Outcomes of combined behavioural, physical and pharmacological therapy compared to a monotherapy approach for overactive bladder syndrome: A systematic review and meta-analysis

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Abstract. Overactive bladder (OAB) syndrome is a prevalent condition characterised by urinary urgency, frequency and nocturia, and is often accompanied by incontinence. OAB is typically managed through pharmacological interventions, such as antimuscarinics or β_3-adrenoceptor agonists, and behavioural therapies, such as bladder training and pelvic floor muscle exercises. However, the effectiveness of combined pharmacological and behavioural approaches remain uncertain. Therefore, the present systematic review and meta-analysis aimed to evaluate the outcomes of combined therapies for the management of OAB. A systematic search was conducted across the PubMed, ScienceDirect and Cochrane Library databases for studies published between January, 2000 and December, 2023. Eligible studies included randomised controlled trials and cohort studies reporting on outcomes of combined pharmacological and behavioural therapies (≥8 weeks) in adult patients with OAB. Data on study design, patient demographics, treatment regimens, follow-up duration, outcome measures and adverse effects were extracted. The quality of the studies was evaluated using established assessment tools. The present study analysed four studies comprising 830 participants. The results of the meta-analysis indicated no significant differences between combination therapy and monotherapy in reducing voiding frequency [mean difference (MD), 0.35; 95% confidence interval (CI), -0.23 to 0.93; P=0.24] and nocturia episodes (MD, 0.04; 95% CI, -0.18 to 0.27; P=0.70). However, combined therapies demonstrated greater symptom improvement and adherence in individual studies, particularly for the urgency and quality of life variables. Adverse events were mild and primarily related to pharmacological agents. Although the results of the meta-analysis suggest comparable efficacy between the combined and single therapies in reducing voiding frequency and nocturia episodes, combined therapies exhibit potential benefits in overall symptom relief, treatment adherence and quality of life. Future research is required to investigate the long-term effects of combined therapies and explore strategies to enhance adherence to treatment.

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Introduction

Overactive bladder (OAB) syndrome is defined by the International Continence Society (ICS) as a symptom of urinary urgency, with or without incontinence. It is usually associated with nocturia and urinary frequency (1). OAB is divided into two types: i) Dry, when urinary incontinence is not present; and ii) wet, when it is present (2). Epidemiological studies have consistently demonstrated that OAB is common among both men and women, with prevalence increasing with age and symptom profiles differing by sex (3,4). However, a study conducted in Indonesia revealed no difference in prevalence between the two sexes, suggesting the need for a different approach to OAB in the Indonesian population (4).

In both men and women, lower urinary tract symptoms (LUTS) associated with OAB can substantially impair daily functioning and overall quality of life. In men, OAB has been linked to a higher prevalence of sexual dysfunction, particularly reductions in erectile function, sexual activity and sexual satisfaction (5). Similar effects have been observed in women: The cross-sectional study by Lin *et al* (6) demonstrated that women with OAB had significantly lower scores on several domains of the female sexual function index (FSFI), including desire, arousal, lubrication, orgasm and sexual satisfaction, with these reductions strongly associated with the severity of OAB. Despite its non-life-threatening nature, OAB is frequently under-recognised and undertreated by both patients and clinicians, even though it can lead to considerable deterioration in quality of life (7).

OAB can be managed using pharmacological therapy, typically antimuscarinic agents or β_3-adrenoceptor agonists, or through conservative approaches such as lifestyle modification and behavioural interventions, including pelvic floor muscle training and bladder training. The most commonly used first-line pharmacological agents are antimuscarinics, which reduce detrusor smooth muscle activity and decrease bladder

outlet resistance (8,9). Current guidelines from the American Urological Association and the European Association of Urology recommend behavioural therapy as the initial treatment option for OAB, with pharmacotherapy introduced as the following step when needed (10). Both pharmacological and behavioural approaches have demonstrated efficacy in reducing OAB symptoms across multiple clinical parameters and validated scoring systems (11).

The previous systematic review and meta-analysis by La Rosa *et al* (12) also found that both therapies have a similar efficacy for the treatment of OAB. However, this statement should be interpreted with caution due to the high risk of bias (12). The combination of both drugs and behavioural therapy could enhance the each other's efficacy or may be more effective than single therapy. However, to date, only a limited number of studies have reported differences between combination therapy and single therapy in patients with OAB (11,12). Shapiro and Brucker (13) found that the combination of behavioural therapy and pharmacological intervention was effective for OAB syndrome. Therefore, the present systematic review and meta-analysis aimed to compile and quantitatively measure the difference between monotherapy and combination therapy in treating the symptoms of OAB.

