Neurogenic gastrointestinal, urinary, and sexual dysfunction in multiple sclerosis: a multidisciplinary framework for clinical practice

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Summary

Neurogenic gastrointestinal, urinary, and sexual symptoms are highly prevalent in people with multiple sclerosis and substantially impair quality of life, daily functioning, and psychosocial well-being. Despite their frequency and clinical relevance, management remains fragmented across specialties, the close interrelationship among these symptoms is often overlooked, and clinicians lack a pragmatic framework adaptable to different healthcare settings. This review translates current evidence into a pragmatic model of care tailored to the realities of European clinical practice and heterogeneous healthcare resources, helping neurologists and multidisciplinary teams identify needs, prioritize interventions, and optimize management. Because these disturbances are multifactorial and closely interconnected, assessment requires a structured, proactive approach integrating symptom screening, contributing factors, and individual patient needs. Early recognition and individualized multidisciplinary treatment are essential to prevent complications and reduce symptom burden. By promoting structured assessment, rehabilitation, patient education, and coordinated care, this framework may reduce variability in management and improve patient-centered outcomes across diverse healthcare settings.

Keywords: Multiple sclerosis; Gastrointestinal dysfunction; Urinary dysfunction; Sexual dysfunction; Pelvic floor rehabilitation; Multidisciplinary care

Introduction

Neurogenic gastrointestinal (GI), urinary and sexual symptoms are among the most common symptoms in multiple sclerosis (MS)[1] and, though significantly decreasing the quality of life of people with MS (pwMS), they are often under-recognized and not appropriately managed. These symptoms are highly interrelated and interdependent and, when left untreated, one symptom can precipitate or exacerbate others. Conversely, effective treatment of one symptom can break this cycle and have a significant beneficial impact on the others.[2] For example, bladder problems can affect sleep and sexual function which in turn have effects on cognition and mood, thus leading to fatigue and hypoactivity with secondary consequences of increased spasticity and constipation. Since limited time during visits is often a barrier, screening and scheduling additional dedicated appointments may be beneficial.

In this review, we aim to translate the available evidence on neurogenic GI, urinary, and sexual symptoms in MS into a pragmatic model of care tailored to the realities of European clinical practice and heterogeneity of healthcare resources, helping neurologists and multidisciplinary teams identify needs, prioritize interventions, and optimize MS care.

Neurogenic gastrointestinal symptoms

Neurogenic GI dysfunction in MS primarily manifests as an impairment of motor rather than sensory or secretory function and more commonly affects the lower GI tract (GIT).[3] The GIT has both an extrinsic (parasympathetic and sympathetic innervation) and intrinsic neural control (by the enteric nervous system, including the myenteric and submucosal plexuses). Vagus nerve and sacral parasympathetic nerves provide excitatory innervation to non-sphincteric GIT muscles, while sympathetic nerves (levels T5-T10) inhibit

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Key points

- Neurogenic gastrointestinal (GI), urinary, and sexual symptoms are highly prevalent in people with multiple sclerosis (pwMS) and can substantially impair quality of life. Since limited time during clinical visits is often a barrier, screening for these symptoms with dedicated questionnaires and scheduling additional dedicated appointments may be beneficial.
- Constipation is the most prevalent GI symptom in MS, followed by fecal incontinence, delayed gastric emptying, delayed colonic transit and accelerated gastric emptying.
- Pharmacological therapies for constipation include laxatives and prokinetics (in patients with slow colonic transit). Transanal irrigation is the treatment of choice for fecal incontinence. Biofeedback therapy is indicated in patients with dyssynergic defecation or fecal incontinence.
- Lower urinary tract symptoms in MS can be due to storage or voiding phase dysfunction. Detrusor overactivity is the most common alteration in pwMS, followed by detrusor-sphincter dyssynergia and less frequently detrusor underactivity.
- Pharmacological therapies for storage symptoms include antimuscarinics and beta3-agonists. Clean intermittent catheterization is indicated in case of high post-void residual. Neuromodulatory options include sacral nerve modulation and percutaneous tibial nerve modulation. Pelvic floor muscle training is indicated for the prevention and treatment of all types of urinary incontinence, with preliminary data on sexual dysfunction.
- Erectile dysfunction (ED) and premature ejaculation (PE) are common sexual complaints in male pwMS, while female pwMS frequently experience decreased vaginal lubrication and difficulties in reaching orgasm.
- Therapeutic strategies for ED include phosphodiesterase-5 inhibitors, vacuum-constriction devices and intracavernous injection of alprostadil. Dapoxetine is the only licensed drug for PE. For women with dyspareunia and/or vaginal dryness, anesthetic and water-soluble lubricants can be used. In case of postmenopausal vaginal atrophy, topical estrogen therapy is indicated. Vibrators can be useful when decreased genital sensation limits intimacy.
- By integrating diagnostic, therapeutic, and rehabilitative strategies across these closely interconnected domains, we propose a framework intended to support neurologists and multidisciplinary teams in identifying patients' needs, prioritizing interventions, reducing variability in care and support MS centers in delivering more comprehensive and patient-centered management.

non-sphincteric muscles and excite sphincters muscles (Fig. 1A). Though recent studies show that intrinsic myenteric neurons can be affected by the disease,[4] damage to the extrinsic neural control of the GIT prevails in MS and explains patients' symptoms. In particular, spinal cord lesions can result in interruption of supraspinal control of the sacral parasympathetic supply[5] while brainstem demyelinating lesions, via disruption of gastric vagal motor circuits, can affect gastric emptying.[6]

