Benefits of cannabis in treating lower urinary tract symptoms: A scoping review

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ABSTRACT

Introduction: Anticholinergics and β3-agonists remain the mainstay for bladder dysfunction but are limited by side effects and poor adherence. Cannabinoids are a potential alternative given receptor distribution in bladder control pathways. Early studies suggested that cannabis may demonstrate benefits in overactive bladder (OAB) and lower urinary tract symptoms (LUTS), but findings are limited by small sample sizes and cross-sectionality. This review investigates the therapeutic utility of cannabis and its impact on LUTS.
Methods: This scoping review was conducted following Cochrane and PRISMA guidelines. Eligible studies included adults with OAB symptoms due to neurogenic disease, benign prostatic hyperplasia (BPH), or cystitis, treated with cannabis vs. placebo, no treatment, or active therapies. Outcomes included urinary function and quality of life. Databases searched included MEDLINE, EMBASE, and CENTRAL. Non-English studies were excluded.
Results: From 998 abstracts, 31 full-text articles were reviewed and 12 were included. Studies showed consistent evidence on the effectiveness of cannabis-based therapies for managing LUTS, particularly in patients with multiple sclerosis (MS). Cannabis interventions, including THC, CBD, and combined formulations, showed some improvements in incontinence episodes, frequency, and quality-of-life measures. Mild adverse effects, including dizziness and dry mouth, were common (2−18%) and sometimes led to treatment discontinuation. Nine of 12 studies were done on MS populations, and only three studies were randomized controlled trials.
Conclusions: Evidence for the benefits of cannabis in treating LUTS is limited and largely observational. While preliminary findings are encouraging, randomized trials focusing on patient-centered outcomes are needed to clarify its role in clinical practice.

INTRODUCTION

Lower urinary tract symptoms (LUTS) encompass various manifestations of bladder dysfunction that can significantly impact quality of life, and include urgency, frequency, nocturia, and urgency incontinence.[1] Bladder dysfunction is prevalent and challenging to manage, especially when associated with advanced age and neurogenic conditions such as multiple sclerosis (MS). Current pharmacotherapy is primarily centered on anticholinergic agents and β3-agonists. However, anticholinergics are associated with adverse effects, including dry mouth, constipation, and cognitive impairment, thereby limiting their tolerability and long-term adherence.[2,3] While β3-agonists have better side effect profile compared to anticholinergics, adherence rates remain low.[4,5]

Both recreational and medicinal use of cannabis and its associated pharmacologic products, has become widespread, especially following its legalization in Canada and parts of the United States. This increased availability has led to a surge in patient-driven exploration of cannabis as a therapeutic option, not only for chronic pain and neurological disorders but also for a range of urological symptoms.[6] The active compounds of cannabis, particularly delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), exhibit anti-inflammatory, analgesic, and spasmolytic properties, suggesting they may demonstrate potential utility in treating LUTS.[7,8]

The potential therapeutic benefits of cannabis for LUTS have been explored in several clinical studies. Two randomized controlled trials found that cannabis-based medicinal extracts significantly improved bladder symptoms, including reduced urinary urgency, frequency, and incontinence episodes in patients with MS.[9,10] Moreover, an observational study utilizing data from the National Health and Nutrition Examination Survey revealed that regular THC users reported significantly fewer LUTS compared to non-users, suggesting a protective effect of cannabis on urinary symptoms in the general population.[11] While these findings are promising, existing literature remains limited in scope and scale, underscoring the necessity for further comprehensive studies to clarify cannabis's role and efficacy in managing LUTS. The aim of this scoping review was to evaluate the available evidence surrounding the therapeutic use of cannabis and its association with LUTS in patients with urological conditions, particularly those with overactive bladder (OAB).

METHODS

The scoping review was completed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping review (PRISMA- ScR) checklist.[12]

Search strategy

A comprehensive search for clinical studies on Cannabis and LUTS through medical databases including MEDLINE, EMBASE and Cochrane CENTRAL was completed in March 2026 References from review articles and those in our initial search were manually searched for additional sources. The complete search strategy and keywords used for each database are detailed in APPENDIX 1.

