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Conservative management for urinary incontinence in neurological patients: A systematic review and meta-analysis☆

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ABSTRACT

Aim: To summarize evidence from a search and review of the 7th International Consultation on Incontinence chapter's section on conservative treatments in neurological patients.
Methods: Searching the Cochrane Incontinence Specialised Register (MEDLINE, CENTRAL, others) on August 2nd, 2022. Quality and certainty evidence were assessed using the Cochrane Risk of Bias Tool and the Grading of Recommendations Assessment, Development and Evaluation.
Results: After screening 5416 records, 40 trials with 2751 participants were included and stratified according to the site and nature of the neurological disease: (1) Brain disorders n = 22; (2) Spinal cord disorders n = 3; (3) Multiple sclerosis (MS) n = 13; (4) Mixed types of neurological diseases n = 2. Pooled analysis from trials in participants with brain disorders showed that, compared to no active treatment, electrical stimulation (EStim) improved UI episodes per day based on very low certainty evidence and improved UI symptom measures based on moderate certainty evidence. Further, compared to usual care, toilet assistance improved neurological quality of life (QoL) measures based on moderate certainty evidence. Pooled analysis from trials in participants with MS showed that, compared to pelvic floor muscle training (PFMT) alone, PFMT plus EStim was effective for improving the number of UI episodes per day based on moderate certainty evidence.
Conclusion: Our review shows that neurological patients could benefit from conservative interventions to improve symptoms of UI, and QoL. Further well-designed trials with larger cohorts and longer-term follow-up are needed given the limited studies in this population.

1. Introduction

Urinary incontinence (UI) is highly prevalent in neurological patients and negatively impacts quality of life (QoL) [1]. Severity and type of UI depend upon the extent, duration and location of the neurological disease [2]. UI experienced by neurological patients are most often caused by storage dysfunction resulting from involuntary detrusor contractions [2]. Brain disorders such as stroke and Parkinson's disease (PD) may include involuntary detrusor contractions after damage to the suprapontine neural circuitry leading to the cessation of tonic inhibition on the pontine micturition centre [2]. Conversely, after spinal cord (SC) disorders such as including SC injury and spina bifida the mechanism of detrusor overactivity is due to disruption or lack of descending inhibitory fibres that leads to involuntary detrusor contractions [2]. Multiple sclerosis present storage and voiding symptoms, or a combination of both, with their manifestation influenced by the duration of the disease and the extent of spinal cord involvement [2]. While conservative interventions are considered the first line of treatment for UI symptoms in the general population [3], their effectiveness has not been clearly established in neurological patients. Clinical practice guidelines therefore recommend pharmacological treatments for UI management in neurological patients given the limited number of studies on conservative interventions [4,5], however concerns about adverse effects [6] significantly affect patients' adherence to treatment [7]. When pharmacological treatments fail, conservative treatments might be a potential alternative to deliver

Abbreviations: CIs, confidence intervals; EStim, electrical stimulation; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICI, International Consultation on Incontinence; MDs, mean differences; MS, Multiple sclerosis; PD, Parkinson's disease; PFMT, pelvic floor muscle training; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; QoL, quality of life; RCT, randomized controlled trials; RoB, risk of bias; RR, risk ratios; SC, spinal cord; SD, standard deviation; SMDs, standardized mean differences; TNS, tibial nerve stimulation; UI, urinary incontinence; UTI, urinary tract infections

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interventions for UI in neurological patients. Conservative treatments refer to interventions not involving drugs or surgery, they have shown to be effective generally safe and less costly [8]. Previous systematic reviews have focused on a select few conservative approaches [9,10], neglecting some of the established first-line conservative interventions. For this purpose, this systematic review synthesizes the evidence on all conservative interventions for UI across different neurological disorders to appraise and guide evidence-based decisions for policy-makers and healthcare practitioners. This systematic review was conducted based on the data provided in the new section on neurological patients of the conservative management for UI chapter in the International Consultation on Incontinence (ICI) 7th edition [11].

2. Material and methods

2.1. Protocol, registration and search methods

This systematic review followed the Cochrane Handbook for Systematic Reviews of Interventions [12] and was reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidance [13]. The protocol was registered on PROSPERO (International Prospective Register of Systematic Reviews, CRD42022310084). Studies were sought on August 2nd, 2022, using the Cochrane Incontinence Specialised Register (includes MEDLINE, CENTRAL, other sources) with no restrictions applied (e.g., publication date or language) (Supplementary Appendix). Evidence was obtained from a search and review of the literature based on the procedures detailed in the 7th ICI [11], specifically in the new section on the "Adult Conservative Management" chapter. The following paper presents the review highlights, meta-analysis and provides the levels of certainty of evidence.

2.2. Eligibility criteria

Studies were eligible for the systematic review using the PICO (population, intervention, comparison, and outcome) model, according to the inclusion and exclusion criteria shown in Table 1. Briefly, included studies were required to meet the following inclusion criteria: randomized controlled trials (RCTs), involving adult participants with neurological conditions, comparing the effectiveness of a conservative intervention [14] for UI compared to either no active treatment, usual care (as defined by trialists) or another conservative treatment. Additionally, studies needed to assess outcomes with patient-reported outcomes recommended by the 7th Edition of the ICI [11] and condition- or neuro-urological-specific measures [15]. Primary outcomes of interest included relief of UI symptoms and/or improvement of urinary symptoms. A comprehensive list of eligibility criteria characteristics, along with definitions of conservative interventions considered for this review, is provided in Table 1.

2.3. Study selection

Records identified were managed using Covidence (https://www.covidence.org). The screening process included titles and abstracts followed by a full-text assessment by at least two independent reviewers (AL, GV, IK, IL, OD, PT and YXH); a third author (CD) resolved any disagreement. Using a standardized data extraction template, two reviewers (GV with AL or OD) collected the studies' main characteristics. The corresponding authors were contacted when relevant data were unclear.

Based on previous evidence [2] and consultation with clinical experts, studies were stratified according to the location and nature of the neurological disease influencing UI patterns differently as follows: (1) Brain disorders, including stroke, PD and cognitive/memory impairments; (2) SC disorders, including SC injury and spina bifida; (3) Multiple sclerosis (MS); (4) Mixed types of neurological diseases. Patients with MS were categorized separately due to the difficulty in defining the extent of the disease and progress of neurological symptoms.

2.4. Data analysis

When at least two studies appeared to be clinically homogeneous with similar outcome variables and time points, they were included in the meta-analysis using Review Manager software (RevMan v.5.4.1; Cochrane, Oxford, UK). In three-arm studies using the same type of conservative intervention with small differences in the treatment protocol (e.g., pelvic floor muscle training (PFMT) with and without biofeedback, or electrical stimulation (EStim) with differences in frequency intensity), the intervention groups were pooled for meta-analysis using the recommendations in the Cochrane Handbook for Systematic Reviews of Interventions [12].

For continuous outcomes, the mean and standard deviation (SD) were used to calculate mean differences (MDs) and 95% confidence intervals (CIs). If investigators reported similar outcomes on different scales, standardized mean differences (SMDs) and 95% CIs were calculated. Different approaches were used to pool the effect measures of continuous data when means and SDs were not reported, and study investigators were not reachable. The estimated mean and SD were calculated for studies reporting only medians and interquartile ranges or the minimum-to-maximum range using https://smcgrath.shinyapps.io/estmeansd/ For dichotomous data, numbers of events in the control and intervention groups of each study were used to calculate risk ratios (RRs) with 95% CIs. Statistical heterogeneity was assessed using the I^2 measure and the following thresholds: <40%: low; 30–60%: moderate; 50–90%: substantial; and >75%: considerable heterogeneity [12].

2.5. Risk of bias in individual studies

Two reviewers (GV and YX) independently assessed risk of bias (RoB) using the Cochrane RoB tool [16] in all included studies. Disagreements were resolved via discussion by consulting a third review author (CD). Using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [17], two independent reviewers (GV and CD) assessed the certainty of the body of evidence.

3. Results

3.1. Study selection

Fig. 1 presents the screening process in a PRISMA flowchart. After screening a total of 5416 records, 113 met the eligibility criteria (Supplementary Table 1). In total, 57 unique studies were included in the systematic review with one study awaiting classification pending further information from authors, and 16 ongoing studies identified as potentially relevant (Supplementary Table 2). Our final dataset contained 40 studies [18–57] that met our eligibility criteria.