Constipation is the most prevalent GI symptom in MS. A recent retrospective cohort analysis of a tertiary MS center studied GI motor function identifying constipation in 82% of MS patients, fecal incontinence (FI) in 33%, delayed gastric emptying in 16%, delayed colonic transit in 7% and a previously unappreciated high prevalence of accelerated gastric emptying in 22% of patients.[7] The study demonstrated that GI symptoms were more prevalent across all domains than in the general population[8] and highlighted that constipation and FI are more prevalent in MS subjects of old age, with spinal cord lesions and a progressive phenotype.[7]

According to the Rome V criteria, chronic constipation is defined by an evacuation frequency of less than 3 times per week, associated with hard feces, strain, feeling of incomplete emptying/obstruction or need for manual maneuvers.[9] Constipation can be a feature of other *disorders of gut-brain interaction*, particularly irritable bowel syndrome with constipation (IBS–C) and opioid-induced constipation.[10] While some abdominal pain can be present in patients with chronic constipation, pain should not be the predominant symptom as in IBS. Moreover, patients with constipation may also display anorectal disorders: FI, anorectal pain, dyssynergic defecation (DD) and rectal hypo- or hyper-sensitivity.[11] While FI only requires the presence of symptoms, a diagnosis of DD or altered rectal sensitivity requires both clinical and physiological testing data. DD is characterized by inadequate propulsive force or paradoxical contraction/inadequate relaxation of the pelvic floor muscles (PFM) during defecation. Only one abnormal physiological testing result is needed for the diagnosis of DD.[11]

The initial workup of MS patients with constipation (Fig. 2) begins with history taking to aid in the identification of secondary causes and establishing the presence of red flags that can point to an underlying neoplasia. Digital rectal examination (DRE) has a sensitivity and specificity in detecting anal-sphincter dyssynergia of around 80%.[12] DRE is performed in the Sims position (left lateral recumbency). It begins with visual inspection to identify structural pathology (e.g., hemorrhoids, anal fissures). Inspection is also performed with straining, evaluating for rectal prolapse. During inspection it is possible to detect paradoxical contraction of the sphincter during straining rather than its normal relaxation. The examiner can appreciate if increased tone of the sphincter is present at rest. The

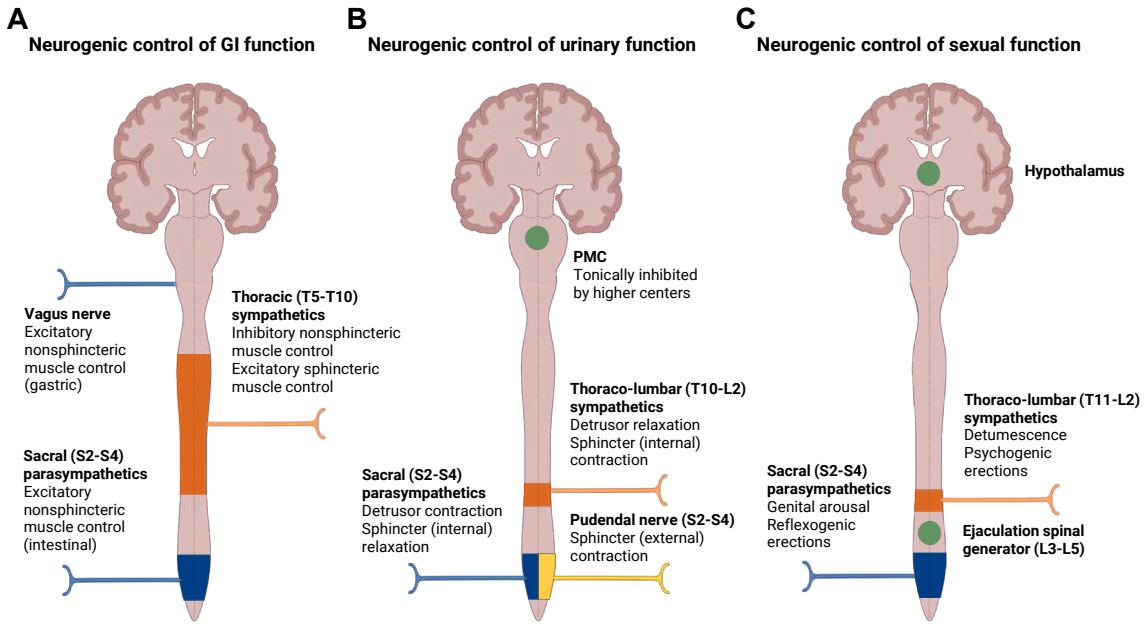


***Fig. 1:* Pathophysiological mechanisms of neurogenic gastrointestinal, urinary and sexual dysfunction in multiple sclerosis.** Schematic overview of the pathophysiological mechanisms underlying neurogenic gastrointestinal, urinary, and sexual symptoms in people with multiple sclerosis. (A) Gastrointestinal dysfunction. (B) Urinary dysfunction. (C) Sexual dysfunction. Across these domains, demyelinating lesions affecting supraspinal, spinal, and peripheral autonomic and somatic pathways may disrupt the coordinated control of visceral and pelvic organ function, leading to impaired sensory processing, abnormal reflex activity, and defective efferent output. The figure summarizes the main neuroanatomical substrates and mechanisms thought to contribute to symptom development in multiple sclerosis. Figure created in BioRender. Abbreviations: PMC = pontine micturition center.

examiner asks the patient to voluntarily contract the sphincter evaluating for its appropriate increase in tone. Then the examiner asks the patient to perform a straining maneuver with the finger still in place. Normal response is an expulsion of the finger towards the outside. If the finger remains in the same position the exam is indicative of PFM weakness. If the finger is constrained, the exam points to paradoxical contraction of the sphincter (DD). If DRE is positive for DD the next diagnostic step is anorectal manometry[13] which evaluates rectal pressure/sensitivity and anal contraction. The physiological response during defecation is an increase in rectal pressure and consensual relaxation of the anal sphincter. Four high-resolution rectal manometry patterns can be distinguished in DD:

Type 1: appropriate increase in rectal pressure but paradoxical contraction of the sphincter; Type 2: no increase in rectal pressure and paradoxical contraction of the sphincter; Type 3: rectal pressure is increased, but the sphincter is not adequately relaxed; Type 4: no increase in rectal pressure and no relaxation of the sphincter. If high-resolution rectal manometry is not available, standard rectal manometry combined with the balloon expulsion test (BET) can identify patients with DD or altered rectal sensitivity.[14] When rectal manometry and BET show equivocal results or discordant findings, defecography can be useful.