Study eligibility

Studies were included if they met the following criteria: 1) included adult patients with any urologic disease or voiding dysfunction including storage-associated LUTS disorders treated with cannabis or cannabis-based pharmacotherapy and 2) reported on any urinary symptom outcome measures or health related quality of life measures. Study types, such as randomized controlled trials, prospective or retrospective comparative studies, single group follow-up reports, retrospective cohorts, and cross-sectional studies, were included in this review. Non-English studies, conference abstracts, case reports, case series, animal studies and studies focusing on pediatric populations were excluded.

Screening

Two blinded reviewers (AC, JK) independently screened titles, abstracts and full-text manuscripts for included studies using Covidence Systematic Review Software (Veritas Health Innovation, Melbourne, Australia).[13] Disagreements were resolved by consensus and a third investigator (UB) when necessary.

Data extraction and analysis

Two authors (AC, JK) extracted data from all articles. One reviewer extracted the information, and the second reviewer counter-verified the accuracy of the extracted data which included study design, participants and setting, intervention(s), outcome measures and results. Outcomes included evidence on the association of cannabis with its use for symptom management in patients with LUTS.

RESULTS

Study identification

A total of 1272 studies were identified in our initial search, of which 274 duplicates were removed, leaving 998 studies for screening. After title and abstract screening, 967 studies were excluded based on inclusion and exclusion criteria and 31 studies full text articles were assessed for eligibility. 19 articles were excluded after full text review given they did not meet the study type inclusion criteria as they were primarily reviews and conference abstracts with no final paper publication. A total of 12 studies were included in this scoping review (Figure 1).

Population characteristics

Of the 12 included studies that assessed the use of cannabis in treating LUTS, nine of them were focused on MS patients, with two studies [11,14] looking at patient data from the National Health and Nutrition Examination Survey (NHANES) database and one study looking at patients attending a neurological rehabilitation clinic.[8] Nine studies were observational in nature, including prospective, retrospective, cross-sectional, and single-group follow-up designs, with the remaining three studies being randomized controlled trials.[8–10]

Treatment characteristics

Cannabis was administered as an oromucosal THC/CBD spray (Sativex/nabiximols) in six studies. Two studies [8,15] involved administration of cannabis as a sublingual THC and/or CBD spray and three cross-sectional studies [11,14,16] included self-reported patient cannabis use. Primary outcome measures varied across the studies and included incontinence diaries [9,10], LUTS questionnaires [11,15,16], Overactive Bladder Symptom Score (OABSS) [14,17], International Prostatic Symptoms Score (IPSS) [18,19] and Urinary Numerical Rating Scales (uNRS).[8,20,21]

Across all included studies, LUTS improved in patients who using any form of cannabis except in the study by Zhu et al. (2023), in which cannabis use increased the incidence and severity of overactive bladder symptoms.[14] However, a significant benefit was mostly seen in observation or open-label trials and not randomized controlled trials (RCTs). In both Kavia et al. (2010) and Wade et al. (2003), the improvements found in the primary endpoints of daily incontinence episodes compared to placebo and improved bladder control were not found to be significant ($p=0.569$ and $p >0.005$ respectively). While cannabis extract and THC significantly reduced urge incontinence episodes by 38% and 33% respectively (compared to 18% for placebo; $p=0.005$ and $p=0.039$) in the RCT by Freeman et al. (2006), these results were limited by substantial missing data, with over 40% of patients failing to provide complete urinary diaries.