3.2. Study characteristics

Table 2 presents general characteristics of the 40 included studies with 2751 participants. Over 50% of studies were published between 2010 and 2019 (n = 21) and conducted in Europe (n = 18). PFMT and EStim (n = 9) and tibial nerve stimulation (TNS) (n = 8) were the most frequently investigated conservative interventions. Supplementary Table 3 provides more information about the interventions. UI episodes (n = 17) and UI symptom questionnaires score (n = 17) were the most frequently reported outcomes. Nineteen studies reported data on adverse events. For quantitative analyses, (n = 33) studies were stratified based on the location and nature of the neurological disease. In this paper, we have included only the results of studies assessed in the GRADE analysis. Additional studies can be found in Supplementary Table 4 and 5.

Table 1
PICO criteria for inclusion and exclusion of studies.

Parameter	Eligibility criteria
Population	Inclusion criteria: Men and women aged 18 years and over with a neurologic disease diagnosis (e.g., Stroke, Parkinson's disease, Alzheimer disease, cognitive/memory impairments, Spinal Cord Injury, Spina Bifida, Multiple Sclerosis, mixed types of neurological disease, cognitive/memory impairments) and any type of urinary incontinence (UI) were included (i.e., urgency, stress, and mixed UI). Exclusion criteria: Participants with secondary neurological consequence of a primary disease (e.g., diabetic neurogenic bladder and human T-lymphotropic virus type 1 (HTLV-I)).
Interventions	Studies including the following conservative treatments: • Pelvic floor muscle training (PFMT): considered repeated exercises that promote the voluntary contraction, strength, endurance, power and relaxation of PFM [14]. The training could be supervised or unsupervised exercises, alone or combined with other types of treatment or devices (e.g., biofeedback, electrical stimulation). • Electrical therapy (EStim): The use of electric potential or currents that target motor or sensory functions [14] (e.g., transcutaneous electrical nerve stimulation and tibial nerve stimulation (TNS)). • Toilet assistance programmes: The use of an established and adjusted voiding schedules which can include a progressive voiding schedule with relaxation and distraction techniques [14] (e.g., timed voiding, bladder training, habit retraining, prompted voiding). These programs may provide simple physical assistance for toilet needs or promote behaviour change by encouraging self-initiated requests for toilet use. • Bladder expression: Comprises different manoeuvres that increases intravesical pressure in order to facilitate bladder emptying [15]. • Triggered reflex voiding: The use of voluntary approaches to provoke a bladder contraction by stimulation of the sacral and lumbar dermatomes (e.g., tapping/jabbing the suprapubic area, squeezing the glans penis or scrotal skin, digital rectal stimulation) [15]. Education (i.e., information provided for the patients regarding mechanisms of UI and/or anatomy and function of PFM) and fluid management (i.e., counselling patients on appropriate fluid intake) were considered an integral part of the conservative intervention program rather than a main intervention itself. We excluded invasive interventions such as percutaneous TNS and other procedures that penetrate the skin or body cavities.
Comparator	No active treatment of UI (which included no treatment, wait list, sham, placebo or usual care not involving UI treatment), usual care or minimal intervention (which included education of UI, healthcare professional visit or advice for UI management), or another conservative treatment.
Outcomes	Primary outcomes: number of participants reporting relief of urinary incontinence symptoms and/or improvement of urinary symptoms. Secondary outcomes: (1) (a) subjective quantification of incontinence symptoms (e.g., number of urinary leakage episodes in the bladder diary); (b) objective quantification of incontinence symptoms (e.g., pad weight or number of pads); (2) UI symptom assessment measures by validated questionnaires including: Bristol Female Lower Urinary Tract Symptoms B-FLUTS, DAN-PSS-1 (Danish Prostatic Symptoms Score), ICIQ-OAB (International Consultation on Incontinence Questionnaire (ICIQ) on Overactive Bladder, ICIQ-UI-SF (ICIQ-Urinary incontinence short form), ISI (Incontinence Severity Index), KHQ (King's Health Questionnaire), OABSS (Overactive Bladder Symptom Score), UDI (Urogenital Distress Inventory), USP (Urinary Symptom Profile); (3) Neuro-urological QoL assessment validated questionnaires for neuro-urological patients [16] including: Qualiveen and IQOL (Incontinence Quality of Life); (4) UI-specific QoL assessment measures by validated questionnaires including: ICIQ-LUTSqol (ICIQ-Lower Urinary Tract Symptoms Quality of Life Module), ICIQ-OABqol (ICIQ-Overactive Bladder Quality of Life Module), IIQ (Incontinence Impact Questionnaire, OABq (Overactive Bladder Assessment questionnaire), OABv8; (5) adverse events.
Study design	Randomized controlled trials (RCT), cluster RCTs, cross-over RCTs and quasi-RCTs
Time-points	End of treatment: post-treatment to ≤ 3 months follow-up Intermediate follow-up: > 3 months to ≤ 12 months follow-up Long-term follow-up: > 12 months follow-up

3.2.1. Brain disorders

Twenty-two trials studied participants with brain disorders, including stroke (n = 14) [19,27–30,36,37,44,48–52,56], PD (n = 5) [18,42,43,46,55] and memory/cognitive impairment (n = 3) [23,31,35], totalling 1745 participants (mean age of 69 years, 52% women). Four studies [23,27,31,49] presented no numerical results for the outcomes included in this review.

3.2.1.1. Conservative vs. no active treatment.

3.2.1.1.1. Tibial nerve stimulation Five trials compared TNS with no active treatment in patients with PD (n = 3) [18,42,46] and stroke patients (n = 2) [19,44]. After treatment, there was no evidence of difference between groups in the relief of UI symptoms in pooled data of two trials with moderate certainty evidence [42,44] (Fig. 2.1.a, Table 3), UI episodes over 24 h in pooled data of two trials with very low certainty evidence [18,42] (Fig. 2.1.b, Table 3), UI symptoms and neuro-urological QoL questionnaires score in one trial [42], and UI-specific QoL questionnaires score in pooled data of two trials with very low certainty evidence [18,46] (Fig. 2.1.e, Table 3). However, one trial [18] reported improvement of urinary symptoms, number of pads used in 24 h, and UI symptom questionnaires score, favouring TNS (Supplementary Table 4). At intermediate follow-up, there was no evidence of difference between groups in the relief of UI symptoms in pooled data of two trials with moderate certainty evidence [19,42] (Fig. 2.1.a, Table 3), UI episodes over 24 h, UI symptoms, and neuro-urological QoL questionnaires score in one trial [42] (Supplementary Table 4). At long-term follow-up, there was no evidence of difference between groups in UI symptom relief in one trial. However, in the same trial, TNS was found to be more effective than no active treatment for