If constipation is mild, conservative treatment can be started. Caloric and liquid intake should be adequate. Only soluble fibers have a significant effect on constipation (e.g., psyllium 5–15 g/day).[15] A small chair can be used to elevate feet from the ground during evacuation and the physiological gastrocolic reflex can be exploited trying to evacuate after meals. Patients with spinal cord lesions who lose sacral parasympathetic control of defecation with constipation and FI are dependent on the reflex rectal stimulation for defecation (abdominal massage and perianal manual stimulation). In cases resistant to conservative treatment, if fecal impaction has been excluded or resolved, pharmacological therapy is indicated. Evidence from multiple randomized controlled trials (RCTs) lasting up to 6 months supports the use of osmotic laxatives as the preferred first-line pharmacological therapy.[16] Macrogol is preferred over lactulose due to less frequent blowing.[17] If after some days of laxative therapy no effect is seen, it is possible to perform a water-enema. In patients with concomitant abdominal pain or IBS-C, pain relief can be obtained using anti-spasmodics like peppermint oil.[18] Patients with constipation can have normal or slow colonic transit (ST-C).

At least half of DD patients can have ST-C, which benefits from prokinetic therapy.[19] In a real-world setting, given the limited availability and cost of

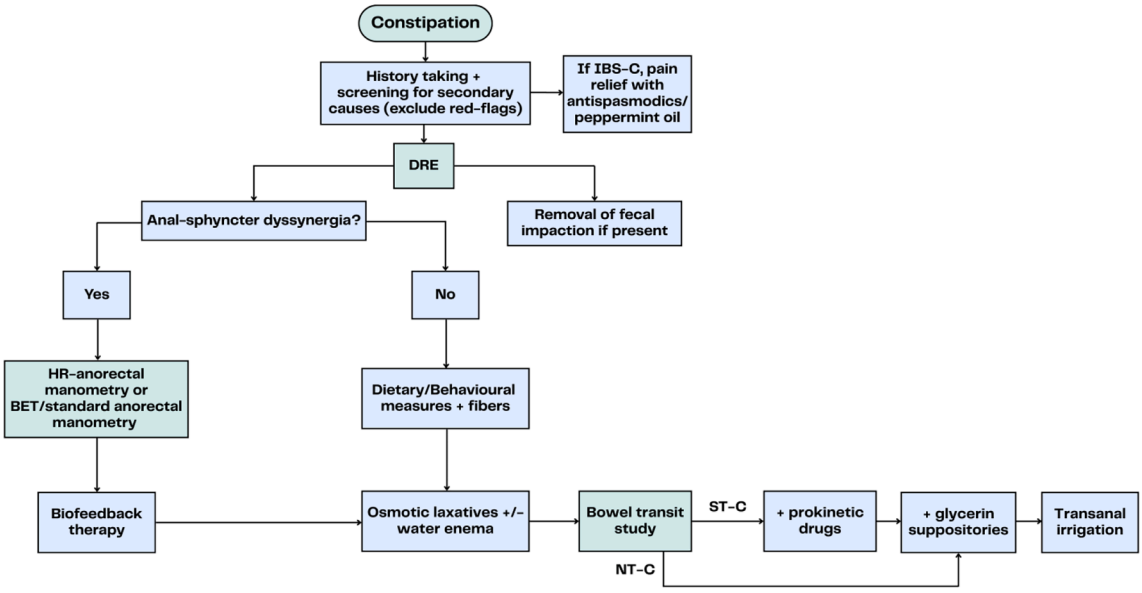


***Fig. 2:* Flowchart of the diagnostic work-up and therapeutic management of constipation in people with multiple sclerosis.** The figure summarizes a stepwise approach from clinical assessment to tailored treatment selection and escalation in refractory cases. Abbreviations: BET = balloon expulsion test; DRE = digital rectal examination; HR = high-resolution; IBS-C = constipation associated with Irritable Bowel Syndrome; NT-C = normal transit constipation; ST-C = slow transit constipation.

colonic transit testing, an empirical trial of a prokinetic agent may be considered in patients with suspected ST-C. Two clinical parameters can help predict ST-C based on history alone: evacuation frequency $\leq$2 per week and Bristol Stool Chart (a validated stool form scale ranging from type 1 [separate hard lumps] to type 7 [liquid stools]) score of 1–2.[20] Prucalopride (2 mg/day), a highly selective agonist of the 5-HT4 receptor, has demonstrated efficacy in ST-C in phase III RCTs.[21] No benefits have emerged with increased dosage. In older patients or in patients with kidney damage or severe hepatic failure, the dose of 1 mg daily is preferred. Patients should be reassessed for drug efficacy after 4 weeks of therapy. Data on intestinal secretagogues for constipation secondary to neurological disorders are limited (options include linaclotide, lubiprostone and plecanatide). Glycerine suppositories are an add-on option in patients with DD who cannot benefit from biofeedback therapy (BT) or do not benefit from laxatives and prokinetic therapy. As a last resort, transanal irrigation (TAI) can be used. TAI is also the treatment of choice for FI.[22] In ST-C patients without evidence of DD (or DD corrected with BT) it is possible to evaluate for surgery or sacral nerve modulation (SNM).[23] In case of rigidity and spasms of the ano-pelvic complex, oral anti-spastic therapy should be considered.