Data and methods

The present study was a systematic review and meta-analysis conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (14).

Study eligibility criteria. All studies on the effect of combination therapy in both male and female patients with OAB syndrome were included. The articles identified during the literature search were first filtered based on their title and abstract to exclude irrelevant studies. The full texts of the selected studies were then thoroughly assessed. The inclusion criteria were as follows: i) Studies reporting the effect of combination therapy on patients with OAB; ii) studies with a follow-up period with ≥8 weeks; iii) studies that contained a detailed explanation of the study treatment, particularly the behavioural therapy conducted; iv) studies that reported the outcome using measurable metrics, such as bladder diary parameters or scoring systems, such as the Overactive Bladder Symptom Score (OABSS). The exclusion criteria were the following: i) Case series studies and case reports; ii) literature reviews; iii) studies without full text available; iv) studies not reported in English or Indonesian.

Literature search strategy. A systematic literature search was conducted on the PubMed, Cochrane Library and ScienceDirect databases to identify studies on the effect of combination therapy using both drugs and behavioural therapy on reducing symptoms of OAB in male and female patients. The search was conducted in August, 2024 using the key words presented in Table I.

Risk of bias assessment. The selected studies were tested for their risk of bias based on their study designs. Randomised controlled trial (RCT) studies were assessed using the Cochrane's Risk of Bias tool, integrated into the Review Manager (RevMan) software version 5.4 (15). Cohort studies were assessed using the Newcastle-Ottawa Scale (NOS) that reviews three risk of bias domains: Selection, comparability and outcome (16). Cross-sectional studies were assessed using the analytical cross-sectional risk of bias checklist from the Joanna-Briggs Institute (JBI) (16).

Data extraction. The data extracted from the selected studies were the following: i) Authors and year of publication; ii) study design; iii) sex prevalence; iv) pharmacological and behavioural therapy regimen; v) sample size in each subgroup; vi) follow-up period; and vii) outcome parameters reported. The data of the general characteristics were then compiled into a table. The outcomes were analysed qualitatively in a systematic review and, when possible, quantitatively in a meta-analysis.

Statistical analysis. The outcomes were analysed qualitatively in a systematic review and, where appropriate, quantitatively in a meta-analysis. For the quantitative synthesis, continuous outcomes were analysed using mean differences (MDs), while categorical outcomes were analysed using odds ratios (ORs), each with corresponding 95% confidence intervals (CIs). Meta-analyses were performed using the inverse-variance method under a random-effects model to account for potential clinical and methodological heterogeneity across studies, irrespective of the observed I^2 values, in accordance with the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. Forest plots were generated to visually present individual study estimates and pooled effect sizes. Pooled estimates and 95% CIs were calculated using study-specific effect measures, and P-values for overall effects were derived from Z-tests.

Statistical heterogeneity was assessed using Cochran's Q (χ^2) test and quantified using the I^2 statistic, with I^2 values >50% indicating substantial heterogeneity. Publication bias was assessed qualitatively by visual inspection of funnel plot symmetry, where applicable. A two-sided P-value <0.05 was considered to indicate a statistically significant difference. All quantitative analyses were conducted using Review Manager (RevMan) version 5.4 (Cochrane Collaboration).

Results

Literature search. A total of 416 records were identified (Fig. 1). After removing 12 duplicates in Zotero, 404 titles and abstracts were screened, of which 399 were excluded based on the pre-defined criteria: Studies not involving OAB populations, not evaluating combined behavioural-pharmacological therapy, using ineligible designs (case reports, case series, reviews and editorials), involving non-adult populations, or lacking measurable clinical outcomes. In total, five full-text articles were assessed, and one article was excluded as it was a narrative review. Thus, four studies met all the eligibility criteria and were included in the present systematic review.

Characteristics of the included studies. The characteristics of the studies included in the present systematic review and meta-analysis are presented in Table II. The table summarises four studies evaluating the effectiveness of monotherapy

Table I. Key words used during systematic searching.

