Use with caution if history of QT-interval prolongation
- Contraindicated if blood pressure severely uncontrolled (systolic ≥ 180 mmHg or diastolic ≥ 110 mmHg)

Clinical question 23. Cholinergic agents

- Side effects include abdominal cramps, vomiting, diarrhoea and bradycardia [13, 29]

Clinical question 24. Desmopressin for nocturia

- Taken at bedtime, desmopressin has been shown to reduce MS related nocturia [81] and overnight catheterisation frequency in SCI-related nocturnal polyuria [82]
- Fluid intake should be restricted for a few hours after taking desmopressin [49]; weight and blood pressure should be monitored
- Common side effects include headache, ankle oedema, nausea, dizziness and hyponatremia, typically occurring early in treatment.
- The risk for hyponatremia is higher in females [27] and the elderly [27, 83], and therefore the standard desmopressin formulations (0.2 mg tablets at bedtime) should not be used for individuals, especially women, above age 65 [27]
- Low-dose desmopressin may, however, be considered for non-frail elderly individuals [21]
- Sodium levels should be checked at baseline, repeated 4–8 days and 1 month after initiation, and then every 3 to 6 months depending on clinical need [27]
- Desmopressin should be discontinued in case of side effects [38]
- Contraindications for desmopressin use include congestive heart failure, polydipsia, and concurrent use of medications with a high risk for developing hyponatremia [27] and persistent ankle oedema

Clinical question 25. α_1-adrenoceptor blockers

α_1-adrenoceptor blockers can cause hypotension, and should be avoided if orthostatic hypotension has been documented

- When initiating treatment, individuals should be advised to take the medication at bedtime and when supine, particularly the elderly, and those with high-level SCI, PD, dementia with Lewy bodies, or MSA, to minimise the risk of developing orthostatic hypotension
- Caution is advised when α_1-adrenoceptor blockers are taken together with PDE5 inhibitors
- Ejaculatory dysfunction is a known side effect, especially with the more selective α_1-adrenoceptor blockers eg. tamsulosin and silodosin [84]

Abbreviations: IC, intermittent catheterisation; MS, multiple sclerosis; MSA, multiple system atrophy; PD, Parkinson's disease; PDE, phosphodiesterase; PTNS, percutaneous tibial nerve stimulation; PVR, post-void residual; SCI, spinal cord injury; UTI, urinary tract infection.

dysfunction, evaluating incidental spinal MRI findings, cases of pelvic trauma, or for medico-legal reasons. The tests should be reserved for specialist settings where they can be accurately performed and interpreted [13, 89, 96].

Recommendation: Diagnostic evaluations such as pelvic neurophysiology and MRI are not recommended for individuals with neurological diseases and sexual problems, except in specific clinical situations. (Consensus-based recommendation; Consensus: 100%).

Clinical Question 30. Should There Be Red Flags That Initiate a Specialist Referral for Individuals With Neurological Disease Reporting Sexual Problems Versus Not Initiating a Specialist Referral?

Individuals with neurological diseases facing sexual issues should seek specialist consultation under specific circumstances.

Recommendation: Neurologists should refer individuals with neurological diseases with complex sexual dysfunction for specialist care to avoid missing potentially treatable conditions. (Good practice statement; Consensus: 97%).

3.4 | Section 4: Treatment of Sexual Symptoms

Table 4 and Appendix S8 present the evidence supporting recommendations made for the treatment of sexual symptoms, and Figure 3 illustrates the assessment and treatment algorithm of sexual symptoms based on the recommendations.

TABLE 3 | Summary of evidence supporting recommendations for the assessment of sexual symptoms.