BT is indicated in patients with DD or FI, based on evidence from multiple RCTs.[24] If rectal hyposensitivity is present, concurrent sensory training (e.g., barostat-assisted sensory training) is needed.[25] In pwMS, cognitive dysfunction and global motor disability can impact BT efficacy and compliance. No universal BT protocol exists establishing a needed number of sessions. Home- and office-based BT have comparable success rates.[26] We routinely perform BET at baseline and encourage patients to continue training with BET independently at home after adequate training.

Neurogenic urinary symptoms

Lower urinary tract symptoms (LUTS) occur in up to 97% of MS patients over the course of the disease, with a median onset of 8 years after diagnosis, and represent the first manifestation of MS in up to 10% of cases.[27] Compared with the general population, LUTS in pwMS are more frequent, occur at a younger age and are generally more severe.[28] LUTS can be related to storage phase dysfunction (frequency of micturition, nocturia, urgency, urge incontinence) or voiding phase dysfunction (hesitancy, straining, slow/interrupted flow, urinary retention).[29]

During bladder filling, sympathetic innervation inhibits the detrusor while sympathetic and pudendal (somatic motor) nerves mediate contraction of the internal (smooth muscle) and external (striated muscle) urethral sphincter respectively (Fig. 1B). When voiding is deemed appropriate, the pontine micturition center loses the tonic inhibition of higher brain centers and the pattern of detrusor inhibition and sphincter contraction reverses. Detrusor contraction is associated with parasympathetic stimulation and is necessary for complete bladder emptying.[30] Lesions at the suprapontine level

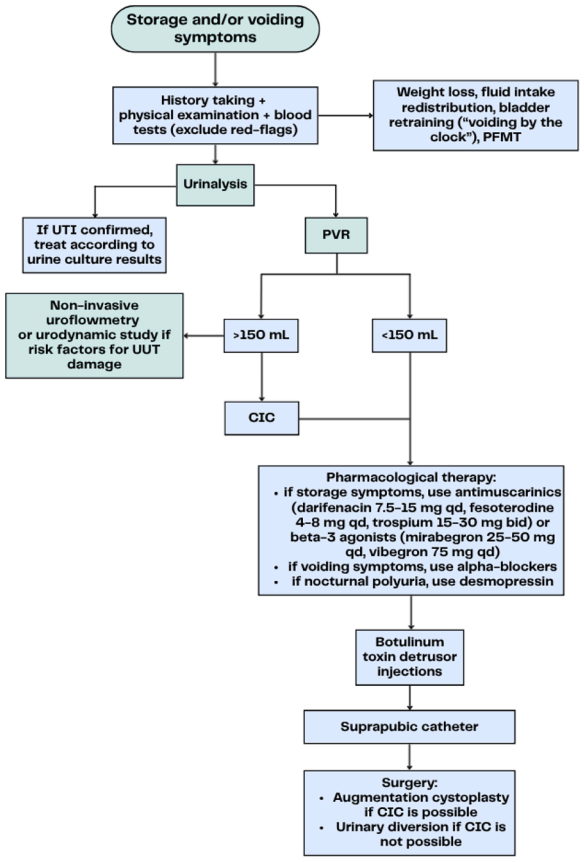
predominantly cause storage symptoms (detrusor overactivity [DO]), infrapontine suprasacral lesions can cause both storage (DO) and voiding (detrusor-sphincter dyssynergia [DSD]) symptoms, while sacral/infrasacral lesions cause predominantly voiding disturbances (detrusor underactivity [DU]).[31] DO is the most common alteration in pwMS, followed by DSD and less frequently DU. DO is characterized by more frequent but normal strength detrusor contractions, thus patients with suprapontine lesions usually have low post-void residuals (PVR). However, if DSD or DU coexist with DO, as frequently seen in MS, PVR can be high. DSD is defined as the involuntary contraction of the external urethral sphincter concurrent with detrusor contraction during voiding, resulting in incomplete bladder emptying. DU is defined as reduced strength or duration of detrusor contractions resulting in prolonged and incomplete bladder emptying and usually appears only later in the course of disease. Patients with high PVR can develop complications, which include raised intravesical pressure, leading to bladder diverticuli and trabeculations, and vesicoureteral reflux (VUR) leading to hydronephrosis, recurrent urinary tract infections (UTIs) and renal damage.[32]

