

# How long do we have to treat overactive bladder syndrome? A questionnaire survey of Canadian urologists and gynecologists

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## Abstract

**Introduction:** Overactive bladder (OAB) syndrome is a highly prevalent and costly condition worldwide, with negative impact on health-related quality of life. Although many guidelines exist and anticholinergics are considered to be the mainstay of pharmacological treatment, data are lacking regarding optimal treatment duration. Therefore, the aim of this study was to determine practice patterns of Canadian urologists and gynecologists regarding duration of OAB pharmacotherapy.

**Methods:** A 14-question survey was designed and survey links (English and French) were sent by email to all practicing urologists and gynecologists registered with the Canadian Urological Association and the Society of Obstetricians and Gynecologists of Canada via the associations' email lists. The SurveyMonkey website served as platform where responses were collected and stored.

**Results:** A total of 301 physicians completed the questionnaire; 250 respondents (83%) prescribe anticholinergics or beta-3-adrenoceptor agonist (mirabegron) in their practice, and 202 (81%) start patient treatment with the lowest recommended medication dose. One hundred and twelve respondents (45% of those who prescribe OAB medications) classified OAB pharmacotherapy as a lifelong management strategy, whereas 130 (52% of those who prescribe OAB medications) think that OAB pharmacotherapy should be administered for a defined time period. Six-month and one-year time periods of drug treatments are the most commonly chosen answers given by physicians who treat their patients for a defined duration.

**Conclusions:** There is general agreement among Canadian urologists and gynecologists that OAB treatment should be started with the lowest recommended medication dose. A slim majority of respondents think that OAB pharmacotherapy should be administered for a defined duration.

## Introduction

Overactive bladder (OAB) syndrome is defined by the International Continence Society as “urinary urgency, usu-

ally accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathologies.”<sup>1</sup> Although OAB is not a life-threatening condition, its impact on quality of life (QoL) plays a major role in the decision to treat patients. It has been demonstrated that OAB significantly affects patients' health status, including physical, emotional, social, sexual, and mental functioning.<sup>2-4</sup> The chronic nature of this condition and its impact can be lifelong, negatively influencing the QoL of affected patients.<sup>5</sup>

For many years, anti-muscarinic medications have been administered in the management of OAB symptoms and are currently recommended by the Canadian Urological Association (CUA) as second-line treatment.<sup>6</sup> The commercially available beta-3-adrenoceptor agonist mirabegron is also currently recommended as an OAB pharmacotherapy option. Adverse event profile and possible contraindications should be considered when prescribing drugs of choice as second-line treatments. Presently- available OAB medications have proven their efficacy and are considered safe and well-tolerated overall. However, available literature does not provide recommendations about how long OAB should be managed pharmacologically.

The purpose of the present study is to ascertain current practices among Canadian urologists and gynecologists regarding OAB pharmacotherapy duration and review available data on this issue to describe standards for this clinical concern.

## Methods

An up to 14-question survey (depending on respondent answers to three skip-logic questions) was designed to assess current Canadian practices in terms of OAB treatment duration. The institutional research ethics committee approved the study, and the principle of implied consent applied: thus, formal consent was not required. Study and consent details were clearly communicated before respondents began answering the questionnaire. Participation was voluntary, and no compensation was given. Survey links (English and French versions) were sent by email to all urologists and gynecologists registered with the CUA and the Society of

Obstetricians and Gynecologists of Canada via the associations' email lists.

Specifically, 623 urologists and 790 gynecologists were invited to participate in the survey over a three-month period. To increase the response rate, a reminder was sent one month after initial contact. The SurveyMonkey website served as platform where responses were collected and stored. The survey was mobile-responsive and optimized for desktop, tablet, and mobile resolutions on Android and iOS devices. Responses were anonymous, and no personal information was collected.

Responses were summarized as descriptive statistics with proportions and percentages. All answers were included in the analysis, irrespective of whether the entire questionnaire was completed or not. Associations between demographic information and other responses were explored by Chi-square test, with p value set at <0.05 to define statistical significance. Data analysis was conducted with IBM SPSS Statistics, version 23.0 (IBM Corporation, Armonk, NY, U.S.).

## Results

### Respondent characteristics

A total of 301 physicians completed the questionnaire. The response rate for urologists and gynecologists was 31% (190/623) and 14% (111/790), respectively. Table 1 details the demographic characteristics of respondents.