Conversely, observational and open-label trials consistently reported broad symptomatic and objective improvements. [15,17,19] Significant reductions were observed in subjective symptom scores such as the OABSS ($p=0.001$) and IPSS ($p=0.0000$), alongside objective urodynamic gains including reduced post-void residual (PVR) volume ($p=0.016$) and improved maximum detrusor pressure ($p=0.0171$). [17,19] Finally, results from large-scale population data were contradictory; cross-sectional analysis of the NHANES database by Fantus et al. (2018) concluded THC use was protective against LUTS (OR 0.55), while a subsequent analysis of the same database by Zhu et al. (2023) identified marijuana as an independent risk factor for OAB (OR 1.39) and increased severity of symptoms (OR 1.45).

Safety

The safety and tolerability of cannabis medicinal extracts were mixed. There were no significant changes to blood work [10,15] or deaths reported but adverse events were common, occurring in up to 42% of participants.[18] Reasons for stopping cannabis use were mainly attributable to side effects such as dizziness and fatigue. Other side effects mentioned included paranoia and depression. Discontinuation rates ranged from 6.3 to 36.2%. [10,15,18,20] In comparison, the study by Kavia et al. (2010) reported that 8.8% of participants in the placebo arm discontinued treatment.

Table 1 summarizes the study population, study design, outcome assessment and findings of the included studies. Table 2 summarizes the discontinuation rates and adverse events reported in the included studies.

DISCUSSION

As interest in the therapeutic use of cannabis for LUTS increases, a deeper understanding of the available evidence is necessary to support clinical decision making. LUTS and OAB have multifactorial causes and continue to carry a significant symptom burden to many patients, posing as a therapeutic challenge. Multiple animal studies and clinical trials haves suggested that cannabinoids may help with LUTS and provide a viable treatment alternative [2,22,23] which underscore the need for further studies to determine efficacy across urological conditions and patient populations.

Our review found that the use of cannabis in patients experiencing LUTS demonstrated promising symptomatic benefits, particularly in populations with MS-associated storage symptoms. Several clinical studies included in this review revealed that oral administration of cannabis extracts, predominantly THC and CBD, effectively improved bladder symptoms in clinically stable adult MS patients with refractory neurogenic detrusor overactivity.[8–10,19] Interestingly, contradictory findings emerged in a study by Zhu et al. (2023), in which regular cannabis use correlated with an increased incidence and severity of overactive bladder symptoms and nocturia. These results contrast directly with the findings of the study by Fantus et al. (2018), who analyzed the same NHANES database but concluded cannabis use may confer a protective effect against LUTS. The discrepancies between these studies could be attributed to differences in cannabis use, targeted populations, and outcome measures, highlighting the complexity of cannabis role in treating LUTS.

Many studies chose a sublingual or oromucosal spray formulation of cannabis for testing treatment effect given its rapid and predictable rate of absorption compared to oral administration which is often subject to unpredictable bioavailability in the gastrointestinal tract.[8,15] This mode of delivery, while central in allowing patients to self-tritate doses and balance symptomatic relief against intoxication side effects, led to a wide range of reported doses ranging from 1 to 39 in the study by Brady et al. (2004). Although this highlights the high degree of inter-individual variability in cannabinoid sensitivity, current research is limited by a lack of standardised uniform dosing schedules. [11,16] Future studies should aim to determine the minimum effective doses and specific dosing schedules to establish symptom relief while minimizing side effects.

The safety and tolerability profiles of cannabis and associated pharmaceuticals have also emerged as critical themes in this review. While cannabis demonstrates potential in managing spasticity-associated bladder symptoms, its risk profile warrants careful evaluation. Short-term adverse effects include mood alterations, memory issues, and possibly psychotic episodes, while long-term consequences may include neurodevelopmental and psychological sequelae, such as depression and paranoia.[24] Cannabis has also been associated with negative impacts on systemic health, including cardiovascular, gastrointestinal, reproductive, and respiratory dysfunction. Particularly relevant to urology is a potential association between regular cannabis use and chronic kidney disease.[25,26]