Assessment (Fig. 3) begins with recording of patients' symptoms, revision of bladder diary (Appendix A—Fig. 1) and physical examination which includes the evaluation of structural abnormalities (e.g., prostate enlargement, pelvic organ prolapses) as well as genital reflexes and perineal sensitivity. In patients with urinary incontinence (UI) and high disability or progressive disease, functional incontinence (whereby a patient cannot reach the toilet in a timely manner) should be excluded. Blood chemistry including renal function testing, urinalysis and PVR measurements are routinely performed. Based on urinalysis results, if UTI is suspected, urine culture is necessary and guides antibiotic treatment. UTIs can exacerbate irritative LUTS, thus antibiotic treatment is recommended in symptomatic patients. Asymptomatic bacteriuria is not routinely treated. Recurrent UTIs should prompt evaluation of urological causes like bladder stones and VUR. Low dose antibiotic prophylaxis is considered in individuals with recurrent UTIs and no identifiable causes. PVR can be measured non-invasively with ultrasound devices.[33] If PVR is >150 mL, clean intermittent catheterization (CIC) with hydrophilic catheters is the management strategy of choice.[34] Proper training of the patient is important in avoiding complications and improving compliance. In female patients, a mirror can be used to aid in the identification of the urethral meatus. If manual dexterity and cognition are barriers to self-CIC, a caregiver should be trained together with the patient to help with CIC. CIC average frequency is 4–6 per day and can be adapted based on PVR (bladder volume at catheterization should not be greater than 400–500 mL). If PVR is low, or in cases where CIC does not lead to sufficient benefit, symptomatic management can be started. The need for invasive urodynamic testing before treatment initiation in MS is debated. A recent RCT showed that performing a whole urodynamic study does not influence treatment choice or outcomes.[35] Thus, in early MS, non-invasive evaluation is probably sufficient to start therapy, reserving invasive studies only for patients refractory to first line treatment or with risk factors for upper urinary tract damage (UUTD). The incidence of UUTD is low in patients with MS. In a recent study[36] assessing 325 MS patients undergoing voiding cystourethrography (VCUG), only 5.5% had VUR and only 3.1% showed hydronephrosis. Among MS patients with VUR, 19% had grade III–IV VUR. Hydronephrosis was observed in all grade III–IV VUR, whereas it was absent in patients with grade I–II VUR. PMS patients were more likely to have VUR compared to RRMS (11.5% vs. 4.1%, $p = 0.04$) and patients with VUR showed a mean glomerular filtration rate decrease of 29% with no evidence of significant renal failure. Thus, patients with risk factors for UUTD should undergo VCUG to assess the presence and entity of VUR.[36]

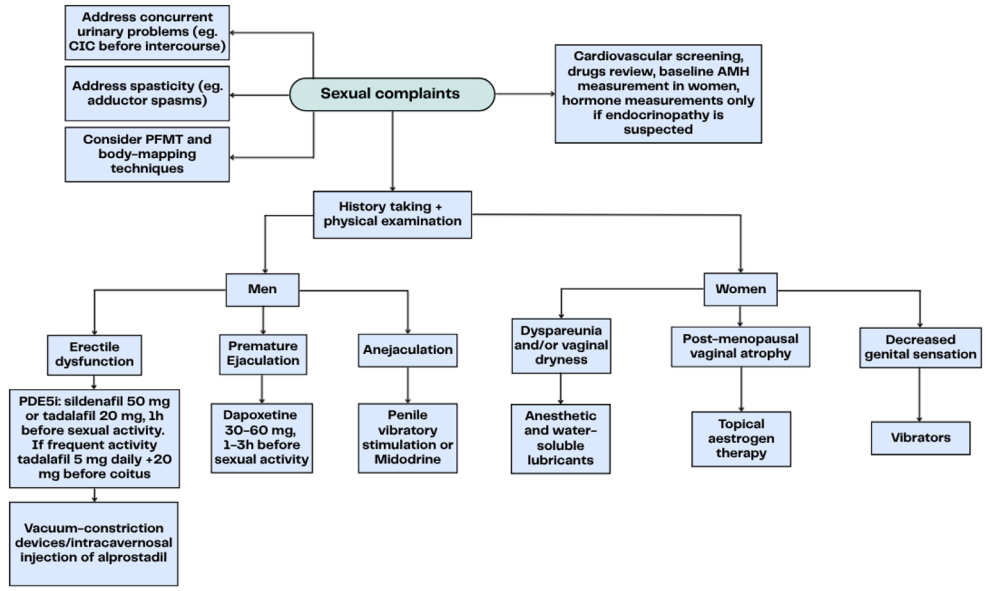
Conservative strategies should be used in all patients and include weight loss, bladder retraining ("voiding by the clock", setting a voiding routine with increasing intervals between voidings),[37] fluid intake review (equally distributing fluids throughout the day) and PFM training (PFMT). In patients with voiding dysfunction, reflex voiding can be triggered by suprapubic tapping or thigh scratching via stimulation of sacral and lumbar dermatomes. Valsalva and Credè maneuvers are not recommended (risk of rising intravesical pressure). A RCT showed limited efficacy of suprapubic vibration devices (no significant reduction in the frequency of micturition or episodes of incontinence compared to no treatment, $p = 0.872$).[38]

If the patient shows nocturia or nocturnal polyuria, desmopressin can be used, based on evidence from prospective and retrospective studies, with caution to monitor sodium, especially in elderly patients.[39] If the patient has storage symptoms, antimuscarinics or beta3-agonists are indicated, based on RCT evidence. Antimuscarinics block muscarinic receptors (mainly M3) in the detrusor muscle competing with acetylcholine, thus inhibiting DO. Highly selective M3 (e.g., Darifenacin 7.5–15 mg qd) or low blood-brain barrier penetrant (e.g., trospium 15–30 mg bid, fesoterodine 4–8 mg qd) antimuscarinics should be preferred due to decreased effects on cognition. Beta3-agonists (e.g., mirabegron 50 mg qd, vibegron 75 mg qd) selectively stimulate beta3 adrenergic receptors in the detrusor and inhibit afferent bladder signaling. Beta3-agonists do not cause the side effects reported with antimuscarinics but mild increases in blood pressure and more rarely palpitations and atrial fibrillation have been reported with mirabegron use.[40]

A


Storage and/or voiding symptoms
History taking + physical examination + blood tests (exclude red-flags)
Weight loss, fluid intake redistribution, bladder retraining ("voiding by the clock"), PFMT
Urinalysis
If UTI confirmed, treat according to urine culture results
PVR
Non-invasive uroflowmetry or urodynamic study if risk factors for UUT damage
>150 mL
<150 mL
CIC
Pharmacological therapy:
• if storage symptoms, use antimuscarinics (darifenacin 7.5–15 mg qd, fesoterodine 4–8 mg qd, trospium 15–30 mg bid) or beta-3 agonists (mirabegron 25–50 mg qd, vibegron 75 mg qd)
• if voiding symptoms, use alpha-blockers
• if nocturnal polyuria, use desmopressin
Botulinum toxin detrusor injections
Suprapubic catheter
Surgery:
• Augmentation cystoplasty if CIC is possible
• Urinary diversion if CIC is not possible