Database	Key words	Hits
PubMed	(pharmacological[All Fields] OR pharmacological therapy[All Fields] OR pharmacological treatment[All Fields] OR pharmacotherapy[All Fields] OR antimuscarinic[All Fields] OR mirabegron[All Fields]) AND (behavioural[All Fields] OR behavioural therapy[All Fields] OR bladder training[All Fields] OR pelvic floor muscle training[All Fields] OR pelvic floor training[All Fields] OR cognitive behavioural therapy[All Fields]) AND (combination[All Fields] OR multimodal[All Fields] OR integrated[All Fields] OR combined modality therapy[All Fields]) AND (overactive bladder[All Fields] OR oab[All Fields])	48
Cochrane	#1 (pharmacotherapy):ti,ab,kw OR (pharmacological):ti,ab,kw OR (antimuscarinic):ti,ab,kw OR (mirabegron):ti,ab,kw OR ('pharmacological treatment'):ti,ab,kw #2 (behavioural):ti,ab,kw OR ('behavioural therapy'):ti,ab,kw OR ('bladder training'):ti,ab,kw OR ('pelvic floor muscle training'):ti,ab,kw OR ('cognitive behavioural therapy'):ti,ab,kw #3 (combination):ti,ab,kw OR ('multimodalities'):ti,ab,kw OR ('combined modality therapy'):ti,ab,kw OR (integrated):ti,ab,kw #4 ('overactive bladder syndrome'):ti,ab,kw OR ('overactive bladder'):ti,ab,kw OR ('OAB syndrome'):ti,ab,kw OR (OAB):ti,ab,kw #5 #1 AND #2 AND #3 AND #4	42
ScienceDirect	(('pharmacological therapy' OR 'antimuscarinic' OR Mirabegron') AND ('behavioural therapy' OR 'pelvic floor muscle training') AND (Combination) AND ('overactive bladder' OR OAB)	326

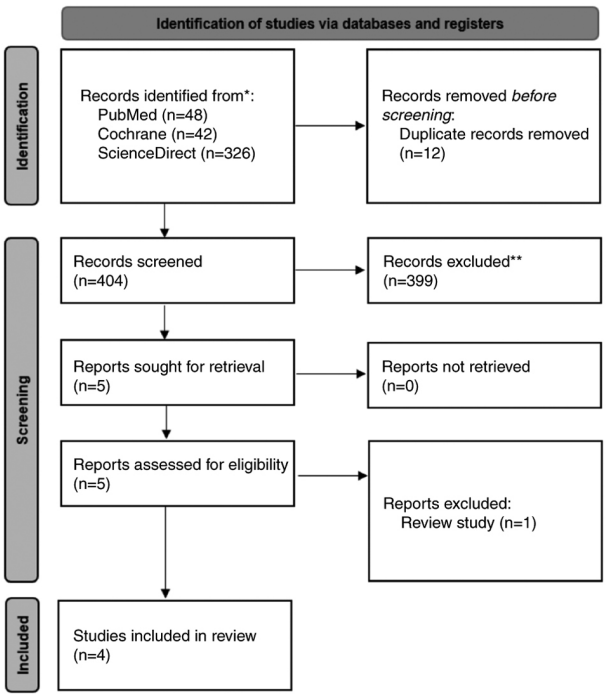

Figure 1. PRISMA flowchart illustrating the process for article selection used in the present study.

and combination therapy for overactive bladder syndrome. Burgio *et al* (17) conducted an RCT in an all-female group, assessed the impact of oxybutynin chloride combined with pelvic floor exercises and urgency control strategies over 8 weeks, focusing on urinary frequency. The second study was by Klutke *et al* (18), who conducted a cohort study with 86% female participants and examined the effect of daily tolterodine extended-release (4 mg), alongside behavioural interventions such as pelvic floor training, over a period of 12 weeks. Their study measured the total micturition, urgency, and nocturia of the patients'. Subsequently, Burgio *et al* (11), conducted another RCT, but in an all-male population. Their study explored the combination of tolterodine and tamsulosin with behavioural therapy and compared it with patients receiving drug therapy alone and behavioural therapy alone over a period of 12 weeks. The researchers measured the frequency, urgency and nocturia of the patients. The final analysed study was by Lin *et al* (19), who also conducted an RCT in an all-male group and investigated the effects of 50 mg of mirabegron daily combined with urge control strategies over a period of 12 weeks. Their study measured the OABSS of the patients, the International Index of Erectile Function-5 (IIEF-5), and International Prostate Symptom Score (IPSS). These studies collectively demonstrate the varied approaches to managing urinary symptoms, with a focus on specific outcomes depending on the demographic and intervention used, providing valuable insight into the effectiveness of these therapies across different patient groups.