Clinical question 26. History taking

History taking should include the following [13, 85–90] (checklist presented in Table 5):

- Sexual dysfunction assessment should include inquiries about primary, secondary, and tertiary contributors to sexual dysfunction [91]
- Consider the importance of an individual's context and psychological framework when assessing sexual function
- Enquire about sexual desire, orgasms, genital sensitivity, and in males erectile dysfunction and ejaculation issues, and in females poor lubrication

Medical history is crucial for identifying the cause of sexual dysfunction, and include onset and duration

- Sexual orientation, gender, relationships, emotional status, past treatments, alcohol/smoking habits, and recreational drug use
- The assessment should include a review of psychological co-morbidities, past sexual trauma and STIs
- Current medications and their impact on sexual functions should be reviewed [92]
- Stroke survivors should have regular inquiries about intimacy and sexual function, with post-stroke counselling at 3, 6, 9, and 12 months
- Several validated questionnaires exist for assessing sexual function in individuals with MS and SCI

Clinical question 27. Targeted physical examination

When appropriate, individuals with neurological disease reporting sexual dysfunction should undergo a targeted physical examination which includes [85, 87, 89, 93, 94]:

- Assessment of vital signs including blood pressure and pulse rate (supine and standing), and weight/height
- Bedside neurological assessment of cognitive, motor, sensory and autonomic functions to evaluate multidimensional contributors that can impact intimacy and sexual performance and management
- Pelvic evaluation includes assessment of sensations in the sacral dermatomes, anal sphincter tone and contractions and reflexes (cremasteric, anal and bulbocavernosus reflex)
- Individuals with suspected urological, gynaecological or endocrinological pathology should be referred for specialist advice

Clinical question 28. Screening laboratory testing

In the appropriate clinical context, individuals with neurological diseases experiencing sexual problems should undergo screening laboratory testing to assess for additional contributing factors. The following should be considered [85, 87, 89, 90, 93, 95–98]:

- Male individuals with neurological disease who report ED should undergo a screening assessment for vascular risk factors (fasting glucose, HbA1c, lipid profile)
- Routine measurement of testosterone in males with neurological diseases and sexual problems is not recommended unless there is suspicion of hypogonadism
- Screening for cervical, ovarian, uterine, breast, prostatic, and testicular cancers may be recommended on an individualised basis
- Screening for STIs, including HIV, when deemed appropriate for the individual patient

Clinical question 29. Diagnostic examinations

Electrodiagnostic tests evaluating the sacral somatic innervation [13, 89, 96]:

- Sensory functions:
  - Pudendal sensory evoked potentials
  - Dorsal penile nerve conductions
- Motor functions:
  - Electromyography of pelvic floor muscles including urethral sphincter, anal sphincter
  - Pudendal motor terminal latency
- Reflex testing:
  - Bulbocavernosus reflex
  - Anal reflex

Electrodiagnostic tests may be helpful in the following situations:

- Unexplained urogenital dysfunction where a neurological cause is suspected (e.g., atypical parkinsonism, unexplained urinary retention in females, genital numbness)
- Further evaluation of abnormal MRI findings such as a thickened filum terminale when the clinical significance is unclear
- History of trauma including individuals with a history of pelvic or perineal trauma where neurological injury is suspected
- Medico-legal considerations involving cases with urogenital symptoms that necessitate evaluating pelvic somatic innervation

(Continues)

TABLE 3 | (Continued)

Clinical question 30. Red-flags for specialist referral
Individuals with any of the following presentations should be referred by their neurologist for specialist assessments [89, 99]: 1. Pain or bleeding during sexual activity 2. Anejaculation 3. Priapism 4. Suspected anatomical changes such as penile curvature or plaque (in male individuals) or pelvic organ prolapse (in female individuals) 5. Suspected endocrinological causes of sexual dysfunction, such as hypogonadism 6. Inadequate response to standard treatments for sexual problems. 7. Male and female individuals seeking treatment for infertility 8. Significant psychological co-morbidities such as depression and anxiety 9. Psychosocial factors including past or current trauma that may impact intimacy or sexual performance

Abbreviations: ED, erectile dysfunction; HIV, human immunodeficiency virus; MS, multiple sclerosis; PE, premature ejaculation; SCI, spinal cord injury; STI, sexually transmitted infection.

Clinical Question 31. Should Education Be Offered to Individuals With Neurological Disease Reporting Sexual Problems vs. Should Not Be Offered?