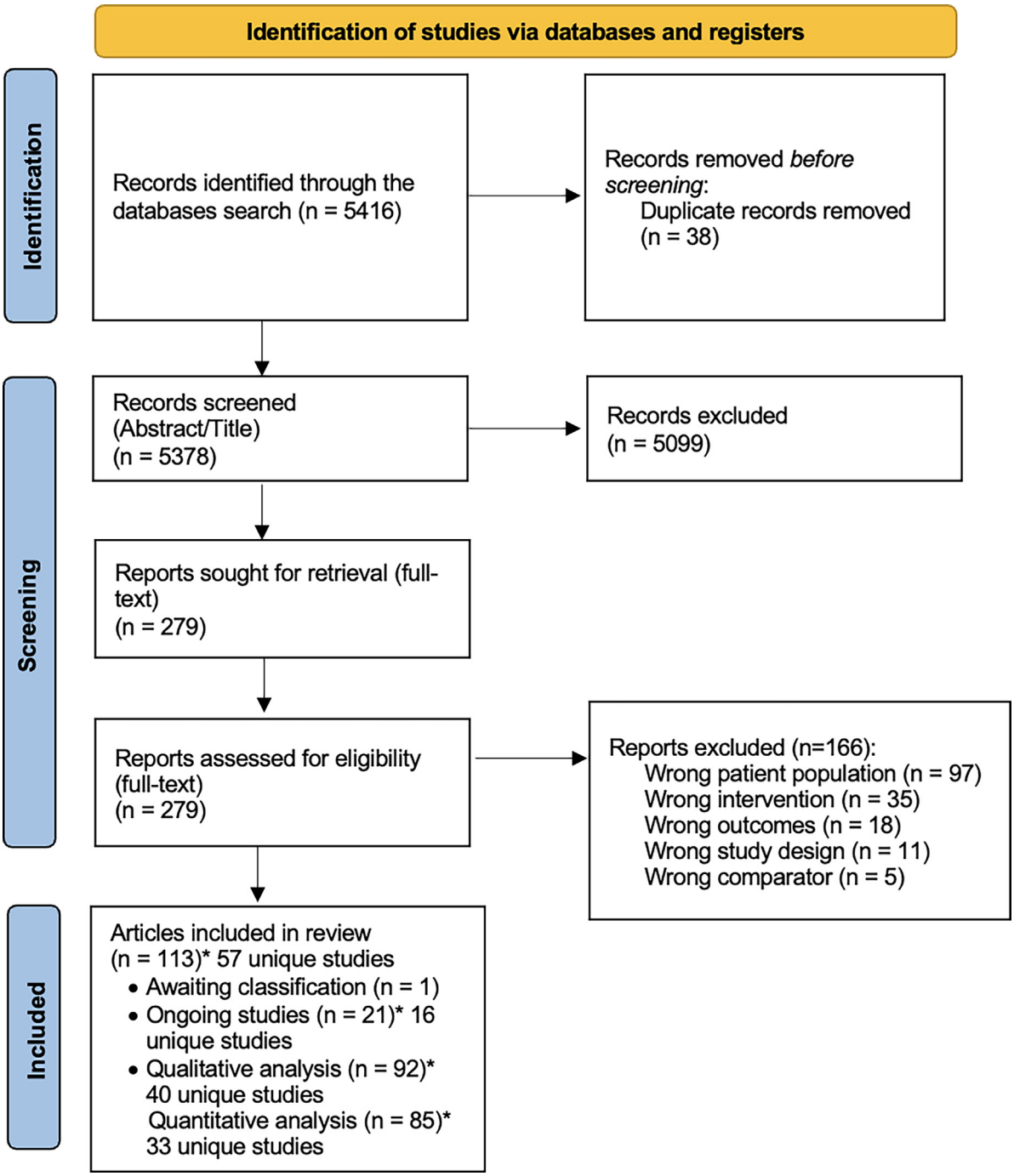

Fig. 1. PRISMA diagram showing the flow of literature through the assessment process.

improvement of urinary symptoms [44] (Supplementary Table 4). Finally, one trial [19] with no timing of the outcome assessment showed no evidence of difference in UI episodes over 24 h and UI-specific QoL questionnaires score between groups. In one trial [19], one participant in each group (TNS versus no active treatment) (2/54 (3.7%)) had residual urine volume > 150 ml. Furthermore, one participant (1/54 (1.85%)) had minor skin irritation (group not reported), and one (1/54 (1.85%)) had ankle cramping (group not reported). Two studies [18,46] reported no data on adverse events and another two studies [42,44] reported no adverse events (Table 2).

3.2.1.1.2. Electrical stimulation Three trials [29,30,37] compared surface (between lumbar level and ischial node) EStim with no active treatment in stoke patients. After treatment, pooled data from two trials [29,37] showed a decrease in UI episodes over 24 h with very low certainty evidence, favouring EStim (Fig. 2.1.b, Table 3). Furthermore, in pooled data from two trials [30,37], EStim was found to be more effective than no active treatment for UI symptom questionnaires score with moderate certainty evidence (Fig. 2.1.c, Table 3). All studies reported no adverse events (Table 2).

3.2.1.2. Conservative treatment vs. usual care.

3.2.1.2.1. Toilet assistance Three trials compared toilet assistance with usual care in patients with PD (n = 1) [43] and stroke (n = 2) [50,56]. Trialists considered usual care as: checking for urinary tract infections (UTI), assessing overflow incontinence through bladder scanning, using containment devices (such as pads) with regular changes, and some form of toileting schedule. After treatment, there was no evidence of difference between groups in UI symptom

Table 2
Summary of the characteristics in the included studies (40 studies).

Study	Design and country	Sample size	Outcome measures	Adverse events	Age (years)	Population and condition	Intervention	Comparator	Time points
1. Brain disorders									
Araújo 2021 [18]	RCT Brazil	Total: 36 TNS: 18 No active: 18	Number of participants reporting improvement of symptoms, 24 h UI episodes and number of pads, UI symptom and UI-specific QoL questionnaires	NR	66.2	100% Women 100% Parkinson's disease	TNS	No active	End of treatment (3 mo) and intermediate follow-up (4 and 6 mo)
Booth 2016[a] [19]	Feasibility RCT UK	Total: 54 TNS: 27 No active: 27	Number of participants reporting relief of UI symptoms, 24 h UI episodes and UI symptom and UI-specific QoL questionnaires	Residual urine volume of > 150 ml: 2 Minor skin irritation: 1 Ankle cramping: 1	67	56% Women 100% Stroke	TNS	No active	End of treatment (6 weeks) and intermediate follow-up (3 and 6.5 mo)
Engberg 2002 [23]	cross-over RCT US	Total: 19 Toilet assistance: 9 No active: 10	UI episodes	NR	83	68% Women 100% Cognitive impairment (Mini-Mental State Examination< 24) 42% Stroke 5% Parkinson's disease	Toilet assistance	No active	End of treatment (2 mo)
Gelber 1997 [27]	RCT USA	Total: 28 Toilet assistance 1: 10 Toilet assistance 2: 18	24 h UI episodes	NR	NR	NR 100% Stroke	Toilet assistance 1	Toilet assistance 2	End of treatment (12 mo)
Gong 2013 [28]	quasi-RCT China	Total: 65 Multimodal intervention: 30 Toilet assistance:35	Number of participants reporting relief and improvement	NR	60.9	42% Women 100% Stroke	Multimodal intervention	Toilet assistance	End of treatment (2 mo)
Guo 2014 [29]	RCT China	Total: 61 EStim: 32 No active: 29	24 h UI episodes	None	66.7	31% Women 100% Stroke	EStim (surface)	No active	End of treatment (2 mo)
Guo 2018 [30]	RCT China	Total: 82 EStim: 41 No active: 41	UI symptom questionnaire	None	63.4	43% Women 100% Stroke	EStim (surface)	No active	End of treatment (10 weeks)
Jirovec 2001 [31]	RCT US	Total: 118 Toilet assistance: 77 No active: 41	UI episodes	NR	79.9	69% Women 100% Memory-impaired elder	Toilet assistance	No active	End of treatment (6 mo)
Lee 2017 [35]	RCT Korea	Total: 98 PFMT + Toilet assistance: 52 Toilet assistance: 46	24 h UI episodes and UI symptom questionnaire	NR	75.1	100% Women 63.4% Cognitive impairment 36.6% Alzheimer disease	PFMT + Toilet assistance	Toilet assistance	End of treatment (3 mo)
Lewis 1990 [36]	RCT USA	Total: 23 Toilet assistance + sensory-motor biofeedback: 11 Toilet assistance: 12	48 h UI episodes	NR	NR	NR 100% Stroke	Toilet assistance + sensory-motor biofeedback	Toilet assistance	End of treatment (2 weeks)
Liu 2016 [37]	RCT China	Total: 81 EStim 1: 27 EStim 2: 27 No active: 27	24 h UI episodes and UI symptom questionnaire	None	66	28% Women 100% Stroke	EStim[b] (surface)	No active	End of treatment (3 mo)
McClurg 2022 [42]	RCT UK	Total: 242 TNS: 121 No active: 121	Number of participants reporting relief of UI symptoms, 24 h UI episodes, UI symptom and neuro-urological QoL questionnaires	None	69	41% Women 100% Parkinson's disease	TNS	No active	End of treatment (6 weeks) and intermediate follow-up (3 mo)
McDonald 2020 [43]	RCT UK	Total: 38 Toilet assistance: 20 Usual care: 18	Number of participants reporting improvement, 72 h UI episodes, UI symptom and UI-specific QoL questionnaires	NR	66.5	NR 100% Parkinson's disease	Toilet assistance	Usual care	End of treatment (3 mo) and intermediate follow-up (5 mo)
Monteiro 2014 [44]	RCT Brazil	Total: 24 TNS: 12 No active: 12	Number of participants reporting relief and improvement	None	60.6	0% Women 100% Stroke	TNS	No active	End of treatment (6 weeks) and long-term follow-up (12 mo)
Perissinotto 2015 [46]	RCT Brazil	Total: 23 TNS: 12 No active: 11	UI episodes, UI symptom and UI-specific QoL questionnaires	NR	63.6	NR 100% Parkinson's Disease	TNS	No active	End of treatment (10 weeks)
Shin 2016 [48]	RCT Korea	Total: 35 PFMT: 18 No active: 17	UI symptom questionnaire	NR	62.5	100% Women 100% Stroke	PFMT	No active	End of treatment (6 weeks)
Smilskalne 2009 [49]	RCT Latvia	Total: 38	UI symptom questionnaire	NR	NR	NR 100% Stroke	Group 1 PFMT Group 2 PFMT + EStim	No active	End of treatment (4 weeks)
Thomas 2014 [50]	cluster RCT UK	Total: 413 Toilet assistance 1: 164 Toilet assistance 2: 125 Usual care: 124	Number of participants reporting relief of UI symptoms and neuro-urological QoL questionnaire	Fall: 31 UTI: 54 Bladder catheterization: 6	77.4	54% Women 100% Stroke	Toilet assistance[d]	Usual care	End of treatment (6 weeks), intermediate follow-up (3 mo) and long-term follow-up (12 mo) post-stroke
Tibaek 2004 [51]	RCT Denmark	Total: 26 PFMT: 14 No active: 12	24 h UI episodes, pad test 24 h, number of pads used, UI-specific QoL questionnaire	NR	64.4	100% Women 100% Stroke	PFMT	No active	End of treatment (3 mo) and intermediate follow-up (6 mo)
Tibaek 2017 [52]	RCT Denmark	Total: 31 PFMT: 16 No active: 15	UI episodes and UI symptom questionnaire	None	66.7	0% Women 100% Stroke	PFMT	No active	End of treatment (3 mo) and intermediate follow-up (6 mo)

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Table 2 (*continued*).