Risk of bias analysis. Risk of bias analysis was conducted based on the designs of the selected studies. For RCT studies, the Cochrane checklist was used, and the results revealed that these studies had a low risk of bias (Fig. 2). However, there was an unclear risk of bias due to the lack of description on how the study concealed the allocation for each patient. The unclear risk of bias was also due to the nature of the study treatment, making it impossible to apply blinding.

For the cohort study by Klutke *et al*, the risk of bias was assessed using the Newcastle-Ottawa scale (Table III). The

Table II. Characteristics of the included studies.

Authors, year of publication	Study design	Sex prevalence	Pharmacological therapy	Combination therapy	No. of samples	Follow-up duration	Outcome measured	(Refs.)
Burgio, *et al* 2000	RCT	All female	Oxybutynin chloride, titrated from 2.5 to 15 mg daily	Oxybutynin chloride, titrated from 2.5 to 15 mg daily + PFMT exercises, urgency control strategies, and a home exercise program	BT group, 55; DT group, 19; CT group, 35	8 weeks	Frequency	(17)
Klutke, *et al* 2009	Cohort	86% female	Tolterodine Extended Release (ER) 4 mg once daily	Tolterodine extended release at 4 mg once daily + pelvic floor muscle training, urgency control strategies, and lifestyle modifications	Total, 416	12 weeks	Frequency, urgency, nocturia	(18)
Burgio, *et al* 2020	RCT	All male	Tolterodine (sustained-release, 4 mg once daily) and tamsulosin (0.4 mg once daily)	Tolterodine (sustained-release, 4 mg and Tamsulosin 0,4 mg + pelvic floor muscle training, urge suppression strategies, delayed voiding, and lifestyle modifications	BT group, 71; DT group, 68; CT group, 65	12 weeks	Frequency, urgency, nocturia	(11)
Lin, *et al* 2023	RCT	All male	Mirabegron at 50 mg once daily	Mirabegron 50 mg + urge control strategy	BT group, 36; CT group, 65	12 weeks	Voiding diary OABSS IIEF-5 IPSS	(19)

BT, behavioural therapy; CT, combination therapy; DT, drug therapy; IIEF-5, International Index of Erectile Function; IPSS, International Prostate Symptom Score; OABSS, Overactive Bladder Symptom Score; RCT, randomized controlled trial.

Table III. Risk of bias analysis for the study by Klutke *et al* (18).

Risk of bias parameters	Klutke *et al* (18)
Representativeness of the exposed cohort (1)	1
Selection of the non-exposed cohort (1)	1
Ascertainment of exposure (1)	1
Demonstration that outcome of interest was not present at start of study (1)	1
Comparability of cohorts on the basis of the design or analysis (2)	2
Assessment of outcome (1)	1
Was follow-up long enough for outcomes to occur? (1)	1
Adequacy of follow up of cohorts (1)	1
Total	9

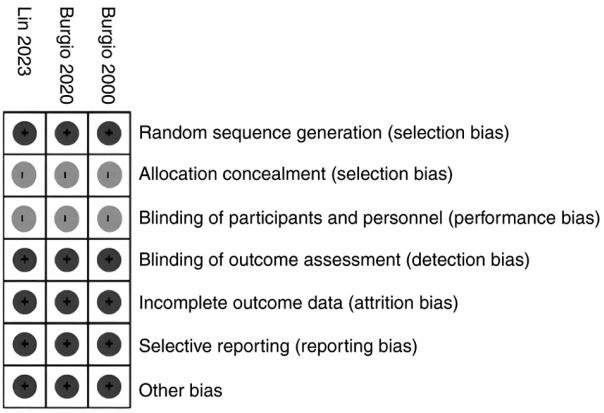

Figure 2. Risk of bias analysis of the randomised controlled trial studies.

results revealed that the study had a low risk of bias with a total score of 9 (Table III). Publication bias was not formally assessed using funnel plots or statistical tests due to the limited number of included studies, as such methods are not recommended when <10 studies are available.

