# Supplementary Online Content

Burgio KL, Kraus SR, Johnson TM II, et al. Effectiveness of combined behavioral and drug therapy for overactive bladder symptoms in men: a randomized clinical trial. *JAMA Intern Med*. Published online January 13, 2020. doi:10.1001/jamainternmed.2019.6398



This supplementary material has been provided by the authors to give readers additional information about their work.

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**eTable 1.** Exclusion criteria

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| • Urinary flow rate < 8.0 mL/sec on a void greater than 125 mL |
| • Post-void residual volume > 150 mL (based on bladder ultrasound after voiding in the presence of a usual urge to urinate) |
| • Urinary tract infection (defined as growth of >100,000 colonies per mL of a urinary pathogen on urine culture). Participants were referred for treatment with antibiotics and could be enrolled if OAB symptoms persisted after the infection resolved. |
| • Transurethral resection of the prostate (TURP), simple prostatectomy, or other BPH related surgery within the past 5 years |
| • Current active treatment for prostate cancer |
| • History of radical prostatectomy. |
| • Previous artificial urinary sphincter, sling procedure, bladder injection of botulinum toxin bladder injections, or implanted sacral neuromodulation device |
| • Poorly controlled diabetes (glycosylated hemoglobin $\geq$9.0 within last 3 months). Subjects with poorly controlled diabetes were offered enrollment if the OAB symptoms persisted after the diabetes was controlled. |
| • Hematuria on microscopic examination in the absence of infection. A urologic consultation was recommended, and enrollment depended on clearance by a urologist and agreement by the Site PI. |
| • Any unstable medical condition (particularly: cancers under active treatment, decompensated congestive heart failure, history of malignant arrhythmias, unstable angina, diagnosed by history or physical exam) |
| • Neurologic conditions such as Parkinson disease, spinal cord injury, multiple sclerosis, or myasthenia gravis |

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|---|
| • Positive screening test for dementia on the Mini-Cog (score ≤ 2) |
| • Unable to toilet independently |
| • Contraindications to the study drugs, including history of postural hypotension with syncope, history of acute urinary retention requiring catheterization, narrow angle glaucoma, or history of gastric retention |
| • Hypersensitivity to tolterodine or tamsulosin |
| • Current use of alpha-blocker. Evaluation was delayed until the drug had been discontinued for 2 weeks. |
| • Current use of an anti-muscarinic or beta-3 agonist for OAB. Evaluation was delayed until the drug was discontinued for 2 weeks. |
| • If on a diuretic, dose had not been stable for at least 4 weeks |
| • If taking dutasteride or finasteride, dose had not been stable for at least 6 months |
| • If on an antibiotic for prostatitis. Participants were offered re-evaluation if OAB symptoms persisted after antibiotics were completed. |
| • Full course of behavioral therapy |

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**eTable 2.** Changes in voiding frequency and other urinary symptoms of participants who completed the study: baseline to 6 weeks of therapy

| | **Behavioral** | **Drug** | **Combined** | **P-Value** |
|---|---|---|---|---|
| **Bladder Diary Variables** | Mean (SD) N=63 | Mean (SD) N=61 | Mean (SD) N=59 | |
| 24-Hour Voiding Frequency | | | | |
| Baseline | 11.8 (2.4) | 11.7 (2.5) | 11.6 (2.3) | 0.8030 |
| Post-treatment | 8.8 (2.2) | 10.2 (2.7) | 8.2 (2.3) | <.0001* |
| Change (baseline to 6 weeks) | 3.0 (2.4) | 1.5 (2.4) | 3.3 (1.8) | <.0001* |
| Percent change | 25.4% | 12.8% | 28.4% | |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| Nocturia | | | | |
| Baseline | 2.1 (1.2) | 2.2 (1.1) | 2.1 (1.3) | 0.7171 |
| Post-treatment | 1.4 (0.8) | 1.8 (1.2) | 1.3 (1.0) | 0.0034 * |
| Change (baseline to 6 weeks) | 0.8 (1.0) | 0.4 (1.0) | 0.8 (1.1) | 0.0034* |
| P-Value (within group)** | <.0001 | 0.0005 | <.0001 | |
| Urgency Score† | | | | |
| Baseline | 1.6 (0.6) | 1.6 (0.5) | 1.5 (0.6) | 0.3781 |
| Post-treatment | 1.6 (0.6) | 1.5 (0.5) | 1.3 (0.7) | 0.0048* |
| Change (baseline to 6 weeks) | -0.1 (0.5) | 0.1 (0.5) | 0.2 (0.6) | 0.0048* |
| P-Value (within group)** | 0.1637 | 0.1280 | 0.0218 | |
| Maximum Urgency Score† | | | | |
| Baseline | 2.3 (0.7) | 2.4 (0.6) | 2.4 (0.6) | 0.8958 |
| Post-treatment | 2.2 (0.7) | 2.2 (0.6) | 1.8 (0.8) | 0.0001* |
| Change (baseline to 6 weeks) | 0.1 (0.6) | 0.2 (0.6) | 0.5 (0.7) | 0.0001* |
| P-Value (within group)** | 0.0613 | 0.0002 | <.0001 | |
| Incontinence (episodes/week) | | | | |
| Baseline | 6.1 (10.0) | 5.9 (10.9) | 6.4 (9.4) | 0.8578 |
| Post-treatment | 2.4 (5.1) | 2.6 (7.0) | 1.0 (3.7) | 0.1423* |
| Change (baseline to 6 weeks) | 3.7 (7.3) | 3.3 (11.1) | 5.4 (8.7) | 0.1423* |
| Percent reduction | 60.7% | 55.9% | 84.4% | |
| P-Value (within group)** | <.0001 | 0.0031 | <.0001 | |
| **Overactive Bladder Questionnaire (OAB-q).** | | | | |
| Baseline | 64.4 (33.4) | 60.4 (32.8) | 63.0 (33.5) | 0.7700 |
| Post-treatment | 41.6 (28.1) | 38.4 (30.4) | 23.5 (22.7) | <.0001* |
| Change (baseline to 6 weeks) | 22.8 (20.1) | 22.0 (28.3) | 39.5 (30.7) | <.0001* |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| **International Prostate Symptom Score (IPSS) §** | | | | |
| Baseline | 15.7 (5.6) | 16.2 (5.7) | 17.3 (6.2) | 0.2193 |
| Post-treatment | 11.2 (5.3) | 11.2 (5.8) | 8.9 (4.7) | <.0001* |
| Change (baseline to 6 weeks) | 4.4 (3.9) | 5.0 (5.9) | 8.4 (4.9) | <.0001* |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |

***** P-value is for an F test adjusting for baseline values and age.

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** P-value (w/ group) compared baseline vs. post-treatment (treatment effects) with Wilcoxon signed rank sum test.

† Scores range from 0 to 3:

0 - None - no urgency

1- Mild - awareness of urgency, but is *easily tolerated*

2 - Moderate - enough urgency discomfort that it *interferes with or shortens* usual activity

3 - Severe - extreme urgency discomfort that abruptly *stops all* activities or tasks

§ Scores range from 0 to 35 with higher scores indicating more frequent lower urinary tract symptoms.

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**eTable 3.** Changes in voiding frequency and other urinary symptoms of participants who completed the study: baseline to 12 weeks of therapy

| | **Behavioral** | **Drug** | **Combined** | **P-Value** |
|---|---|---|---|---|
| **Bladder Diary Variables** | Mean (SD) N=63 | Mean (SD) N=61 | Mean (SD) N=59 | |
| 24-Hour Voiding Frequency | | | | |
| Baseline | 11.8 (2.4) | 11.7 (2.5) | 11.6 (2.3) | 0.8030 |
| 12-weels treatment | 8.1 (2.2) | 8.6 (2.4) | 8.0 (2.2) | 0.2902* |
| Change (Baseline to 12 weeks) | 3.8 (2.3) | 3.2 (2.5) | 3.6 (2.0) | 0.2902* |
| Percent change | 32.2% | 27.4% | 31.0% | |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| Nocturia | | | | |
| Baseline treatment | 2.1 (1.2) | 2.2 (1.1) | 2.1 (1.3) | 0.7171 |
| 12-weels treatment | 1.2 (0.9) | 1.4 (1.1) | 1.2 (1.0) | 0.3594 * |
| Change (Baseline to 12 weeks) | 0.9 (1.0) | 0.7 (1.0) | 1.0 (0.9) | 0.3594* |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| Urgency Score† | | | | |
| Baseline treatment | 1.6 (0.6) | 1.6 (0.5) | 1.5 (0.6) | 0.3781 |
| 12-weels treatment | 1.5 (0.6) | 1.5 (0.6) | 1.2 (0.6) | 0.0534* |
| Change (Baseline to 12 weeks) | 0.1 (0.6) | 0.2 (0.6) | 0.2 (0.6) | 0.0534* |
| P-Value (within group)** | 0.4471 | 0.1191 | 0.0058 | |
| Maximum Urgency Score† | | | | |
| Baseline treatment | 2.3 (0.7) | 2.4 (0.6) | 2.4 (0.6) | 0.8958 |
| 12-weels treatment | 2.0 (0.8) | 2.0 (0.8) | 1.8 (0.8) | 0.0602* |
| Change (Baseline to 12 weeks) | 0.3 (0.7) | 0.4 (0.7) | 0.6 (0.8) | 0.0602* |
| P-Value (within group)** | 0.0001 | <.0001 | <.0001 | |
| Incontinence (episodes/week) | | | | |
| Baseline treatment | 6.1 (10.0) | 5.9 (10.9) | 6.4 (9.4) | 0.8578 |
| 12-weels treatment | 1.0 (2.5) | 1.0 (3.1) | 1.1 (3.2) | 0.9805* |
| Change Baseline to 12 weeks) | 5.1 (8.8) | 5.0 (10.5) | 5.3 (8.4) | 0.9805* |
| Percent reduction | 83.6% | 84.7% | 82.8% | |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| **Overactive Bladder Questionnaire (OAB-q).** | | | | |
| Baseline treatment | 64.4 (33.4) | 60.4 (32.8) | 63.0 (33.5) | 0.7700 |
| 12-weels treatment | 22.0 (22.1) | 26.4 (25.3) | 18.3 (18.7) | 0.0829* |
| Change (Baseline to 12 weeks) | 42.4 (30.0) | 34.0 (29.8) | 44.7(33.0) | 0.0829* |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |
| **International Prostate Symptom Score (IPSS) §** | | | | |
| Baseline treatment | 15.7 (5.6) | 16.2 (5.7) | 17.3 (6.2) | 0.2193 |
| 12-weels treatment | 8.2 (5.4) | 8.8 (4.7) | 7.9 (4.8) | 0.3353* |
| Change (Baseline to 12 weeks) | 7.5 (5.3) | 7.5 (6.0) | 9.3 (5.4) | 0.3353* |
| P-Value (within group)** | <.0001 | <.0001 | <.0001 | |