Study	Design and country	Sample size	Outcome measures	Adverse events	Age (years)	Population and condition	Intervention	Comparator	Time points
Vaughan 2019 [55]	RCT USA	Total: 53 PFMT + Toilet assistance: 26 No active: 27	UI episodes and UI-specific QoL questionnaire	NR	70.3	26% Women 100% Parkinson's disease	PFMT + Toilet assistance	No active	End of treatment (2 mo)
Watkins 2022 [56]	RCT UK	Total: 157 Toilet assistance: 79 Usual care: 78	UI symptom and neuro-urological QoL questionnaire	NR	74.9	48% Women 100% Stroke	Toilet assistance	Usual care	End of treatment (post-hospital discharge) and intermediate follow-up (3 and 6 mo) post-randomization
2. Spinal cord Disorders									
Daia 2019 [20]	RCT Romania	Total: 332 EStim: 162 No active: 170	Short-term quantity of urine lost (LOSS 24 h)	None	39.8	30% Women 100% spinal cord injury	EStim (surface)	No active	End of treatment (1 mo)
Elmelund 2018 [22]	RCT Denmark	Total: 36 PFMT + EStim: 19 PFMT: 17	Number of participants reporting improvement of symptoms, 24 h UI episodes, Pad-test 24 h and UI symptom questionnaire	PFMT + EStim: none PFMT: soreness in PF area (n = 1)	53.8	100% Women 100% incomplete spinal cord injury	PFMT + EStim (intravaginal)	PFMT	End of treatment (3 mo) and intermediate follow-up (6 mo)
Khan 2015 [33]	RCT Australia	Total: 54 Multimodal intervention: 27 Usual care: 27	UI symptom and UI-specific QoL questionnaires	None	33.3	57% Women 100% Spina Bifida	Multimodal intervention	Usual care	End of treatment (3 mo)
3. Multiple Sclerosis									
Darwish 2022 [21]	RCT Egypt	Total: 40 PFMT + EStim: 20 PFMT: 20	Number of UI episodes	NR	31.4	0% Women 100% Multiple Sclerosis	PFMT + EStim (surface)	PFMT	End of treatment (1 mo)
Ferreira 2016 [24]	RCT Brazil	Total: 24 PFMT + EStim: 12 PFMT: 12	Neuro-urological QoL and UI-specific QoL questionnaires	NR	43.3	100% Women 100% Multiple Sclerosis	PFMT + EStim (surface)	PFMT	End of treatment (6 mo)
Ferreira 2019 [25]	RCT Brazil	Total: 31 PFMT + EStim: 16 PFMT: 15	Neuro-urological QoL and UI-specific QoL questionnaires	NR	44.2	100% Women 100% Multiple Sclerosis	PFMT + EStim (intravaginal)	PFMT	End of treatment (6 mo)
Gaspard 2014 [26]	RCT Belgium	Total: 31 PFMT: 16 TNS: 15	24 h UI episodes, UI symptom and neuro-urological QoL questionnaires	None	42	48% Women 100% Multiple Sclerosis	PFMT	TNS	End of treatment (8 weeks) and intermediate follow-up (6 mo)
Khan 2010 [32]	RCT Australia	Total: 74 Multimodal intervention: 40 Usual care: 34	Number of participants reporting improvement of symptoms and UI symptom questionnaire	None	50.5	73% Women 100% Multiple Sclerosis	Multimodal intervention	Usual care	End of treatment (12 mo)
Klarskov 1994 [34]	RCT Denmark	Total: 20	Number of participants reporting improvement of symptoms, 24 h UI episodes, pad-test 1 h and number of pads per day	NR	58.4	75% Women 100% Multiple Sclerosis	PFMT	PFMT	NR
Lucio 2011 [38]	RCT Brazil	Total: 35 PFMT: 18 No active: 17	Number of participants reporting relief of UI symptoms, pad test 24 h, number of pads, UI symptom and UI-specific QoL questionnaires	NR	35.4	100% Women 100% Multiple Sclerosis	PFMT	No active	End of treatment (3 mo)
Lucio 2016 [39]	RCT Brazil	Total: 30 PFMT + EStim: 10 PFMT + TNS: 10 PFMT: 10	24 h UI episodes	NR	40.2	100% Women 100% Multiple Sclerosis	Group 1: PFMT + EStim (intravaginal) Group 2: PFMT + TNS	PFMT	End of treatment (3 mo)
McClurg 2006 [40]	RCT UK	Total: 30 PFMT + EStim: 10 PFMT 1: 10 PFMT 2: 10	Number of participants reporting relief of UI symptoms, 24 h UI episodes, UI symptom and UI-specific QoL questionnaires	PFMT + EStim: Intervention physically and psychologically demanding (n = 1) Tingling in the posterior aspect of the right thigh (n = 1)	50.5	100% Women 100% Multiple Sclerosis	PFMT + EStim (intravaginal)	PFMT[c]	End of treatment (9 weeks) and intermediate follow-up (4 and 6 mo)
McClurg 2008 [41]	RCT UK	Total: 74 PFMT + EStim: 37 PFMT: 37	24 h UI episodes, pad test 24 h, UI symptom and UI-specific QoL questionnaires	None	50.2	77% Women 100% Multiple Sclerosis	PFMT + EStim (intravaginal or intra-anal)	PFMT	End of treatment (9 weeks) and intermediate follow-up (4 and 6 mo)
Perez 2020 [45]	RCT Spain	Total: 48 PFMT 1: 24 PFMT 2: 24	72 h UI episodes, 3 UI symptom and UI-specific QoL questionnaires	NR	46.9	NR 100% Multiple Sclerosis	PFMT	PFMT	End of treatment (3 mo)
Prasad 2003 [47]	cross-over RCT UK	Total: 28	UI episodes	None	49	64% Women 100% Multiple Sclerosis	Group 1 Bladder expression Group 2 Bladder expression	Usual care	End of treatment (2 weeks each)
Vahtera 1997 [54]	RCT Finland	Total: 80 PFMT + EStim: 40 No active: 40	Questionnaires of subjective severity and urinary symptoms	None	43.7	63% Women 100% Multiple Sclerosis	PFMT + EStim (intravaginal or intra-anal)	No active	End of treatment (6 mo)
4. Mixed neurological disorders									
Tornic 2020 [53]	pilot RCT Switzerland	Total: 9 TNS: 5 No active: 4	Number of participants reporting relief of UI symptoms	None	52.9	22% Women 34% spinal cord injury 22% Multiple sclerosis 22% Cervical disc hernia 11% Parkinson's disease 11% Hydrocephalus internus	TNS	No active	End of treatment (6 weeks)

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Table 2 (*continued*).

Study	Design and country	Sample size	Outcome measures	Adverse events	Age (years)	Population and condition	Intervention	Comparator	Time points
Welk 2020 [57]	RCT Canada	Total: 30 TNS: 16 No active: 14	Pad test 24 h and neuro-urological QoL questionnaire	None	54.9	67% Women 73% Multiple sclerosis 17% spinal cord injury 7% Lipomyelomeningocele 3% Parkinson's disease	TNS	No active	End of treatment (3 mo)

EStim = electrical stimulation; h = hour(s); LOSS = quantity of urine lost; NR = not reported; ml = millilitre; mo = months; PFMT = pelvic floor muscle training; QoL = quality of life; RCT = randomized controlled trial; TNS = transcutaneous tibial nerve stimulation; UI = urinary incontinence; UK = United Kingdom.