Bladder diary variable. A total of two studies compared changes in bladder diary data between combination and single therapy regimens. Burgio *et al* (11) reported baseline, post-treatment and the change in the number of voiding frequencies, mean nocturia, mean urgency score and maximum urgency score. Their study found that compared to behavioural therapy or drug therapy, combination therapy was superior in reducing daytime frequency (reduction of 3.8±2.1 vs. 3.7±2.3 vs. 3.2±2.5 episodes; P=0.33), mean nocturia (reduction of 1.0±1.0 vs. 0.9±1.0 vs. 0.8±1.0 episodes; P=0.34), mean urgency (reduction of 0.3±0.6 vs. 0.1±0.6 vs. 0.2±0.6 episodes; P=0.06) and maximum urgency score (reduction of 0.6±0.8 vs. 0.3±0.7 vs. 0.4±0.7 episodes; P=0.07). However, after 12 weeks, there was no statistically significant difference between the three groups (11).

Lin *et al* (19) compared urge control behavioural therapy alone with a combination of behavioural therapy and mirabegron 50 mg. At 12 weeks, combination therapy resulted in a greater reduction in daytime voiding frequency compared with behavioural therapy alone (mean reduction, 1.3±2.7 vs. 0.6±1.8 episodes), although this difference did not reach statistical significance (P=0.198) (19). A quantitative synthesis of the two included studies using a random-effects model demonstrated no statistically significant difference between combination therapy and behavioural therapy alone in reducing daytime frequency (MD, 0.35; 95% CI, -0.23 to 0.93; P=0.24) (Fig. 3). Heterogeneity across studies was low (I^2=4%).

The studies by both Burgio *et al* (11) and Lin *et al* (19) evaluated changes in nocturia episodes; however, their findings were inconsistent. Burgio *et al* (11) reported a greater reduction in nocturia episodes with combination therapy, whereas Lin *et al* (19) observed no significant differences between the treatment groups. Consequently, a random-effects meta-analysis was conducted to estimate the overall effect of combination therapy compared with behavioural therapy alone. The pooled analysis demonstrated no statistically significant difference in nocturia reduction between the two groups (MD, 0.04; 95% CI, -0.18 to 0.27; P=0.70) (Fig. 4). No significant heterogeneity was observed among the studies (I^2=0%).

Klutke *et al* (18) conducted a one-group cohort study to assess the combined effects of tolterodine extended release and behavioural intervention in patients with OAB syndrome who were dissatisfied with their prior antimuscarinic treatments. Their study was conducted over a period of 16 weeks and included 416 participants who received 4 mg tolterodine extended release along with a self-administered behavioural intervention for the first 8 weeks. In their study, significant improvements were observed in the bladder diary variable, including up to -3.0 episodes reduced in total micturition per 24 h, -5.0 episodes reduced in urgency-related micturition, -1.0 episodes reduced in urgency urinary incontinence and -1.0 episode reduced in nocturnal micturitions (18).

Burgio *et al* (17) examined the effects of combination therapy and monotherapy on reducing incontinence episodes, specifically among patients converting from monotherapy to combination therapy. Their study initially assessed the effectiveness of monotherapies, either using oxybutynin therapy or behavioural therapy through pelvic floor muscle training and urge control strategy. The group that received behavioural therapy alone demonstrated a mean reduction in incontinence of 84.1%. By contrast, the group treated with oxybutynin alone exhibited a mean reduction of 71.8%. The placebo group, which received no active treatment, exhibited a mean reduction in incontinence of 60.5% (17).

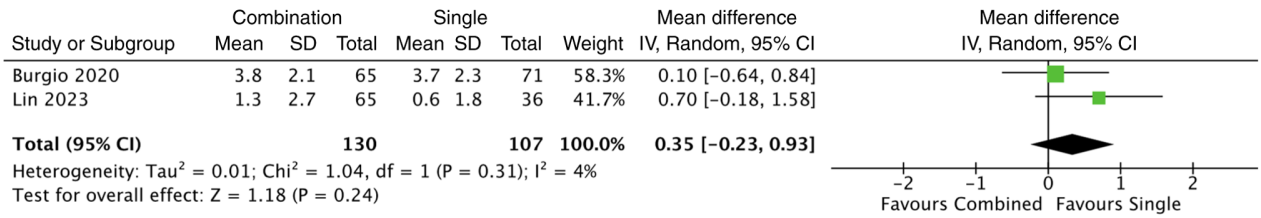

Figure 3. Forest plot comparing reduction of voiding frequency episodes.