***** P-value is for an F test adjusting for baseline values and age.

** P-value (w/in group) compared baseline vs. 12-weeks (treatment effects) with Wilcoxon signed rank sum test.

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§ Scores range from 0 to 35 with higher scores indicating more frequent lower urinary tract symptoms.

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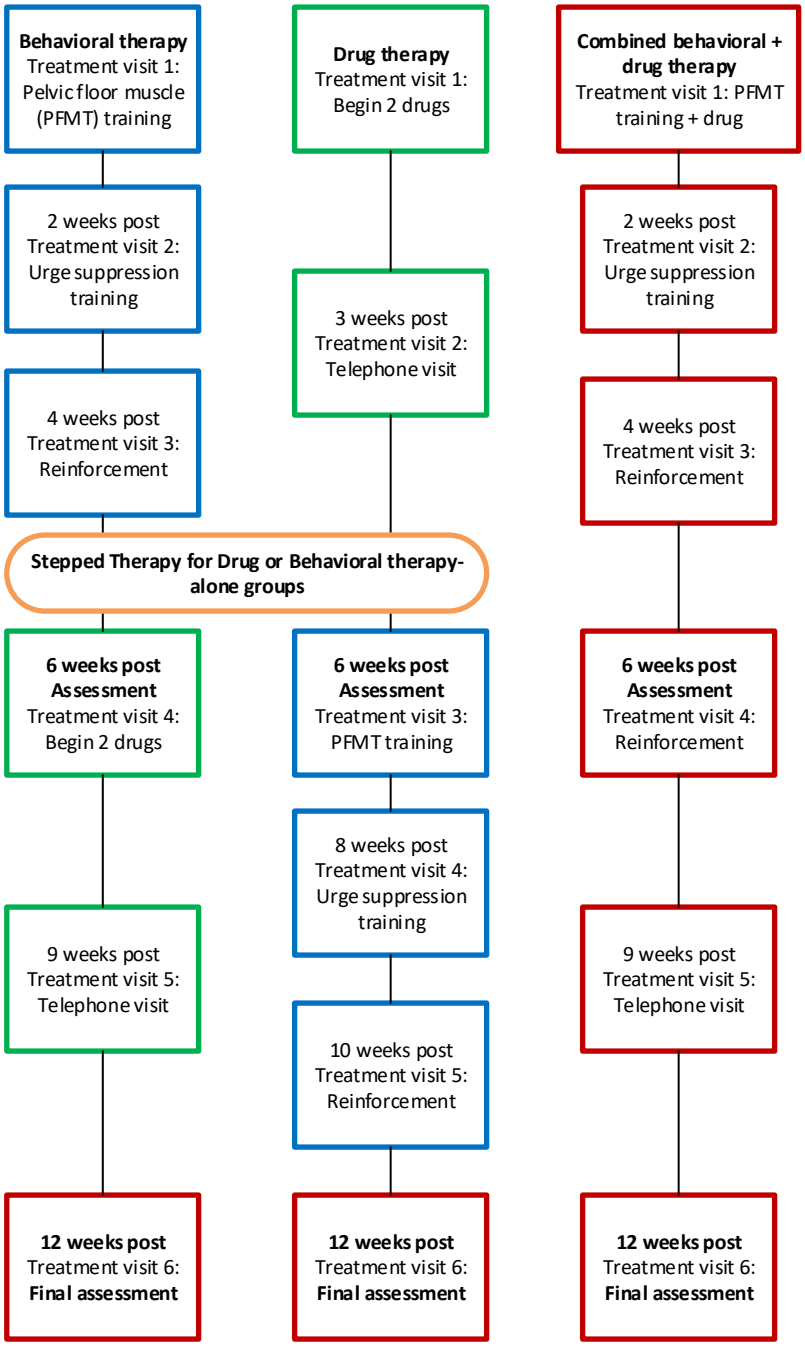
**eFigure.** Overview of study design

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