This scoping review indicated that cannabis demonstrates a mixed safety profile, with some studies reporting significant adverse event rates. For instance, Paolicelli et al. (2016) noted that adverse events occurred in 40.2% of their study participants, resulting in discontinuation of the therapy in 36.2% of patients; the most common adverse were being dizziness and fatigue. Freeman et al. (2006) reported predictable adverse effects that were generally well-tolerated, while Sacco et al. (2022) reported a similar tolerability profile, with a high continuation rate of 93.7% after 12 weeks. These findings underscore the necessity for clinicians to weigh therapeutic benefits against potential risks, especially in populations vulnerable to cognitive and psychiatric complications. Likewise, trials of non-psychoactive cannabinoids, like CBD, may be particularly promising because of their higher tolerability profile.

Several limitations within the included studies must be considered. Although LUTS encompass a wide range of urological conditions, most of the literature found on this subject was centered on MS patients without significant cardiovascular, psychiatric, or cognitive comorbidities. Despite examining the outcomes of cannabis therapy in LUTS, the large heterogeneity of included studies and over reliance on papers with neurogenic dysfunction involving MS patients limit the generalizability the findings and may not accurately represent the benefit of cannabis in treating the general population of patients suffering from LUTS or OAB. [27,28] Additionally cross-sectional analyses using the NHANES database inherently lack the capacity to establish causality or temporal relationships due to their observational nature, and potential biases such as under-reporting cannabis usage due to cannabis's illicit status during data collection could skew results. Furthermore, included randomized controlled trials also displayed methodological limitations. For instance, Freeman et al. (2006) had significant baseline symptom imbalances and substantial missing data. Kavia et al. (2010) demonstrated improvements only in secondary outcomes without significant changes in primary LUTS measures as the study failed to meet its primary endpoint of a statistically significant reduction in daily incontinence episodes. There is a clear need for well-designed, adequately powered randomized controlled trials to rigorously test cannabinoid treatments for LUTS.

There is a clear need for well-designed, adequately powered randomized controlled trials that directly address patient-important outcomes such as quality of life. Such trials must extend beyond the overrepresented MS population to encompass broader LUTS etiologies including idiopathic OAB, benign prostatic hyperplasia and interstitial cystitis, thereby enhancing generalizability. Future research should also standardize outcome assessment and reporting methodologies to enhance comparability across studies, addressing issues such as varied questionnaires and analytical approaches. Finally, comprehensive long-term efficacy and safety evaluations of specific cannabinoid formulations (THC, CBD, and combinations) are crucial to clarify their definitive role in LUTS management, building on initial suggestions of anti-inflammatory, analgesic, and spasmolytic properties. Addressing these gaps will provide the robust evidence necessary to inform clinical decision-making and optimize therapeutic strategies for LUTS.

CONCLUSIONS

This scoping review found that cannabis-based therapies may offer symptom relief for certain LUTS, primarily for patients with neurogenic bladder conditions such as those secondary to MS. However, the variability in outcomes and reported adverse effects indicates a cautious approach and emphasizes the need for well designed, adequately powered randomized controlled trials to rigorously test cannabinoid treatments for LUTS.

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FIGURES AND TABLES

Figure 1. PRISMA flow diagram. The PRIMSA flow diagram details our search and selection process and shows the reasons papers were excluded.