Healthcare professionals should discuss issues related to sexual function, sexual activity, and sexuality with their patients while respecting professional boundaries and considering the individual's interest [89, 93, 95, 96, 110, 111].

Recommendation: Individuals with neurological diseases having sexual problems should be informed about factors that can impact sexual activity and intimacy. (Good practice statement; Consensus: 94%).

Clinical Question 32. Should Lubricants Be Used for Individuals With Neurological Disease Reporting Sexual Problems vs. no Treatment?

When suggesting the use of lubricants, it is important to consider compatibility with condoms, individual sensitivity, and the presence of possible skin irritants. There are several available products on the market, and there is insufficient evidence to recommend using one product type over another [100, 101].

Recommendation: Vaginal lubricants may be considered for female individuals with neurological diseases who experience dyspareunia or vaginal dryness. The benefits and potential risks/burdens should be discussed. (Consensus-based recommendation; Consensus: 97%).

Clinical Question 33. Should Vibrators Be Used for Individuals With Neurological Disease Reporting Sexual Problems vs. no Treatment?

Evidence on the use of vibrators for individuals with neurological disease is limited, primarily based on expert opinion without randomised controlled trials. Individuals should consult trained healthcare professionals to select suitable vibrators and consider contraindications and risks [102, 103].

Recommendation: The use of vibrators may be discussed with individuals with neurological diseases experiencing sexual problems. The benefits and potential risks/burdens should be discussed. (Good practice statement; Consensus: 85% in Delphi round 2).

Clinical Question 34. Should Vacuum Devices Be Used for Individuals With Neurological Disease Reporting Sexual Dysfunction vs. Placebo or no Treatment?

Individuals should consult healthcare professionals to select and learn to integrate appropriate vacuum devices into sexual relationships according to their preferences. While no guidelines address vacuum device use for female sexual issues, the FDA has approved a device to enhance female sexual function, addressing sensation, lubrication, and orgasmic ability [13, 87].

Recommendations: Vacuum devices may be offered as a second-line treatment to male individuals with neurological diseases who experience ED. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: weak; LoE III; Consensus: 88% for recommendation wording and 88% for recommendation strength).

To make an evidence-based recommendation for female individuals, more research is required. However, the panel agrees that vacuum devices may be discussed with female individuals with neurological diseases having sexual arousal problems. (Consensus-based recommendation; Consensus: 82% in Delphi round 2).

Clinical Question 35. Should Phosphodiesterase-5 (PDE5) Inhibitors Be Used for Individuals With Neurological Disease Reporting Sexual Problems vs. Placebo or no Treatment?

Evidence supporting PDE5 inhibitors stems from two high-quality guidelines and five randomized controlled trials across various neurological conditions, including SCI, MS, and PD. Given their potential side effects, PDE5 inhibitors should be prescribed by and discussed with a qualified healthcare professional [13, 85].

Recommendation: PDE5 inhibitors should be offered as a first-line treatment to male individuals with neurological diseases who experience ED. The benefits and potential risks/burdens

TABLE 4 | Summary of evidence supporting recommendations for the treatment of sexual symptoms.

Clinical question 31. Education

Clinicians should inform individuals with neurological diseases experiencing sexual problems about the factors that can influence sexual activity and intimacy. Clinicians should [87–89, 93, 96]:

- Discuss the impact of sexuality and fertility on individuals' lives
- Explore how the underlying neurological condition affects relationships
- Review the effects of medications used for treating neurological symptoms on sexual functions
- Address the effects of alcohol, tobacco and recreational drugs on sexual response and fertility
- Highlight the influence of unhealthy eating habits and obesity on sexual function and fertility
- Emphasise lifestyle modifications, such as diet optimization and increased physical activity targeting weight loss, which may improve sexual function in men with ED
- Consider the use of educational media when appropriate
- Tailor education to meet individuals' needs, life contexts, feelings, and previous sexual experiences
- Involve partners in discussions about sexual dysfunction when relevant and appropriate
- Maintain professional boundaries during discussions and ensure any used educational media complies with legal standards and is suitable for the person