[a] Data extracted as reported on: Thomas LH, Coupe J, Cross LD, Tan AL, Watkins CL. Interventions for treating urinary incontinence after stroke in adults. Cochrane Database Syst Rev. 2019 Feb 1;2(2):CD004462. doi: 10.1002/14651858.CD004462.pub4.

[b] This study used two EStim groups (EStim 1 = 20 Hz and EStim 2 = 75 Hz) that were merged in the current review.

[c] This study used two PFMT groups (PFMT 1 = PFMT with biofeedback and PFMT 2 = home PFMT) that were merged in the current review.

[d] This study used two toilet assistance groups that were merged in the current review.

questionnaires score in pooled data from two trials with low certainty evidence [43,56] (Fig. 2.1.c, Table 3) and UI-specific QoL questionnaires score in one trial [43] (Supplementary Table 4). However, one trial [43] reported an improvement in urinary symptoms and UI episodes over 72 h, favouring toilet assistance (Supplementary Table 4). Pooled data from two trials with moderate certainty evidence [50,56] reported improvement in neuro-urological QoL questionnaires score, favouring toilet assistance (Fig. 2.1.d, Table 3). At intermediate follow-up, there was no evidence of difference between groups in UI symptoms relief in one trial [50], UI episodes over 72 h in one trial [43], UI symptom questionnaires score in pooled data from two trials with low certainty evidence [43,56] (Fig. 2.1.c, Table 3), and UI-specific QoL questionnaires score in one trial [43] (Supplementary Table 4). At long-term follow-up, there was no evidence of difference between groups in UI symptoms relief and neuro-urological QoL questionnaires score in one trial [50] (Supplementary Table 4). Two studies [43,56] reported no data on adverse events. In the other trial [50], 31/413 (7.5%) participants reported falling, which included 16/124 (12.9%) in usual care group and 15/289 (5.2%) in toilet assistance group, most likely to be related to the intervention according to the trialists. A total of 54/413 (13%) participants reported UTI, which included 13/124 (10.5%) in usual care and 41/289 (14.2%) in toilet assistance group. Furthermore, 6/413 (1.5%) participants reported bladder catheterization (n = 6) 1/124 (0.8%) in usual care and 5/289 (0.7%) in toilet assistance group (Table 2).

3.2.2. Spinal cord disorders

Three trials involved participants with SC disorders, two [20,22] included participants with SC injuries and one [33] included participants with spina bifida, totalling 422 participants with a mean age of 42, of which 39% were women (Table 2). No trials were included in the GRADE assessment.

3.2.3. Multiple sclerosis

13 trials [21,24–26,32,34,38–41,45,47,54] included participants with MS, totalling 545 participants (mean age 45 years, 72% women) (Table 2). Three studies [34,47,54] presented no numerical results for the outcomes included in this review.

3.2.3.1. Conservative vs conservative treatments.

3.2.3.1.1. Pelvic floor muscle training with electrical stimulation vs. pelvic floor muscle training Six trials [21,24,25,39–41] compared PFMT with EStim versus PFMT alone. For four trials, surface EStim (hypogastric nerve region) [21,24] and intravaginal [25,39] EStim were used to decrease detrusor overactivity. For two trials [40,41], surface and intravaginal or intra-anal EStim with two different EStim protocol parameters were used to decrease detrusor overactivity and encourage the correct use of PFM. After treatment, there was no evidence of difference between groups in the relief of UI symptoms and UI symptom questionnaires score in one trial [40] (Supplementary Table 4), neuro-urological QoL questionnaires score in pooled data from two trials with low certainty evidence [24,25], and UI-specific QoL questionnaires score in pooled data from three trials with very low certainty evidence [24,25,40] (Fig. 2.2.c, Table 3). However, pooled data from three trials [39–41] reported improvement in UI episodes over 24 h with moderate certainty evidence (Fig. 2.2.a, Table 3), UI episodes in one trial [21], and 24 h pad tests in one trial [41], favouring PFMT with EStim (Supplementary Table 4). At intermediate follow-up, there was no evidence of difference between groups in the relief of UI in one trial [40] (Supplementary Table 4), UI episodes over 24 h in pooled data from two trials with moderate certainty evidence [40,41] (Fig. 2.2.a, Table 3), and UI symptom questionnaires score in one trial [40] (Supplementary Table 4). However, one trial [41] reported improvement in 24-h pad tests, and another trial [40] in UI-specific QoL questionnaires score, favouring PFMT with EStim (Supplementary Table 4). Intragroup comparison showed improvements in UI episodes over 24 h for both groups in three studies [39–41], and for PFMT with EStim in one study [21] when compared to baseline. Furthermore, there was a significant improvement in 24-h pad tests [39], UI symptom questionnaires score [40], neuro-urological QoL questionnaires score [24,25] and UI-specific QoL questionnaires score [24,25,40] for both groups after intervention when compared to baseline. Among these studies, seven [21,24,25,39] reported no data on adverse events and five [41] reported no adverse events (Table 2). For one study [40] one participant reported that the protocol was physically and psychologically demanding 1/10 (10%) and a second participant reported tingling in the posterior right thigh 1/10 (10%) in the PFMT with EStim group (Table 2).

3.2.4. Mixed neurological disorders

Two trials [53,57] included participants with mixed neurological disorders (i.e., MS, SC injury, PD), totalling 39 participants (mean age 54, 56% women) (Supplementary Table 4). No trials were included in the GRADE assessment.

3.3. Methodological quality assessment

The RoB assessment identified two trials [19,42] classified as having overall low RoB. The remaining trials were classified as having some concerns. See Fig. 3 and Supplementary Figure 1.

4. Discussion

4.1. Main findings

This is the first systematic review and meta-analysis of clinical trials evaluating a wide range of conservative interventions for managing UI and UI-specific QoL in neuro-urological disorders. Forty studies were identified including 1745 participants (n = 22 studies) with brain disorders, 422 participants (n = 3 studies) with SC disorders, 545 participants (n = 13 studies) with MS, and 39 participants (n = 2 studies) with mixed neurological conditions, totalling 2751 participants. The populations, conservative interventions, outcomes, and time points differed considerably, limiting meta-analysis. Only studies included in the GRADE analysis will be discussed here.

Table 3
Summary of findings and certainty of evidence assessment using GRADE (16 studies).

	Summary of findings			Certainty of evidence assessment (GRADE)					
	n of Participants (studies)	I^2 %	Effect size (95% CI)	Risk of Bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Publication bias[e]	Certainty of evidence
Relief of UI symptoms									
Brain disorders									
TNS vs no active									
End of treatment	230 (2)	36%	RR 1.12 (0.55 to 2.27)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[f]
Intermediate follow-up	247 (2)	0%	RR 1.12 (0.54 to 2.33)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[f]
UI episodes over 24 h									
Brain disorders									
TNS vs no active									
End of treatment	243 (2)	88%	MD −1.14 (−2.80 to 0.53)	No serious problems	Very serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕OOO VERY LOW[g]
EStim vs no active									
End of treatment	**142 (2)**	**97%**	MD −4.13 (−7.94 to −0.32)	No serious problems	Very serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕OOO VERY LOW[h]
Multiple Sclerosis									
PFMT + EStim vs PFMT									
End of treatment	**117 (3)**	**0%**	MD −0.62 (−1.15 to −0.10)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[i]
Intermediate follow-up	100 (2)	0%	MD −0.19 (−0.60 to 0.22)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[i]
UI symptoms questionnaire									
Brain disorders									
EStim vs no active									
End of treatment	**163 (2)**	**0%**	SMD −0.84 (−1.17 to −0.51)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[i]
Toilet assistance vs usual care									
End of treatment	144 (2)	0%	SMD −0.16 (−0.48 to 0.17)	No serious problems	No serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕⊕OO LOW[j]
Intermediate follow-up	107 (2)	0%	SMD −0.00 (−0.38 to 0.38)	No serious problems	No serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕⊕OO LOW[k]
Neuro-urological QoL questionnaire									
Brain disorders									
Toilet assistance vs usual care									
End of treatment	**192 (2)**	**0%**	MD −3.17 (−6.01 to −0.33)	No serious problems	No serious inconsistency	No serious indirectness	Serious imprecision	Undetected	⊕⊕⊕O MODERATE[f]
Multiple Sclerosis									
PFMT + EStim vs PFMT									
End of treatment	54 (2)	0%	MD −0.21 (−0.52 to 0.11)	No serious problems	No serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕⊕ *OO* LOW[k]
UI-specific QoL questionnaire									
Brain disorders									
TNS vs no active									
End of treatment	43 (2)	68%	MD −6.66 (−16.54 to 3.23)	No serious problems	Serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕OOO VERY LOW[l]
Multiple Sclerosis									
PFMT + EStim vs PFMT									

(*continued on next page*)

Table 3 (*continued*).