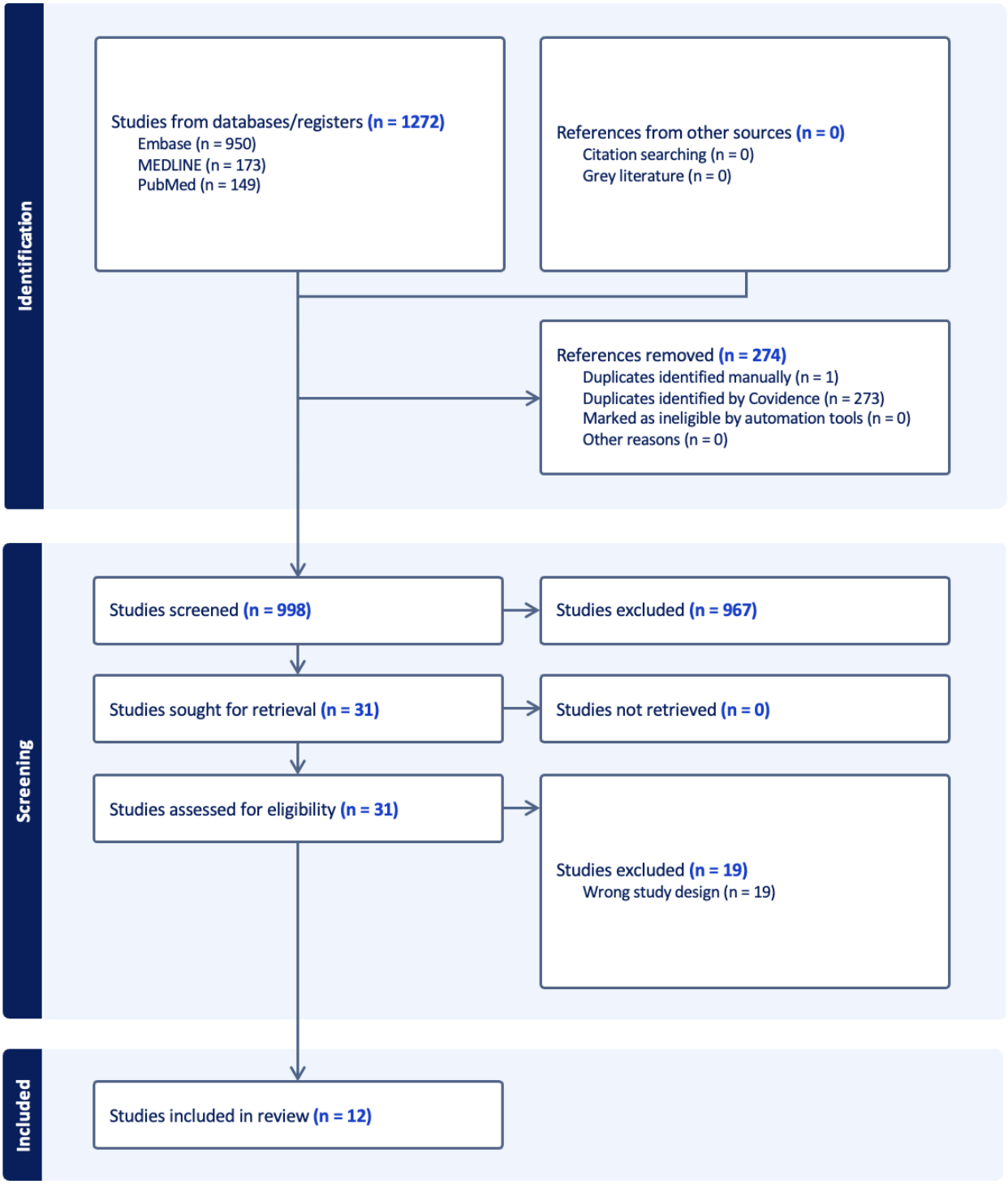

Table 1. Summary of studies on cannabis and lower urinary tract symptoms (LUTS)							
Reference	**Country**	**Study design**	**Sample size (n)**	**Patient population/ characteristics (mean age ± SD)**	**Intervention/ exposure**	**LUTS-specific outcomes measured**	**Key LUTS-related findings**
Brady et al, 2004	U.K.	Open Label Trial	21	Advanced MS patients (Kurtzke score ≤ 6.5) with persistent LUTS unresponsive to conventional treatments and confirmed detrusor overactivity. (Mean age: 48, Range: 31-64)	THC/CBD extract (2.5 mg each per spray) for 8 weeks, then THC-only extract (2.5 mg per spray) for 8 weeks	Daily incontinence episodes, volume of incontinence, nocturia, daytime urinary frequency, total voided volume, catheterized volume, urinary incontinence pad weights	Significant decrease in daily incontinence episodes, volume of incontinence, nocturia, and daytime urinary frequency on both extracts. Significant decrease in daily total voided, catheterized, and urinary incontinence pad weights. Cannabis-based medicinal extracts were safe and effective for urinary and other problems in this population.
Fantus et al, 2018	U.S.	Cross-sectional Study (NHANES database)	3037 men	Men aged 20-59 who completed urinary and substance abuse questionnaires. LUTS defined as ≥2 symptoms (nocturia ≥2, hesitancy, incomplete emptying, or incontinence).	Self-reported regular THC use (at least once per month in past 30 days)	Prevalence of LUTS, individual LUTS symptoms	Regular THC users significantly less likely to report LUTS (OR 0.55; P < .01) compared to non-regular users. No statistically significant difference in the prevalence of individual LUTS symptoms.
Freeman et al, 2006	U.K.	Randomized Controlled Trial	630	MS patients (18-64 years) with clinically	THC capsules (2.5 mg Δ9-THC	Incontinence episode rates	Both cannabis extract (38% reduction) and THC (33%

		(RCT) (CAMS substudy)		definite MS, problematic spasticity. Specifically focused on urge incontinence.	equivalent) or Cannabis extract capsules (2.5 mg Δ9-THC equivalent, 1.25 mg CBD)		reduction) significantly reduced adjusted incontinence episode rates compared to placebo (18% reduction). Both active treatments showed significant effects over placebo (p=0.005 for cannabis extract; p=0.039 for THC).
Kavia et al, 2010	U.K.	RCT	135	Adults with MS and OAB symptoms unresponsive to first-line therapies (e.g., anticholinergics). (Mean age: 47.7 ± 10.3)	Sativex (nabiximols) as an add-on therapy	Change in incontinence episodes (primary); nocturia episodes, overall bladder condition (OBC), number of voids/day, Patient's Global Impression of Change (PGIC), daytime voids, Incontinence Quality of Life (I-QOL)	Primary endpoint (incontinence episodes) showed little difference. Four out of seven secondary endpoints significantly favored Sativex: nocturia episodes (p=0.010), OBC (p=0.001), number of voids/day (p=0.001), and PGIC (p=0.005). Daytime voids also significantly improved (p=0.044).