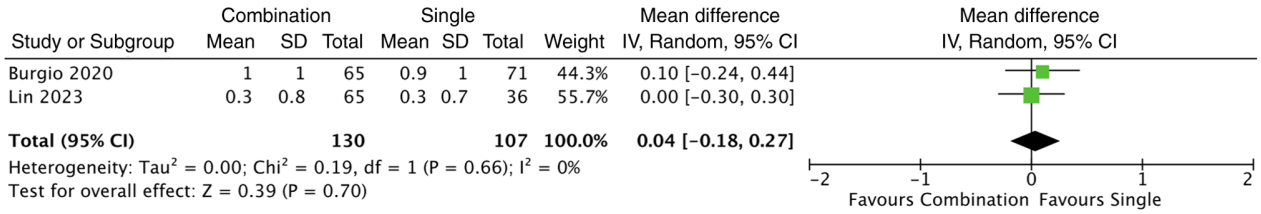

Figure 4. Forest plot comparing reduction of nocturia episodes.

Upon completion of the initial monotherapy for at least 8 weeks, some participants opted to switch to a combination therapy, adding either behavioural therapy to their drug regimen or vice versa. The transition to combined therapy yielded significant improvements in incontinence reduction for these participants. The participants who initially received behavioural therapy and subsequently added oxybutynin experienced an increase in incontinence reduction from 57.5% (±29.4%) after only receiving behavioural therapy to 88.5% (P=0.034) following the combination therapy (17). Similarly, participants who began with oxybutynin and then incorporated behavioural therapy into their treatment plan saw their incontinence reduction rise from 72.7% (±24.9%) after only drug therapy to 84.3% (P<0.001) following the combination therapy (17).

OABSS. Lin *et al* (19) reported a detailed assessment of OABSS changes between combination therapy and monotherapy. Both groups began with similar baseline scores. After treatment, both showed improvements across all subgroups, including daytime frequency, nocturia, urgency, urinary incontinence, and total OABSS score. The changes were slightly more pronounced in the combination group, particularly in urgency and total OABSS score. However, the differences between the groups were not statistically significant (P>0.05). Overall, both therapies were effective, with no clear superiority of one over the other (19). The study by Burgio *et al* (11) demonstrated that combining behavioural therapy with drug therapy achieved superior outcomes compared to either treatment alone. This was evident in the Overactive Bladder Questionnaire (OAB-q) scores, where the combination therapy group had a much lower mean score [mean (SD): 23.8 (22.1)] than the behavioural therapy group [43.0 (28.2)] and the drug therapy group [39.5 (30.0)]. The difference was statistically significant (P<0.001), indicating better symptom improvement with the combination approach (11).

IPSS score. Lin *et al* (19) evaluated the effects of combination therapy on the IPSS of patients with OAB syndrome. Their results revealed that both the behavioural and combination therapy groups experienced improvements over period of 12 weeks. However, the changes in the combined therapy group did not differ significantly from those of the monotherapy group, indicating the comparable efficacy of both therapies (19).

However, the study by Burgio *et al* (11) on the effects of combination therapy on the IPSS of patients demonstrated that combination therapy was more favourable, with a lower mean score [mean (SD): 9.2 (4.8)] compared to behavioural therapy alone [11.4 (5.3)] and drug therapy alone [11.5 (5.8)]. This finding was also statistically significant (P<0.001), further supporting the greater efficacy of the combination treatment in managing symptoms (11).

Sexual function. The study by Lin *et al* (19) also used the IIEF-5 to assess the effects of combination therapy on sexual function. Their data demonstrated that both behavioural and combination therapies led to slight improvements in sexual function over a period of 12 weeks. However, the changes in the IIEF-5 scores were not statistically significant (19).

Moreover, the same study used the Male Sexual Health Questionnaire-Ejaculatory Dysfunction Short Form (MESH EjD SF) to investigate the effects of combination therapy on sexual function (19). The MESH EjD SF scores in that study assessed various aspects of ejaculatory function, including frequency, strength, semen volume and overall satisfaction over a period of 12 weeks. At baseline, both groups had similar scores for frequency, strength and semen volume. Over the period of 12 weeks, there were slight improvements in each aspect, although there were no significant differences. The total scores for Q1-Q3 (frequency, strength and volume) remained relatively stable, with only minimal differences from the baseline (19).