B


Address concurrent urinary problems (eg. CIC before intercourse)
Address spasticity (eg. adductor spasms)
Consider PFMT and body-mapping techniques
Sexual complaints
Cardiovascular screening, drugs review, baseline AMH measurement in women, hormone measurements only if endocrinopathy is suspected
History taking + physical examination
Men
Women
Erectile dysfunction
Premature Ejaculation
Anejaculation
Dyspareunia and/or vaginal dryness
Post-menopausal vaginal atrophy
Decreased genital sensation
PDE5i: sildenafil 50 mg or tadalafil 20 mg, 1h before sexual activity. If frequent activity tadalafil 5 mg daily +20 mg before coitus
Dapoxetine 30–60 mg, 1–3h before sexual activity
Penile vibratory stimulation or Midodrine
Anesthetic and water-soluble lubricants
Topical aestrogen therapy
Vibrators
Vacuum-constriction devices/intracavernosal injection of alprostadil

In patients with overactive bladder and insufficient benefit from CIC and pharmacological treatment or discontinuation of treatment because of side effects, botulinum toxin detrusor injections can be considered, based on phase III RCT data.[41] The licensed preparation for urological indication is onabotulinumtoxinA (TB-A). The procedure consists of 20–30 injections into the bladder wall via cystoscopy under local anesthesia. Repeat injections are required every 6–9 months. Failure rates have been reported in 6–32% and to increase over time.[42] A consensus definition of TB-A treatment failure was recently proposed[43] based on clinical and urodynamic criteria: DO persistence with maximum detrusor pressures >40 mmHg and/or poor compliance and persistence of UI and/or urgency and/or self-CIC >8/day and/or TB-A clinical benefit <3 months. Upon failure, reinjection of a higher dose of the same TB-A or switching to another toxin variation can be tried before transitioning to more invasive treatments.

SNM and percutaneous tibial nerve modulation (PTNM) are also available. In SNM, a device in implanted subcutaneously with a lead in the sacral foramen stimulating the S3–S4 nerves. Adverse events include: pain, hematoma, infection and displacement requiring surgical revision (pooled incidence 7%).[44] Evidence on SNM efficacy for neurogenic LUTS is limited by small sample sizes, retrospective design and lack of urodynamic data. With the advent of MRI-compatible devices, SNM use and research is expected to increase. A systematic review of observational studies on SNM in MS found response rates of 51–83% with more benefits in patients with predominant storage symptoms.[45] PTNM is obtained via the insertion of a needle electrode at the medial malleolus bilaterally, stimulating the posterior tibial nerve and indirectly the sacral nerves. In MS, PTNM can improve DO but not DSD with an overall response rate of around 66% in prospective cohort studies.[46]

If symptoms become refractory to the above treatments, an indwelling suprapubic catheter can be offered with intermittent bladder drainage via a catheter valve, unless the bladder capacity is not enough to store urine, in which case a leg bag is needed. Finally, surgical options include midurethral sling (in stress incontinence), augmentation cystoplasty (if CIC is possible) and urinary diversion (if CIC is not possible).[47]

Neurologists should be aware that patients with spinal cord lesions at or above T6 may display autonomic dysreflexia manifesting as sudden rises in systolic blood pressure of >20 mmHg, triggered by stimuli (e.g., urinary symptoms, urological procedures) originating below the level of injury.[48] If removal of the trigger is not sufficient to manage an episode, short acting anti-hypertensive medications can be used.

Neurogenic sexual symptoms

Sexual dysfunction is reported in more than 80% of pwMS, causing a high prevalence of sexual hypoactivity, to a greater extent than in other chronic diseases.[49,50]

Sacral parasympathetic innervation (S2–S4) mediates genital arousal leading to vasodilation and tumescence (Fig. 1C). Tonic sympathetic innervation (T11-L2) mediates detumescence. Erections can be psychogenic, reflexogenic or nocturnal. Psychogenic erections are mediated by sympathetic preganglionic neurons while reflexogenic erections are mediated by parasympathetic preganglionic neurons. Nocturnal erections are less well understood. Ejaculation is a primarily sympathetic phenomenon with a spinal generator at L3-L5 receiving inputs from the brainstem and hypothalamus.[51]

Primary sexual dysfunction is due to lesional disruption of the hypothalamic–pituitary–gonadal axis and spinal cord.[52] Lesions above T11 can impair psychogenic erections while lesions below T11 can affect both psychogenic and reflexogenic erections. In both cases ejaculation can be affected. Secondary sexual dysfunction is a consequence of fatigue, spasticity, cognition, decreased mobility and increasing disability. At a tertiary level, comorbid depression or anxiety and psychological factors can contribute to sexual dysfunction in both sexes (poor sexual self-image is one of the most common contributing causes of sexual dysfunction in pwMS).[53]

Sexual dysfunction is classified by the ICD-11 into: hypoactive sexual desire dysfunction (decreased libido), sexual arousal dysfunction (decreased genital/non-genital response and sexual arousal/pleasure despite adequate desire and stimulation; it includes male erectile dysfunction [ED]), ejaculatory dysfunction (premature [PE], delayed or retrograde ejaculation in males) and orgasmic dysfunction (reduction in frequency or intensity of orgasm experience). Sexual pain disorders (vaginismus, dyspareunia) have been separated from sexual dysfunctions but are likewise important to address. Neurologists should also be aware that rare sexual disorders, like restless genital syndrome, also exist.[54]