Kim-Fine et al, 2021	Canada	Cross-sectional Study	775	People with MS or Clinically Isolated Syndrome (CIS) aged >18. (Mean age: 51.1 ± 12.6)	Self-reported cannabis consumption in the past 3 months	Perceived benefits on bladder symptoms (urinary frequency, urgency, leakage, pad use, bladder emptying)	Among those using cannabis for bladder symptoms, 89.5% reported "better" bladder symptoms. Cannabis consumption was associated with a two-fold increased odds of reporting

							improvement in urinary frequency, urgency, bladder leakage and wetness, pad use, and bladder emptying.
Maniscalco et al, 2018	Italy	Observational Study	15	MS patients with moderate-to-severe spasticity and OAB symptoms refractory to conventional treatments (antispastic and anticholinergic). (Mean age: 56.1 ± 8.6)	THC/CBD oromucosal spray as add-on medication	Overactive Bladder Symptom Score (OABSS); urodynamic measures (postvoid residual volume (PVR), bladder volume at first desire (BVFD), cystometric capacity (CCmax), detrusor pressure max (Pdet max))	THC/CBD treatment successfully reduced OAB symptoms (p = 0.001). PVR was significantly reduced (p = 0.016). BVFD and CCmax showed increases, but not statistically significant.
Paolicelli et al, 2016	Italy	Observational Cohort Study (40-week postmarketing experience)	102	MS patients treated with THC/CBD spray (Sativex). (Mean age: 48.8 ± 10.4)	THC/CBD spray (Sativex)	International Prostatic Symptoms Score (IPSS) for bladder dysfunction	Among 46 patients with bladder dysfunction, the IPSS score showed a significant improvement (P = .001).
Sacco et al, 2022	Switzerland	Observational Cohort Study	95	MS patients (McDonald 2017 criteria) starting nabiximols treatment. (Mean age: 53)	Nabiximols (titrated up to 10 sprays/day)	Numerical Rating Scale for urinary symptoms (uNRS)	Urinary symptoms (uNRS) significantly decreased after 12 weeks of treatment (p < 0.001).
Torriclerici et al, 2023	Italy	Prospective Cohort Study	31	MS patients (RRMS, SPMS, PPMS) with anamnestic report of urinary disturbances. (Mean age: 51.3 ± 7.9)	Nabiximols oromucosal spray (THC and CBD)	IPSS total score, subscores, IPSS Quality of Life (QoL); urodynamic parameters (detrusor	Mean IPSS total score, its subscores, and IPSS QoL significantly decreased from baseline to 6 months (p = 0.000). Pdet improved