Clinical question 32. Lubricants

Consider vaginal lubricants for females with neurological diseases experiencing dyspareunia or dryness, and discuss benefits and risks [100, 101]:

- Assess lubricant compatibility with condoms, sensitivity, and potential irritants
- Consider local oestrogen therapy for these symptoms when appropriate
- Note insufficient evidence for recommending specific products, but consider:
  - Water-based lubricants may dry quickly, causing discomfort
  - Oil-based lubricants are incompatible with condoms
  - Silicone-based lubricants are condom compatible and don't cause dryness
- Inform individuals with spina bifida about the higher risk of latex allergy
- Possible adverse effects include skin irritation, dermatitis

Clinical question 33. Vibrators

Discuss vibrator use with individuals having neurological diseases and sexual problems, weighing benefits and risks [87, 100, 102, 103]:

- Vibrators may enhance arousal and erectile function in individuals with SCI
- Consult healthcare professionals (nurse practitioners, physiotherapists, sex therapists, andrologists, gynaecologists, or midwives) for appropriate selection and usage guidance
- Note limited studies suggest potential negative impacts on partner-related sexual function
- Be aware of contraindications like autonomic dysreflexia in T6 or above SCI and risk of skin breakdown from friction

Clinical question 34. Vacuum devices

Vacuum devices are a second-line treatment for ED in men with neurological diseases; benefits and risks should be discussed [13, 87, 89, 95]

- Efficacy for satisfactory erections is high, up to 90%, with satisfaction rates between 27% and 94%
- Devices are cost-effective but require manual dexterity
- For female sexual arousal disorder, significant symptom improvement with vacuum devices was noted, with no adverse events [104].
- SCI individuals need a recumbent position for effective use.
- Individuals should be advised never to leave the constriction ring on for over 30 min
- Partner assistance may be needed, especially in tetraplegia
- Most adverse events are minor, including penile petechiae, discomfort, and difficulty with ejaculation
- Common complaints: unnatural erections, coldness, pain, lack of spontaneity
- Caution is advised for men on anti-coagulants, bleeding disorders, or priapism history

(Continues)

TABLE 4 | (Continued)

Clinical question 35. PDE5 Inhibitors

PDE5 inhibitors are recommended as a first-line treatment for ED in males with neurological diseases, emphasising the need to discuss benefits and potential risks [13, 85, 95, 105]

- Oral sildenafil is effective and well-tolerated for ED in individuals with SCI
- In individuals with MS, sildenafil and tadalafil showed significant improvement in ED in two studies, though another reported no benefit
- Individuals with PD experienced improved erectile function and significant IIEF-15 score enhancement with sildenafil 100 mg compared to placebo
- Effective PDE5 inhibitor therapy requires some residual nerve function to induce erection
- Side effects include headaches, flushing, nasal congestion, dizziness, and rarely vascular insufficiency and priapism
- PDE5 inhibitors might cause orthostatic intolerance or hypotension, especially in individuals with tetraplegia/high-level paraplegia, neurodegenerative diseases, (autonomic) neuropathies, or neurovascular diseases
- PDE5 inhibitors are contraindicated in individuals taking nitrates including glyceryl trinitrate, isosorbide mononitrate and isosorbide dinitrate
- Caution is advised when PDE5 inhibitors are coadministered with α_1-adrenoceptor blockers
- Contraindications include hereditary degenerative retinal disorders, history of non-arteritic anterior ischaemic optic neuropathy, recent history of myocardial infarction or stroke, systolic blood pressure < 90 mmHg, individuals in whom sexual activity is inadvisable

Clinical question 36. Intracavernous prostaglandin injections

Intracavernous injections of prostaglandin are recommended as a second-line treatment for ED in males with neurological diseases, with a discussion on benefits and risks being essential [13, 85, 87, 89]:

- A meta-analysis showed a 90% satisfactory erection response rate with prostaglandin injections in individuals with SCI
- Prostaglandin injections have proven efficacy for achieving satisfactory erectile rigidity and duration in individuals with SCI and MS through home administration
- Intraurethral application of alprostadil presents a less invasive, albeit less effective, alternative for those seeking other treatments
- Quality of erection with intraurethral prostaglandin is reported to be less rigid compared to intracavernous injections, highlighting a difference in effectiveness
- Side effects of intracavernous prostaglandin injections include injection site pain and penile scarring, the latter often detectable only via ultrasound after repeated use [13, 87]. Some studies have shown a 40% discontinuation rate
- The risk of priapism following intracavernous prostaglandin injections is considered low, under 1%, according to guidelines for individuals without neurological disease
- Contraindicated if sexual activity is inadvisable

Clinical question 37. Multidimensional Factors

Address multidimensional factors affecting sexual activity and intimacy in individuals with neurological diseases, including secondary factors (spasticity, fatigue, incontinence, cognitive co-morbidities, medication side effects) and tertiary factors (changes in self or body image), through regular discussions due to their dynamic nature [85, 87, 91, 106]

- Inform individuals with spasticity that its level may change during sexual intercourse, potentially impacting sexual activity
- Offer baclofen, tizanidine, or botulinum toxin to reduce limb spasticity in individuals with stroke, SCI, and MS, facilitating sexual movements
- Advise individuals with SCI about the possibility of bowel or bladder incontinence during sexual intercourse, which may cause anxiety and deter sexual relations. Recommend bladder and/or bowel care prior to sexual activity and establish a contingency plan in case incontinence were to occur
- Assess individuals with neurological disorders for depression or other psychological disorders that could affect libido. Treat co-morbid depression with psychological and medication interventions to potentially improve sexual desire. If depression is treated or ruled out, provide suggestions for managing stress and fatigue
- Promote a positive body image, as sexual function can be adversely affected by poor self-perception post-SCI. Encourage counselling and open discussions about body image, ensuring comfort with personal and medical equipment
- Several medications used in neurology practice may cause sexual dysfunction, necessitating a review and possible adjustment of medication [92]

Abbreviations: ED, erectile dysfunction; IIEF, International Index of Erectile Function; MS, Multiple sclerosis; PDE-5, phosphodiesterase-5; SCI, spinal cord injury.

should be discussed. (Evidence-based recommendation; Strength: strong; LoE II; Consensus: 100% for recommendation wording, 97% for recommendation strength).

Clinical Question 36. Should Prostaglandins Be Used for Individuals With Neurological Disease Reporting Sexual Problems vs. Placebo or no Treatment?

TABLE 5 | Urogenital symptoms checklist.

Bladder functions

☐ Urinary symptoms

Storage symptoms	**Voiding symptoms**
Daytime urinary frequency	Hesitancy
Nocturia/nocturnal polyuria	Inability to void
Urgency	Straining to void
Sensations of bladder filling • Normal, increased or reduced	Slow stream
Incontinence • Urgency • Stress • Enuresis • Insensible • Continuous • Disability-associated (impaired cognition and/or mobility) • Sexual activity related	Intermittency **Post-micturition symptoms** Feeling of incomplete emptying Double voiding Post-micturition dribble

☐ Symptom frequency and severity

☐ Variation between night-time and daytime symptoms

☐ Precipitating or relieving factors

☐ Prior treatments and their success

☐ Strategies used by the patients to improve their symptoms

☐ Pad and catheter use

☐ Recent UTIs, painful urination, haematuria

☐ The impact of the symptoms on quality of life and social function

☐ Bowel symptoms, incontinence, constipation, urgency

☐ Patient and caregiver expectations

Sexual functions

☐ Sexual symptoms

- ☐ Altered libido
- ☐ Arousal (Males: erectile dysfunction; Females: lubrication)
- ☐ Ejaculation (Males): anejaculation, delayed ejaculation, premature ejaculation
- ☐ Dyspareunia or discomfort
- ☐ Anorgasmia
- ☐ Patient and partner expectations
- ☐ Multidimensional contributors

Multidimensional contributors to sexual dysfunction [91]