Adverse events. Klutke *et al* (18) reported that the adverse events observed during their study period were associated with treatment with tolterodine. Their study demonstrated that the the majority of common adverse events associated with standard treatments were dry mouth in 25 patients (6%)

and constipation in 20 patients (5%) (18). The majority of the adverse events in the study by Burgio *et al* (11) were observed in patients who underwent the drug therapy (79% of patients, or 44 of 65), and 2% (1 of 65) were classified as extreme adverse events (11).

Discussion

The present systematic review and meta-analysis evaluated the efficacy of a combination of behavioural and pharmacological therapy compared with monotherapy in patients with OAB syndrome. Across the four included studies, the pooled analyses revealed no significant differences between combination therapy and monotherapy in reducing voiding frequency (MD, 0.35; 95% CI, -0.23-0.93; P=0.24) or nocturia episodes (MD, 0.04; 95% CI, -0.18-0.27; P=0.70) over the short-term follow-up. However, individual studies reported trends favouring combination therapy for specific symptoms, particularly urgency scores and quality of life measures, suggesting that the combination approach may offer modest additional benefits in selected patients.

The absence of statistically significant differences in the meta-analysis may be partially explained by variability in the behavioural interventions used across studies. For instance, pelvic floor muscle training (PFMT) as implemented in the study by Burgio *et al* (11) demonstrated substantial improvements in the bladder diary parameter even when delivered without pharmacotherapy, indicating that well-structured behavioural therapy can independently produce strong clinical responses. By contrast, the urge-control strategy used in the study by Lin *et al* (19) appears to yield more modest effects, which may reduce the incremental value observed when pharmacotherapy is added. These differences highlight the importance of the type, intensity and quality of behavioural interventions when evaluating the effectiveness of combined therapy for OAB.

Furthermore, PFMT has been proven effective in controlling OAB symptoms and is recommended by the ICS (1). Its benefits are attributed to three key mechanisms: i) Enhancing pelvic floor muscle strength through repetitive contractions that support the urethra; ii) improving timing and coordination, enabling anticipatory contractions during urgency or leakage triggers; and iii) engaging core musculature, which promotes reflexive co-activation of the pelvic floor (20-22). Evidence across diverse populations supports these mechanisms: The study by Bo *et al* (20) found that five of 11 RCTs demonstrated a significant improvement in OAB symptoms among pregnant women. In another study, Tibaek *et al* (21) demonstrated reductions in urinary frequency in patients post-stroke; and the study by Hagovska *et al* (23) reported improved LUTS in men with benign prostatic hyperplasia when PFMT was combined with Silodosin. Together, these findings highlight PFMT as a versatile and effective behavioural intervention for the management of OAB.

The minor differences between combination therapy and monotherapy observed in the studies included in the present systematic review and meta-analysis may be due to the short follow-up durations, which were limited to a maximum of 12 weeks. Early improvements were consistently noted, such as the symptom reductions at 4 weeks in the study by Lin *et al* (19) and at 6 weeks in the study Burgio *et al* (11). However, these advantages did not persist by week 12, where the outcomes of combination therapy and monotherapy converged (11,19) Similar early responses were reported in the studies by Burgio *et al* (17) and Klutke *et al* (18), both of which demonstrated symptom improvement by 8 weeks. This pattern suggests that OAB treatments often produce an initial response followed by a therapeutic plateau, reducing the observable differences between treatment strategies over time (24).

Another contributing factor is poor long-term treatment adherence, which is a well-recognised challenge in the management of OAB. Enemchukwu *et al* (25) reported that treatment adherence within 1 year decreased to 32% for behavioural therapy and 15-40% for pharmacotherapy due to side-effects, limited perceived benefit, treatment-related fatigue and communication barriers. Even for mirabegron, which is known to have better adherence than solifenacin or oxybutynin, only 25% of women continued therapy after 1 year. These adherence limitations likely blunt the sustained effects of prolonged treatment, limiting the ability of short-term studies to capture meaningful differences between combination therapy and monotherapy (24,25).

Moreover, Lin *et al* (19) did not directly compare the behavioural urge control strategy alone with pharmacological mirabegron alone. Thus, it is unclear which type of therapy has a greater impact on clinical improvement in patients with OAB (19,24). However, the finding that combination therapy is not significantly different from behavioural therapy alone suggests that the addition of mirabegron therapy to patients with OAB already undergoing urge control therapy does not provide significant clinical benefits (25). Similar findings were also reported in male sexual function, measured by IIEF-5 and IPSS. Mirabegron is a selective β_3-adrenoceptor agonist that inhibits β-adrenergic receptors in detrusor muscles, causing relaxation of those smooth muscles (26). Studies have demonstrated that, compared to the placebo, mirabegron is as effective as peripheral tibial nerve stimulation in reducing LUTS symptoms in patients with OAB (24,27).