	Summary of findings			Certainty of evidence assessment (GRADE)					
	n of Participants (studies)	I^2 %	Effect size (95% CI)	Risk of Bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Publication bias[e]	Certainty of evidence
End of treatment	83 (3)	58%	SMD −0.45 (−1.15 to 0.26)	No serious problems	Serious inconsistency	No serious indirectness	Very serious imprecision	Undetected	⊕OOO VERY LOW[l]

CI = confidence intervals; EStim = electrical stimulation; GRADE = Grading of Recommendations Assessment, Development and Evaluation; MD = mean difference; n = sample size; PFMT = pelvic floor muscle training; QoL = quality of life; RR = risk ratio; SMD = standard mean difference; TNS = tibial nerve stimulation; UI = urinary incontinence.

[a] Risk of bias: downgraded by 1 level if > 25% of the participants were from trials with an overall high risk of bias, and downgraded by 2 levels if > 50% of the participants were from trials with an overall high risk of bias.

[b] Inconsistency: downgraded by 1 level if considerable heterogeneity was presented (i.e., I^2 > 50%), and downgrading by 2 levels if evidence of serious inconsistency (i.e., I^2 >75%).

[c] Indirectness: generalizability of the findings; downgraded by 1 level if the majority of studies were outside the PICO.

[d] Imprecision: we used generic thresholds for dichotomous and continuous outcomes from the GRADE handbook as follows: in cases where studies included relatively few patients and few events, and thus had wide CIs around the estimate of the effect, that is, the results were imprecise.
Dichotomous outcomes: (A) When there was only 1 study or when there was more than 1 study, but the total number of events was less than 100 per study, we downgraded the evidence by 1 level on this criterion. (B) When the 95% CI around the pooled or best estimate of effect included both (i) no effect and (ii) appreciable benefit or appreciable harm, we downgraded the evidence by 1 level. We downgraded the evidence by 2 levels when there was imprecision due to both (A) and (B).
Continuous outcomes: (A) When there was only 1 study or when there was more than 1 study but the total sample size was less than 100 per study, we downgraded the evidence by 1 level. (B) When the 95% CI around the pooled or best estimate of effect included no effect and the CI crossed an effect size of SMD = 0.5 or MD greater than 6 of the scale in either direction, we downgraded the evidence by 1 level. We downgraded the evidence by 2 levels when there was imprecision due to both (A) and (B).

[e] Publication bias, using funnel plots if at least 10 studies examining the same intervention and comparison were included in the same outcome.

[f] Downgraded one level for imprecision: 1/2 studies fewer than 100 participants.

[g] Downgraded two levels for inconsistency: I^2 > 75%, and by one level for imprecision: 1/2 studies fewer than 100 participants.

[h] Downgraded two levels for inconsistency: I^2 > 75%, and by two levels for imprecision: all studies fewer than 100 participants and 95% CI for absolute effects include no effect and appreciable benefit/harm.

[i] Downgraded one level for imprecision: all studies fewer than 100 participants.

[j] Downgraded two levels for imprecision: 1/2 studies fewer than 100 participants and 95% CI for absolute effects include no effect and appreciable benefit/harm.

[k] Downgraded two levels for imprecision: all studies fewer than 100 participants and 95% CI for absolute effects include no effect and appreciable benefit/harm.

[l] Downgraded one level for inconsistency: I^2 > 50%, and by two levels for imprecision: all studies fewer than 100 participants and 95% CI for absolute effects include no effect and appreciable benefit/harm.

4.2. Implications for clinical practice

Although there is no similar reporting of adverse events, conservative interventions were found to have low risk of adverse events.

4.2.1. Brain disorders

There is very low to moderate certainty evidence in favour of EStim compared with no active treatment for UI episodes in 24 h and UI symptoms. These findings provide evidence that EStim may be a treatment option for patients. Our results are consistent with early evidence from systematic reviews reporting a reduction of UI symptoms following EStim in neurological patients [9,58,59]. Toilet assistance may improve specific neuro-urological QoL with moderate certainty evidence. On the other hand (low certainty of evidence) there is not enough evidence to determine whether toilet assistance is more effective than usual care for UI symptoms. Moderate certainty evidence shows that TNS is not superior to no active treatment for relief of UI symptoms in neurological patients. Very-low certainty evidence is uncertain to determine whether TNS is more effective than no active treatment for UI episodes over 24 h and UI-specific QoL. TNS alone therefore might not be sufficient for relief of UI symptoms and might need to be accompanied by other management strategies.

4.2.2. Spinal cord disorders

There were not enough trials to generate sufficiently robust data for a quantitative analysis and certainty of evidence. Nonetheless, a study [33] showed significant improvement in UI symptoms and QoL when comparing multimodal rehabilitation with usual care. This suggests a potentially promising intervention for upcoming clinical trials within this population.

4.2.3. Multiple sclerosis

PFMT with EStim may reduce the number of UI episodes over 24 h (moderate certainty evidence) but did not improve neuro-urological QoL and UI-specific QoL based on low and very low certainty of evidence respectively. Although PFMT is established as a first-line treatment of UI in non-neurological patients [11], its effectiveness in patients with suboptimal pelvic floor function has not been clearly identified. When intravaginal or intra-anal EStim was used in addition to PFMT, studies reported improvement in pelvic floor muscle function [39–41,54]. This improvement may augment the control of muscle function, and enhance proprioception, structural support and have a beneficial effect on detrusor overactivity.

4.2.4. Mixed neurological disorders

There were not enough trials to generate sufficiently robust data for a quantitative analysis and certainty of evidence.

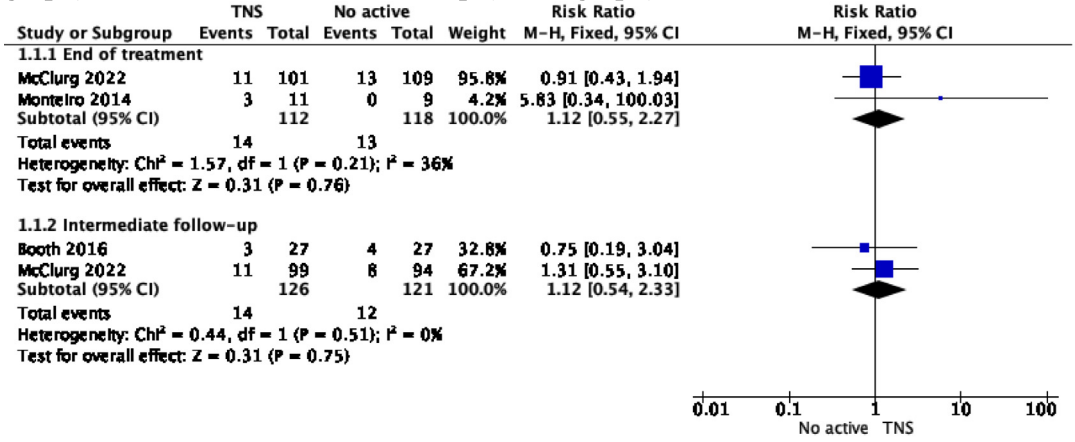
4.3. Strengths and limitations

The present review has covered all neurological disorders, stratified by location and nature of the neurological disease, while also including all conservative interventions. Furthermore, the review incorporated an extensive and comprehensive literature search, maintaining consistent broad study screening across all languages and dates. Methodological and evidence assessments were conducted by independent reviewers following a pre-registered protocol. The review also encompassed clinical trials, which represent the highest level of evidence and patient-important outcomes.