	Definition	**Symptoms**
Primary	Result of neurologic changes that directly affect sexual feelings and/or sexual response	Impaired genital sensation, decreased libido, Males: inability to achieve or maintain an erection; Females: genital numbness, pain, burning, decreased vaginal lubrication

(Continues)

TABLE 5 | (Continued)

Secondary	Related physical changes that affect the sexual response indirectly	Fatigue, muscle tightness, weakness, spasms, bladder and bowel dysfunction, incoordination, cognitive difficulties, numbness, pain in non-genital areas, side effects from medications
Tertiary	Psychological, emotional, social, and cultural aspects that impact sexuality	Negative changes in self-image, body image, feeling less confident about one's sexuality, worries about sexually satisfying one's partner, difficulty communicating with one's partner

Intracavernous prostaglandin injections can be a treatment especially when oral PDE5 inhibitors fail or are not advisable due to severe cardiovascular conditions (like unstable angina, recent stroke or heart attack, or significant liver impairment), following high-quality guidelines for individuals with neurological disease [13]. This treatment should be offered by a trained professional [13, 85, 87, 89, 93, 95, 112].

Recommendation: Intracavernous injections of prostaglandin should be offered as a second-line treatment to male individuals with neurological diseases who experience ED. The benefits and potential risks/burdens should be discussed. (Evidence-based recommendation; Strength: weak; LoE: III; Consensus: 91% for recommendation wording, 82% for recommendation strength).

Clinical question 37. Should treatment of secondary causes (e.g., spasticity/fatigue/incontinence/pain/depression) and tertiary causes (e.g., loss of self-esteem/poor body image) be offered to individuals with neurological disease reporting sexual problems vs no treatment?

Secondary and tertiary factors contributing to sexual dysfunction (listed in Table 5) should be addressed and managed [85, 87].

Recommendation: Multidimensional factors interfering with sexual activity and intimacy (including secondary factors such as spasticity, fatigue, incontinence, cognitive co-morbidities, medication side effects and tertiary factors such as changes in self or body image) should be addressed in individuals with neurological disorders experiencing sexual problems. Given their dynamic nature, these factors should be discussed on a regular basis. (Good practice statement; Consensus: 100%).

4 | Discussion

Several high-quality guidelines on the assessment and management of neurogenic urinary and sexual dysfunction have already been published. However, these guidelines have not been specifically tailored toward neurologists, making it challenging to integrate many of the recommendations into neurology practice. The development of NEUROGED guidelines uniquely involved neurologists, urologists, and patient representatives from the onset. This collaborative effort aimed to ensure that the recommendations would be relevant and practical for neurological practice, addressing the specific needs and challenges faced by neurologists in managing neurogenic urogenital dysfunction.

Anticipating low levels of evidence for several of the PICO-structured clinical questions, the steering committee received methodological advice to develop recommendations using existing guidelines and adopted the ADAPTE framework.

Guidelines of the highest quality, as determined by the AGREE II tool, were given preference. However, lower quality guidelines were also reviewed for PICOs where there were few or no existing recommendations. This approach allowed the committee to address questions that were clinically relevant to individuals with neurological disorders where there were low levels of evidence. Consequently, there were only 11 evidence-based recommendations, and just 6 received a strong strength of recommendation. There is a need for further research to address gaps in the evidence, particularly the PICOs that received consensus-based recommendations.

The recommendations were developed collaboratively between neurologists and urologists across a wide spectrum of healthcare settings and were prepared with an international audience of practising neurologists in mind. The guidelines empower neurologists to assess and manage urinary and sexual symptoms reported by their neurological patients; however, they importantly define limits to practise through red flag symptoms and test findings that would warrant a sharing of care with their urology colleagues. A limitation of adapting the guideline using the ADAPTE framework was that the primary evidence base was reviewed only for PICOs where recommendations were not available in existing guidelines and had to be developed de novo. Despite the focus on developing practical recommendations, challenges in their implementation will be expected due to limited expertise and time and resource constraints, and this will be addressed separately. The task force intends for the NEUROGED guidelines to also serve as a framework for training neurologists in the assessment and treatment of urogenital symptoms.