Screening questionnaires like the *Multiple Sclerosis Intimacy and Sexuality Questionnaire* can be useful to identify areas that deserve discussion. Cardiovascular risk factors also need to be considered as they can

***Fig. 3:* Flowcharts of the diagnostic work-up and therapeutic management of urinary (A) and sexual (B) dysfunction in people with multiple sclerosis.** The figure summarizes a stepwise approach from clinical assessment to tailored treatment selection and escalation in refractory cases. Abbreviations: AMH = anti-mullerian hormone; CIC = clean intermittent catheterization; PDE5i = phosphodiesterase inhibitors; PFMT = pelvic floor muscle training; PVR = post-void residual; UTI = urinary tract infection; UUT = upper urinary tract.

interfere with endothelial function and lead to impaired engorgement of cavernosal tissue. Hormonal tests are not routinely indicated (Fig. 3). Pelvic neurophysiology enables assessment of sacral somatic innervation but is not routinely recommended in pwMS, as it does not influence clinical management.[55] However, when guided by a specific clinical question, it may be performed in selected cases to exclude alternative causes (e.g., cauda equina syndrome or chronic pelvic pain).[56]

For ED, phosphodiesterase-5 inhibitors (PDE5i) can be used on demand (e.g., sildenafil 50 mg or tadalafil 20 mg, 1 h before sexual activity),[57] increasing the dose if erection is not maintained. However, if frequent sexual activity is expected, tadalafil 5 mg daily with booster dose (20 mg) before coitus is preferred.[58] The patient should use the same drug at least 6–8 times before deeming it ineffective, in which case another PDE5i can be tried. Unlike tadalafil, Sildenafil should be taken with no food or alcohol. PDE5i adverse effects

Fig. 4: **Examples of pelvic floor muscle training exercises that may be recommended for people with multiple sclerosis and urinary dysfunction.** Exercises should be performed in different starting positions (lying, sitting, and standing), with progressive incorporation of functional challenges, such as standing up from a chair, jumping, coughing, or performing a Valsalva manoeuvre, and integrated into the patient's everyday routine. Figure created using artificial intelligence.

include headache, flushing, nasal congestion and blurred vision. If pharmacological therapy is not effective, vacuum-constriction devices can be used as an add-on option to PDE5i.[59] Vacuum devices are used in conjunction with penile rings to maintain erection and should not be used for more than 30 min to avoid risk of ischemia. Petechiae and subcutaneous hemorrhages can appear and the device should be avoided in anticoagulated patients. Another option is the intracavernosal injection of alprostadil.[60] Injections can cause petechiae and intracavernous fibrosis. For PE, dapoxetine (30–60 mg, 1–3 h before sexual activity) is the only licensed drug.[61] Penile vibratory stimulation (provided autonomic dysreflexia is absent) and Midodrine can be tried in cases of anejaculation.[62]

For women with dyspareunia and/or vaginal dryness, anesthetic and water-soluble lubricants can be used. In case of postmenopausal vaginal atrophy, topical estrogen therapy is indicated. Vibrators can be useful when decreased genital sensation limits intimacy and higher frequencies can enhance effectiveness. In case of vaginismus, pelvic-floor relaxation training and vaginal dilator therapy can be used.

Drugs should be reviewed and trials of suspension should be done to verify causality.[63] A recent meta-analysis identified five drugs with the highest frequency of sexual dysfunction among anti-depressants (fluoxetine, paroxetine, citalopram, venlafaxine, sertraline). Beta-blockers inhibit the sympathetic nervous system and decrease testosterone levels contributing to sexual dysfunction. In males, baclofen can cause ED and anejaculation. Among neuropathic pain medications, gabapentin is less frequently associated with sexual dysfunction, while pregabalin effects on sexual function seem to be dose independent. Combined oral contraceptive pills can decrease libido and a pill switch can be tried.

In women with urinary dysfunction, CIC can be performed before sexual intercourse. Moreover, if antimuscarinics cause vaginal dryness, lubricants may be helpful. If spasticity is present (e.g., adductor spasms), anti-spasticity agents can be used 1 h before sexual activity or, in severe cases, botulinum toxin treatment can be proposed. Physiotherapy is important in optimizing motor compensations during sexual activities and individuating optimal sexual positions. Psychological aspects of sexual dysfunction may benefit from psychotherapy (e.g., cognitive behavioural therapy) and body-mapping techniques can help identify alternative erogenous zones (e.g., tactile stimulation above the lesional cord level).

Pelvic floor muscle training

Current evidence supports the use of PFMT for the prevention and treatment of all types of UI[64] with preliminary data on sexual dysfunction.[65,66] The 5 Fs model (Find, Feel, Force, Follow-through, Functional training) can guide physiotherapists providing adequate PFMT education. *Find and Feel* indicate the need to become aware of all the different PFMs with the aim of avoiding co-contraction of surrounding muscles. *Force* states that training should involve maximal voluntary repetitive contractions of PFMs, providing sufficient relaxation time between contractions. Exercises should be performed in different starting positions, training should be continued for prolonged periods of time (*Follow-trough*) and should be implemented in the everyday routine (*Functional training*) (Fig. 4).