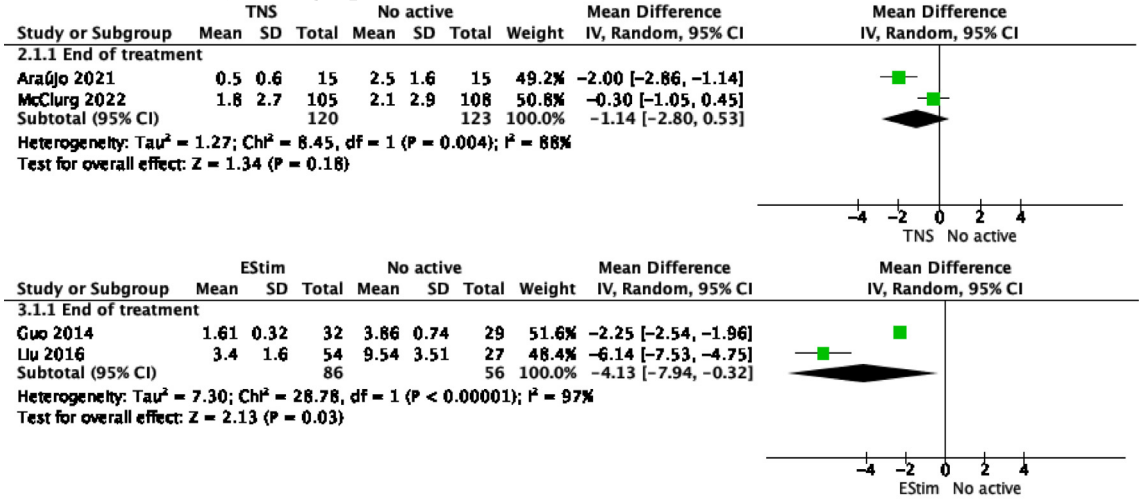
Results should be interpreted with caution due to small sample sizes per trial, especially for SC injuries and MS, incomplete descriptions of interventions, and a high number of unclear RoB domains.

1. Brain disorders

1.a. Relief of UI symptoms – TNS vs no active treatment - at end of treatment period (upper graph) and at intermediate follow-up (lower graph)



1.b. UI episodes over 24 hours – TNS vs no active treatment (upper graph); EStim vs no active treatment (lower graph) – both at end of treatment



1.c. UI symptoms – EStim vs no active treatment – at end of treatment (upper graph); toilet assistance vs usual care – at end of treatment (middle graph) and at intermediate follow up (lower graph)

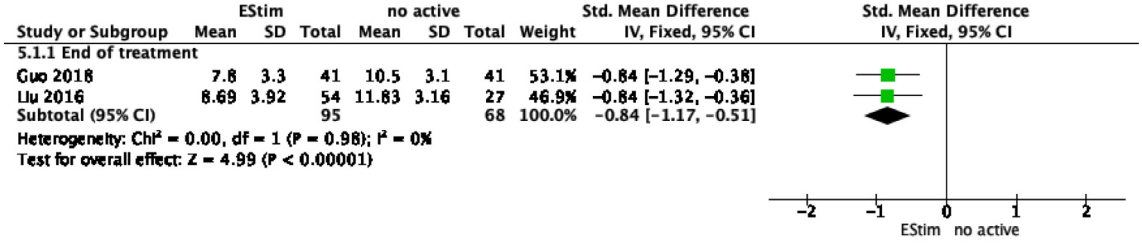
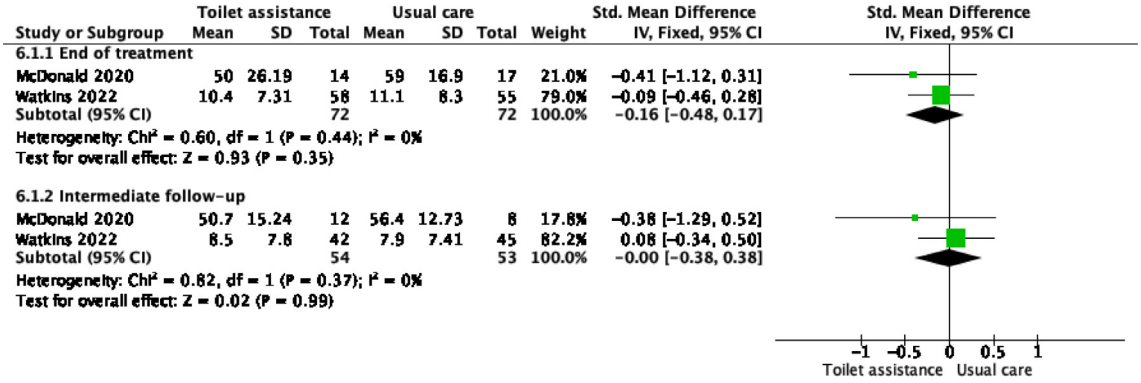
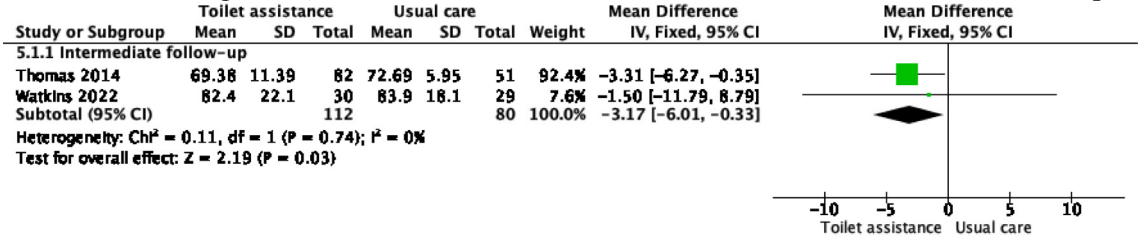


Fig. 2. Forest plots comparing conservative interventions for (1) brain disorders and (2) multiple sclerosis. CI = confidence interval; EStim = electrical stimulation; IV = inverse of the variance; M-H = Mantel–Haenszel; PFMT = pelvic floor muscle training; QoL = quality of life; SD = standard deviation; TNS = transcutaneous tibial nerve stimulation; UI = urinary incontinence.

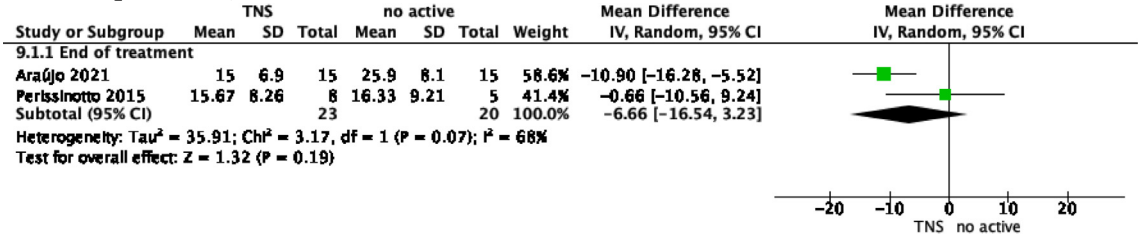
These concerns are particularly prevalent in studies published earlier, specifically between 1990–1997. Additionally, the meta-analysis was underpowered as it was not possible to pool outcome data from trials investigating the same neurological condition, intervention, outcomes, and time-points. The existing evidence is contradictory, and the conclusions drawn from this review emphasize the necessity for more well-designed studies to evaluate first-line conservative management of UI in neurological patients. These studies should utilize self-reported UI relief or improvement, evaluate adverse events, and incorporate condition-specific symptom and QoL measures [11], all with longer-term follow-up. First, considering the challenges associated with conducting trials involving neurological patients and achieving a



1.d. Neuro-urological QoL – toilet assistance vs usual care – at intermediate follow up



1.e. UI-specific QoL – TNS vs no active treatment – at end of treatment



2. Multiple Sclerosis

2.a. UI episodes over 24 hours – PFMT + EStim vs PFMT alone – at end of treatment (upper graph) and at intermediate follow-up (lower graph)

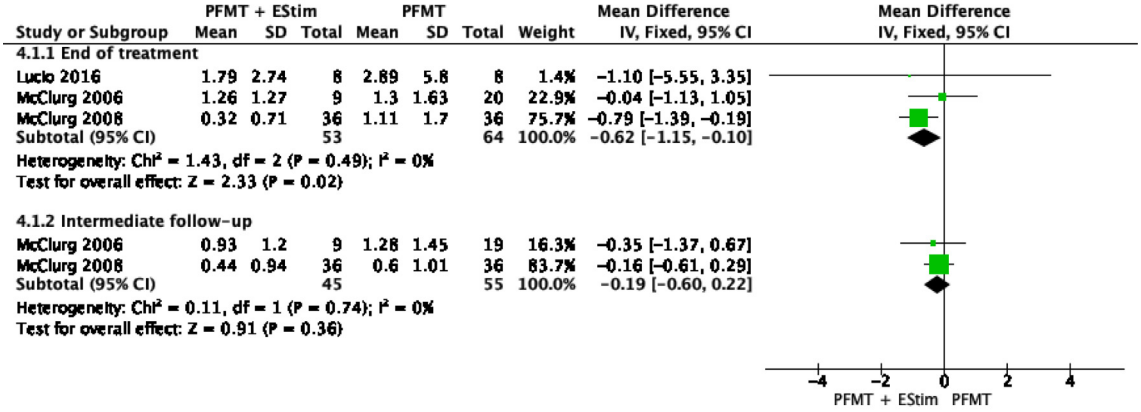


Fig. 2. (*continued*).