						pressure (Pdet), cystometric capacity (CCmax))	significantly ($p = 0.0171$). CCmax marginally changed ($p = 0.0494$). All patients with overactive bladder showed improvement in urodynamic assessment based on a significant reduction of Pdet ($p = 0.0138$).
Vermersch, 2016	Italy	Prospective Cohort Study	433	MS patients (age ≥ 18) with moderate-to-severe MSS, prescribed THC:CBD oromucosal spray. (Mean age: 50.4 ± 10.4)	THC:CBD oromucosal spray (Sativex)	Number of urinary incontinence events per week	Statistically significant improvements in various symptoms, including the number of urinary incontinence events per week ($p < 0.0001$).
Wade et al, 2003	U.K.	Series of Double-Blind, Randomized, Placebo-Controlled Single-Patient Cross-over Trials	24	Patients with a neurological diagnosis and troublesome symptoms, including impaired bladder control, unresponsive to standard treatments.	Sublingual cannabis medicinal extracts (THC-rich, CBD-rich, and 1:1 THC:CBD)	Visual analogue scales for symptoms	Impaired bladder control was improved by CME in some patients with these symptoms.
Zhu et al, 2023	U.S.	Cross-sectional Study (NHANES database)	18736	Participants aged 20-59. Regular marijuana users defined as using at least once a month for over a year.	Self-reported marijuana exposure	Relationship between marijuana use and overactive bladder (OAB) symptoms and severity	Marijuana exposure may be an independent risk factor for OAB (OR 1.39; 95% CI, 1.16-1.66). Associated with the severity of OAB (OR 1.45; 95% CI, 1.30-1.60).

							Consistent effects across all frequencies of regular use.

AEs: adverse events; BVFD: bladder volume at first desire; CBD: cannabidiol; CC: cystometric capacity; CCmax: cystometric capacity maximum; CIS: clinically isolated syndrome; CME: cannabis medicinal extracts; CAMS: cannabinoids in multiple sclerosis; I-QOL: incontinence quality of life; IPSS: International Prostatic Symptoms Score; LUTS: lower urinary tract symptoms; MS: multiple sclerosis; MSS: multiple sclerosis spasticity; NA: not applicable; NHANES: National Health and Nutrition Examination Survey; NRS: numerical rating scale (generally, or specific applications like spasticity NRS); OAB: overactive bladder; OABSS: Overactive Bladder Symptom Score; OBC: overall bladder condition; OR: Odds Ratio; Pdet: Detrusor Pressure; PGIC: Patient's Global Impression of Change; PPMS: primary progressive multiple sclerosis; PVR: postvoid residual volume; QMax: bladder compliance; QoL: quality of life; RCT: randomized controlled trial; RRMS: relapsing-remitting multiple sclerosis; SD: standard deviation; SPMS: secondary progressive multiple sclerosis; THC: Δ9-tetrahydrocannabinol; UDS: urodynamic study; uNRS: numerical rating scale for urinary symptoms/