Data regarding the appropriate PFMT regimen are lacking, with studies using highly heterogeneous regimens and assessments.[67] More intense and more frequent PFMT increases benefits. A recent systematic review identified that at least 6–12 weeks of continued treatment are needed with more than 3 sessions (<45 min each) per week.[67] Supervised training is significantly superior to unsupervised training.[68] However, evidence shows that unsupervised training with appropriate patients' education and regular reassessment may be non-inferior to supervised PFMT. Moreover, group-based PFMT has been shown to be non-inferior to individual PFMT.[69] In patients with limited access to rehabilitation services, access to PFMT can be ensured using telerehabilitation.[70]

Among add-on therapies to PFMT, cones[71] are beneficial but not superior to PFMT in stress UI while electrical stimulation[72] is beneficial in cases of urge UI. Electromyographic biofeedback has not been shown to improve effectiveness of PFMT,[73,74] whereas pressure-mediated biofeedback might be beneficial but needs further validation.[75] The most promising add-on is transcranial direct current stimulation which has recently been shown to significantly enhance PFMT efficacy in MS.[76]

Our approach is to use group-based or individualized/telerehabilitation PFMT protocols with proper individual patient education at the beginning of training and frequent reassessments, helping patients implement functional PFMT exercises during daily life activities with continuation of exercises even after continence has been achieved. In the absence of reliable clinical outcome measures, scales commonly used in the research setting (e.g., the International Consultation on Incontinence Questionnaire-Short Form, the modified Oxford Scale and the 1 h pad test) may be employed.[77–79]

Conclusion

In an era in which early diagnosis and high-efficacy disease-modifying therapies have reshaped the natural history of MS, optimizing quality of life and addressing persistent, burdensome symptoms have become increasingly important priorities. The framework

Search strategy and selection criteria

A comprehensive literature search was initially performed using PubMed from database inception to May 15, 2026, with the following terms: "multiple sclerosis" AND ("gastrointestinal" OR "constipation" OR "fecal incontinence" OR "dyssynergic" OR "urinary" OR "detrusor" OR "sexual" OR "erectile" OR "ejaculation" OR "orgasm" OR "biofeedback" OR "pelvic floor muscle training"). Previously published reviews on gastrointestinal, urinary and sexual symptoms in neurological disorders as well as European clinical guidelines were scanned for additional references. Only English-language studies were included, and the final reference lists were generated according to the scope and relevance of this review.

proposed in this review seeks to translate available evidence into a practical, multidisciplinary model of care that may also be extended to other autoimmune demyelinating and spinal cord disorders commonly encountered in neurological practice.

Patient and caregiver education is essential to improve awareness and adherence to therapeutic strategies, particularly given that neurogenic GI, urinary and sexual symptoms in MS frequently coexist and influence one another. In this regard, PFMT offers a unique educational opportunity, helping patients recognize the interrelationship between symptoms and the benefits of a single intervention across multiple domains.

In centers where dedicated expertise is available, the establishment of a multidisciplinary MS team enables pwMS to access coordinated, patient-centered care through a single point of contact. Close collaboration between neurologists, urologists, gastroenterologists, gynaecologists, rehabilitation physicians, physiotherapists, psychologists, and MS specialist nurses facilitates timely, integrated management, reducing fragmentation of care and delays associated with multiple independent specialist referrals. Regular multidisciplinary case discussions further promote individualized, holistic care and facilitate communication among healthcare professionals.

In our experience, inpatient neurorehabilitation provides a unique opportunity to implement this multidisciplinary approach, allowing simultaneous optimization of pharmacological, rehabilitative, and behavioural interventions, with real-time assessment of treatment response and adjustment of management strategies. Moreover, peer support among patients can promote self-awareness, improve treatment adherence, and provide ongoing psychological support.

However, many patients are managed in centers without access to multidisciplinary expertise or advanced diagnostics. Here, neurologists play a pivotal role in early symptom recognition and initial management. Careful screening, focused pelvic examination and bladder ultrasound for PVR can substantially improve outcomes and guide specialist referral. Developing structured referral pathways, collaboration with tertiary centers, and access to specialist telemedicine consultations can ensure timely expert input while maintaining the neurologist as care coordinator. Group-based rehabilitation and telerehabilitation may improve PFMT access where resources are limited. MS specialist nurses represent a key resource across all settings, contributing to symptom screening, education, functional assessment, PVR monitoring, and follow-up.

By combining structured assessment, evidence-based treatment, rehabilitation, and education, this model may help reduce variability in care and support MS centers in delivering more comprehensive and patient-centered management, including where multidisciplinary specialist resources are limited.

Contributors

Giorgio Guido: conceptualization, data curation, investigation, methodology, project administration, visualization, writing—original draft, and writing—review & editing.

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Declaration of interests

Giorgio Guido has nothing to disclose. Agostino Nozzolillo has nothing to disclose. Manuela Tutolo has nothing to disclose. Patrizia Giollo has nothing to disclose. Maria Assunta Rocca received consulting fees from Biogen, Bristol Myers Squibb, Roche; and speaker honoraria from Alexion, Biogen, Bristol Myers Squibb, Celgene, Horizon Therapeutics Italy, Merck Serono SpA, Mitsubishi-Tanabe Pharma, Neuraxpharm, Novartis, Roche, Sandoz, and Sanofi. She receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla. She is Associate Editor for *Multiple Sclerosis and Related Disorders*; and Associate Co-Editor for Europe and Africa for *Multiple Sclerosis Journal*. Massimo Filippi is Editor-in-Chief of the *Journal of Neurology*, Associate Editor of *Human Brain Mapping*, *Neurological Sciences*, and *Radiology*; received compensation for consulting services from Almirall, Biogen, Bristol-Myers Squibb, Eli Lilly, Merck, Novartis, Roche, Sanofi; speaking activities from Amgen, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eisai, Eli Lilly, Fujirebio, Genzyme, Janssen, Merck, Neopharmed Gentili, Neuraxpharm, Novartis, Novo Nordisk, Roche, Sanofi, Takeda; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Eli Lilly, GE Healthcare Ltd, Merck, Neuraxpharm, Novartis, Roche, Sandoz, Sanofi, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla.

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creation of Fig. 4 only. AI was not used for the creation of the remaining figures.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2026.101824.

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