substantial sample size, it would be interesting to include a range of neurological disease types categorized by the location of the lesion, as this categorization could potentially influence the pattern of UI. Second, a complete replicable description of the interventions provided to the patients is not consistently reported by authors. Even when reported, the descriptions may lack clarity. However, by neglecting this crucial information, investigators hinder the ability of clinicians and researchers to accurately interpret the findings. Furthermore, the absence of a clear intervention description renders the replication of these studies and, consequently, the interventions themselves impractical. Third, exploring combined interventions could prove beneficial for neurological patients. It is important to consider that certain interventions alone may not yield significant benefits for the participants. However, when combined with other interventions, they may yield useful results given the complexity of the patient population. This consideration is particularly important, as conservative interventions typically demonstrate low rates of adverse events and can be easily self-administered at home. In the present review, the use of combined interventions, such as PFMT with EStim, when compared to PFMT alone, leads to an improvement in UI frequency. Fourth, the included studies exhibit

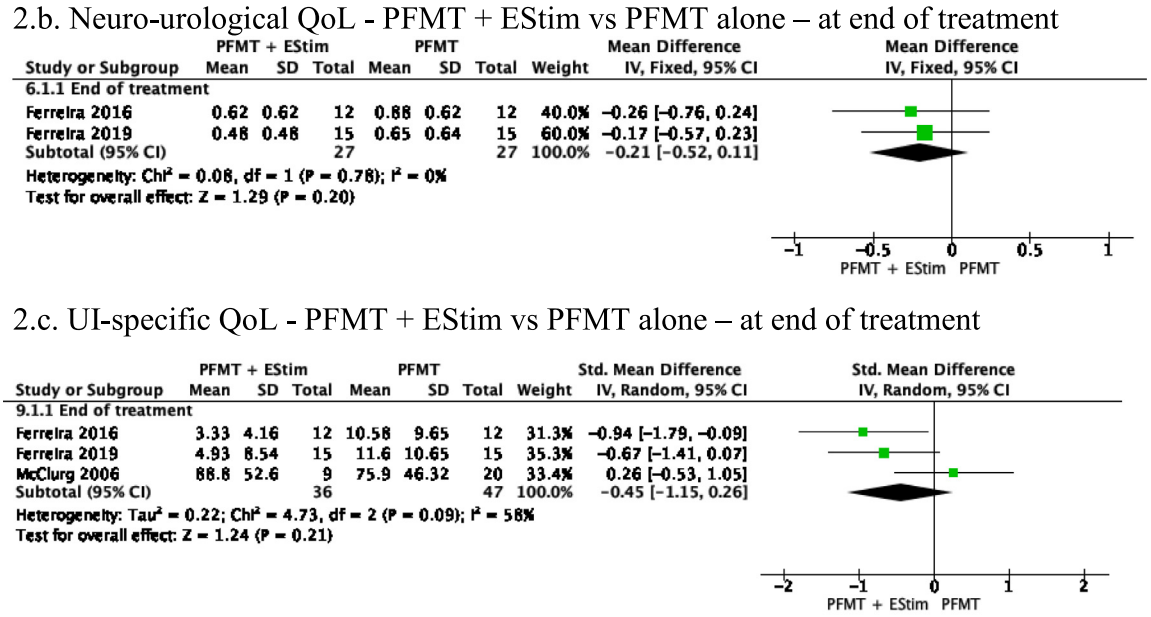


Fig. 2. (*continued*).

a significant variability in the assessed outcomes, encompassing both the types of outcomes and the timing of outcome assessment. Currently, there is no standardized core outcomes set for UI in patients with neurological conditions. Nevertheless, it is plausible that research utilizing patient-reported, validated, reproducible, and widely accepted instruments to assess participants' response to treatment and long-term effects would greatly benefit patients, clinicians, and researchers in managing and addressing incontinence. As an alternative for measuring the outcomes, the Standardization Committee of the International Continence Society has proposed the following outcomes for women with UI: patient's observations (symptoms), quantification of symptoms (e.g., urine loss), clinician's observations (anatomical and functional), QoL, and socioeconomic measures [60]. Furthermore, another limitation of the reviewed studies included is the inconsistent reporting of data on adverse events. For the few studies that did report adverse events, standard terminology was not used. This lack of uniformity extended to the different forms of outcome measurements used during the study and the way in which these events were reported. Trialists should pre-specify and include more clinically relevant adverse events to conservative treatments for both clinicians and patients (e.g., pain, discomfort, fatigue, UTI, bladder catheterization). Following these recommendations will help to improve the quality, clinical relevance, and credibility of trials evaluating the effectiveness of conservative treatments for neurological patients, ultimately improving readability for clinicians and researchers.

5. Conclusion

This systematic review presents some evidence suggesting that conservative options for patients with brain disorder may include EStim and toilet assistance. Additionally, PFMT combined with EStim may offer benefits for individuals with MS. These findings are crucial for informing evidence-based decisions for healthcare practitioners and decision-makers. However, the overall evidence for other conservative interventions remains uncertain given the lack of evidence for conservative interventions in SC disorders and mixed neurological patients. To address this evidence gap, further trials, particularly larger, high-quality and adequately powered RCTs are necessary.

CRediT authorship contribution statement

Giovana Vesentini: Conceptualization, Protocol design and registration, Data collection and extraction, Data analysis, Data interpretation, Writing – original draft, Critical revision. **Jalesh Panicker:** Writing – original draft, Critical revision. **Sheila A. Wallace:** Acquire data, Critical revision. **Chantal Dumoulin:** Conceptualization, Protocol design and registration, Data collection and extraction, Data interpretation, Writing – original draft, Critical revision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Giovana Vesentni reports financial support was provided by University of Montreal. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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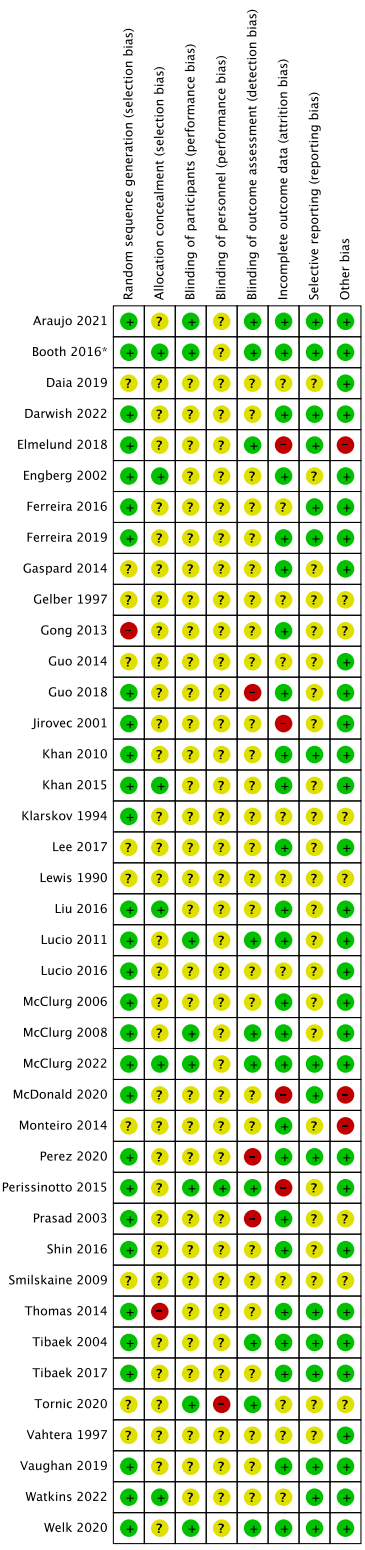

Fig. 3. Risk of bias summary: reviewer's judgements about each risk of bias item for each included study. *Other bias: classified according to the information provided about funding source and/or baseline comparability (age, urinary incontinence severity).

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.cont.2024.101222. Supplementary Table 1. References to studies included in this review.

Supplementary Table 2. Characteristics of ongoing studies.

Supplementary Table 3. Summary of the protocol interventions in the included studies.

Supplementary Table 4. Effect sizes for outcome measures for all time-points available in neurological patients.

Supplementary Figure 1. Risk of bias graph.

Supplementary Appendix 1. Literature search methods.

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