Table 2. Summary of discontinuation rates and adverse events reported

Study (first author, year)	Discontinuation rate	Types of adverse events (AEs) reported
Brady et al, 2004	Approximately one quarter to one third of recruited participants did not complete the initial 16-week course.	Symptoms typical of intoxication (drowsiness, disorientation, altered time perception); hallucinations (visual and auditory); worsening of dry mouth; and mouth soreness at the drug administration site.
Fantus et al, 2018	Not reported (cross-sectional study).	Not reported
Freeman et al, 2006	Not reported	Urinary tract adverse events, primarily Urinary Tract Infections (UTIs). Rare instances of urinary retention were reported in both active and placebo groups.
Kavia et al, 2010	The overall withdrawal rate was approximately one in eight subjects (12.6%), with a slightly higher incidence in the active treatment group. Withdrawal specifically due to treatment-related adverse events was low (7 active vs 3 placebo).	Central Nervous System (CNS)-related effects (most commonly dizziness, as well as disorientation and dissociation); headache; vomiting; nausea; diarrhea; weakness; pharyngitis; nasopharyngitis; feeling drunk; constipation; balance impaired; paraesthesia; cystitis; and serious events like a possible transient ischemic attack or haemorrhagic cystitis.
Kim-Fine et al, 2021	Not reported (cross-sectional study).	Not reported
Maniscalco et al, 2018	The analyzed cohort focused only on the 15 patients completing the 4-week protocol. Only one patient reported an AE but maintained adherence.	Only one mild adverse event was reported: dizziness.
Paolicelli et al, 2016	Overall discontinuation was just over one third (36.2%) during the 40-week observation period. Adverse event incidence contributed significantly, with 7.8% stopping solely due to AEs in the first month.	Dizziness, Asthenia (weakness/lack of energy), Bewilderment (confusion), Drowsiness, Dysgeusia/oral hyperalgesia (altered taste/mouth pain), Anxiety, Decline in attention and/or concentration, Diarrhea, Alterations of dental enamel, Lack of appetite, and Seizures.

Sacco et al, 2022	The discontinuation rate over the 12-week study was low (6.3%), primarily driven by adverse side effects.	Dizziness, confusion/ideomotor slowing, fatigue, and pharyngeal irritation.
Torriclerici et al, 2023	The withdrawal rate by the 6-month endpoint was high, exceeding 40%. Adverse events were the primary reported cause of treatment withdrawal (7 patients, 22.5% of the enrolled cohort).	CNS symptoms (disorientation, speech disturbance, vertigo); local/allergic reactions (oral mucosal irritation, lip edema, skin rash); tachycardia; and spasticity worsening.
Vermersch, 2016	Overall patient attrition by 3 months was over one third. Discontinuation specifically due to adverse drug reactions was low (6.3% of the safety population).	Most common reported adverse drug reactions (ADRs) were dizziness, confusion/confusional state, asthenia, somnolence (sleepiness), and fatigue. Other reported events included balance disorder, brain stem syndrome, dysarthria, headache, memory impairment, mental impairment, paraesthesia, slow speech, tremor, anxiety, apathy, bradyphrenia, nervousness, suicidal ideation, abdominal pain, diarrhea, dry mouth, nausea, pain, tachycardia, back pain, and dyspnoea.
Wade et al, 2003	The withdrawal rate during the initial phase was approximately one in six (16.7%). Withdrawal reasons included lack of therapeutic window (benefit without intoxication) and acute side effects (vasovagal episode, local irritation).	Symptoms of intoxication; central nervous system effects such as dizziness and somnolence (sleepiness); transient hypotension; headache; nausea; vomiting; diarrhoea; sore mouth/sublingual burning sensation; fall; cough; impaired balance; fatigue; influenza-like symptoms; thirst; disturbance in attention; hypoaesthesia; anxiety; and depressed mood.
Zhu et al, 2023	Not reported (cross-sectional study).	Not reported