In conclusion, guidelines for the assessment and management of urogenital symptoms specifically intended for practising neurologists have been prepared for the first time. They have been approved on 6th December 2024 and will be formally updated after 5 years in 2029.

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Acknowledgements

The authors would like to acknowledge the contributions of Ms. Toni Tan for methodological support and Ms. Helena Markulin for conducting the literature search. J.N.P. is supported in part by funding from the United Kingdom's Department of Health NIHR University College London Hospitals Biomedical Research Centres funding scheme. K.P.S.N. is partly supported by the National Institute for Health and Care Research (NIHR) Sheffield Biomedical Research Centre (BRC) and NIHR Sheffield Clinical Research Facility (CRF). G.P. is supported by the National Institute for Health and Care Research (NIHR) Applied Research Collaboration East of England (NIHR ARC EoE) at Cambridgeshire and Peterborough NHS Foundation Trust. The views expressed are those of the author[s] and not necessarily those of the NIHR or the Department of Health and Social Care. M.H. acknowledges support from the Croatian Science Foundation. The project was funded by the EAN, EFAS, and INUS, and task force members received no remuneration for their work. The NEUROGED guidelines have been endorsed by the European Research Network for Rare Neurological Disorders. The American Academy of Neurology affirms the value of the EAN/EFAS/INUS guidelines for practising neurologists on the assessment and treatment of neurogenic urinary and sexual symptoms (NEUROGED guidelines) as an educational tool for neurologists.

Conflicts of Interest

J.N.P.: Consultant (Idorsia, Coloplast, Medice), Speaker Honorarium (Coloplast, Wellspect), Royalties (Cambridge University Press).

A.F.: Royalties from Springer Verlag, speaker fees, and honoraria from Theravance Biopharma, GE Health Care, Bial, CNSystems, Broadview Ventures, KABEG, Austrian Autonomic Society, Elsevier, International Parkinson Disease and Movement Disorders Society, Austrian Neurology Society, Austrian Autonomic Society, and research grants from the FWF-Austrian Science Fund, Medical University of Innsbruck, US MSA Coalition, Dr. Johannes and Hertha Tuba Foundation, and Austrian Exchange Program, outside of the present work. M.K.S.: Participated as a clinical investigator and/or received speaker fees fromSanofi Genzyme, Merck, Novartis, and Roche. I.A.: Participated as a clinical investigator and/or received consultation and/or speaker fees from Biogen, Sanofi Genzyme, Merck, Novartis, Roche, and AstraZeneca. M.A.A.: Consultant (Coloplast), speaker honorarium (Medtronic, Coloplast, GSK, Boston Scientific). J.M.P.: Speaker Honorarium (Asofarma, Convatec). A.B.: Has received a speaker honorarium from Ipsen Pharma and receives royalties from the book "Understanding Parkinsonism" (Jaypee brothers 2017). B.B.: Consultant (Coloplast), Speaker Honorarium (Coloplast), Research Grant (Axonics). C.H.: Consultant: Convatec, BBraun. Speaker: IPSEN, Abbvie, Hollister Inc., Convatec. K.P.S.N.: Has led clinical trials on spasticity in M.S. for Celgene and GWS pharma and received royalties from Cambridge University Press. M.S.: Honoraria from Abbvie. R.D.T.: Lecture and consultancy fees from Medtronic, UCB, Theravarance, LivAssured, Zogenix, Novartis, and Arvelle, and grants from Medtronic and NewLife Wearables. M.T.: Works as a DBS (deep brain stimulation) consultant for Medtronic. M.H.: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Novartis, Roche, Astra Zeneca, and received funding from the Croatian Science Foundation. T.K., K.A., P.G., N.C., F.L., S.S., I.S., S.W., M.J.H., T.M.K., H.M., K.R.N., A.P.L.T., M.P., G.P., M.P., R.S., U.S., W.S., K.I.T., D.B.V., and G.W.: None declared.

Data Availability Statement

The data that supports the findings of this study are available in the Supporting Information of this article.

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Co-funded by the European Union