Studies comparing combination therapy with monotherapy for OAB have yielded mixed results. Lin *et al* (19) reported improvements in OABSS and IPSS scores in both groups, with slightly greater, although not statistically significant, reductions in urgency and total scores in the combination group (P>0.05). By contrast, Burgio *et al* (11) observed significantly improved outcomes with combined behavioural and pharmacological therapy, including lower OAB-q and IPSS scores (P<0.001), suggesting a potential advantage for combination approaches. However, all the studies included in the present systematic review had relatively short follow-up durations, with none extending beyond 12 weeks. Earlier studies, such as those of Burgio *et al* (17) and Klutke *et al* (18) demonstrated symptom improvement by 8 weeks, while the studies by Burgio *et al* (11) and Lin *et al* (19) reported early benefits at 6 and 4 weeks, respectively. Notably, although both studies observed better early improvements with combination therapy, these differences were no longer significant by week 12 (11,19). This pattern suggests that the long-term efficacy of combination therapy may converge with that of monotherapy, although longer follow-up studies are needed to confirm this trend (24,25).

The findings of the present systematic review and meta-analysis indicate that both behavioural and pharmacological therapies remain effective options for the management of OAB, and combination therapy may provide modest short-term advantages in certain domains, such as urgency and quality of life outcomes. However, the lack of sustained superiority at 12 weeks underscores the need for clinicians to set realistic expectations with patients regarding the expected trajectory of symptom improvement and the potential for therapeutic plateau (24,25). As urge-control strategies and PFMT can independently produce significant improvements, sometimes comparable to those achieved with medication, behavioural therapy should remain a cornerstone of first-line management (20,21). Pharmacotherapy, including mirabegron, may still be valuable as an adjunct, particularly for patients who do not achieve adequate relief with behavioural therapy alone. However, clinicians should emphasise the importance of treatment adherence to achieve durable symptom control (26,27). Overall, individualised treatment selection that considers patient preference, symptom burden, and motivation is essential to optimise real-world outcomes in the management of OAB.

The present systematic review has several limitations. First, all the included studies had short follow-up durations of a maximum of 12 weeks, which is a key limitation given that OAB is a chronic condition requiring long-term management. Second, treatment adherence remains a major challenge in the treatment of OAB, particularly for pharmacotherapy, and poor compliance may influence the observed outcomes across studies. Another limitation concerns the variability in treatment protocols; both behavioural interventions and physical therapies, such as PFMT, differed across studies, making direct comparisons difficult. Additionally, heterogeneity in outcome reporting meant that many parameters were derived from a single study, and only two studies contributed data to the meta-analysis of voiding frequency, nocturia and OABSS. The generally small sample sizes further limited the robustness and generalisability of the findings.

Despite these limitations, however, the present systematic review has several strengths. It included three randomised controlled trials with low risk of bias, providing a relatively strong evidence base. The diversity of reported outcomes allowed the review to explore the impact of combination therapy across multiple clinical domains, including LUTS symptoms, sexual function and adverse effects. Collectively, these strengths contribute valuable insight into the comparative effectiveness of combination therapy vs. monotherapy in the management of OAB.

In conclusion, the present systematic review and meta-analysis found no significant difference between combined behavioural-pharmacological therapy and monotherapy in reducing voiding frequency or nocturia in patients with OAB over a short-term follow-up period. Although some studies reported modest early advantages with combination therapy, these benefits were not sustained by 12 weeks. Behavioural interventions, particularly PFMT and urge-control strategies, demonstrated potent independent effects, while pharmacotherapy remains a useful adjunct for selected patients. Overall, both treatment approaches are effective, and clinical decisions should be individualised based on symptom burden, patient preference, and likelihood of adherence. Further high-quality trials with longer follow-up periods are required to clarify the long-term comparative effectiveness of combination therapy.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

AMMA and FW conceived and designed the study. AMMA conducted the literature search and data extraction. FW and HER analysed and interpreted the data. AMMA drafted the manuscript. FW and HER critically revised the manuscript. FW and HER confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, AI tools were used to improve the readability and language of the manuscript or to generate images, and subsequently, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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