### Specific questions

Two hundred fifty respondents (83%) prescribe anticholinergics or beta-3-adrenoceptor agonist (mirabegron) in their practice. They include 181 urologists (95% of participating urologists) and 69 gynecologists (62% of participating gynecologists); 202 (81%) of these physicians start patient treatment with the lowest recommended medication dose. They include 140 urologists (77% of those who prescribe OAB medications) and 62 gynecologists (90% of those who prescribe OAB medications). Thirty-four urologists (19%) and six gynecologists (5%) declared that they start treatment with the highest recommended dose. In this specific group of respondents, the majority are male (35, 88%), with more than 10 years of clinical experience (24, 60%), but not specifically trained in functional urology with adequate fellowship (35, 88%). Table 2 details the demographic characteristics of physicians who answered this question. Statistically significant correlations are found between specialization/gender and dose preference ( $p=0.04$  and  $p=0.0007$ , respectively).

Participants were asked when they wish to see their patients after they started treatment and whether they realistically see them. Fig. 1 presents the overall results. One hundred and ten

respondents (44%) wish to see their patients 4–8 weeks after they started treatment, whereas 96 (38%) like to follow them up 8–12 weeks after initiating pharmacotherapy. In reality, however, 92 (37%), 76 (30%), and 69 (28%) of respondents admitted to seeing their patients 8–12 weeks, >12 weeks, or 4–8 weeks, respectively, after initiation of treatment.

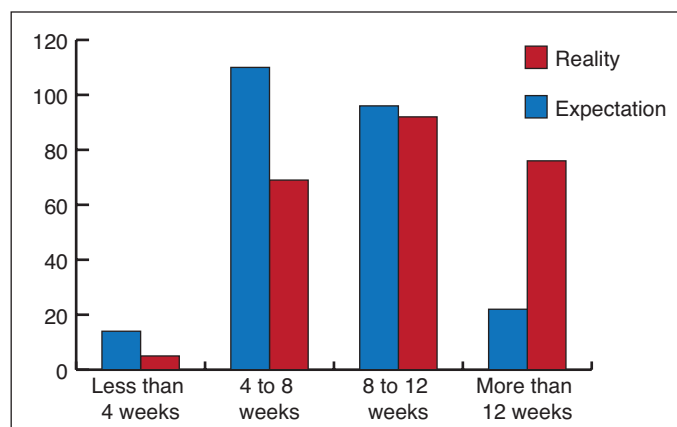
Further questions aimed to standardize OAB treatment duration. Physicians were queried whether OAB pharmacotherapy (medications) is needed lifelong or just for a defined time period. One hundred and twelve respondents (45% of those who prescribe OAB medications) classified OAB pharmacotherapy as a lifelong management strategy; 130 (52% of those who prescribe OAB medications) thought that OAB pharmacotherapy should be given for a defined time period. Table 3 reports the demographic aspects of this question. Correlations between urologists and gynecologists are statistically significant ( $p=0.03$ ).

In a group of respondents who think that OAB medications should be prescribed for a defined time period, the leading answers are “six months” indicated by 53 physicians (41%), and “one year” (32, 25%); 99 physicians (76%) treating OAB for a defined time period suggest self-titration of the medication dose by patients, and 95 (73%) see their patients at the end of treatment. Those who see their patients at the end of treatment were further asked about when it usually takes place. The leading answer is “three months” (32, 34%), fol-

**Table 1. Demographic characteristics of respondents**

	Urologists n=190 (%)	Gynecologists n=111 (%)	All respondents n=301 (%)
Gender			
Male	144 (76%)	24 (22%)	168 (56%)
Female	32 (17%)	82 (74%)	114 (38%)
Number of years of practice			
<5	41 (22%)	33 (30%)	74 (25%)
5–10	36 (19%)	21 (19%)	57 (19%)
11–20	46 (24%)	35 (32%)	81 (27%)
>20	53 (28%)	17 (15%)	70 (23%)
Practice			
Academic	53 (28%)	37 (33%)	90 (30%)
Community	83 (44%)	39 (35%)	122 (41%)
Academic and community	40 (21%)	30 (27%)	70 (23%)
Fellowship			
Functional urology/neurourology-trained	35 (18%)	7 (6%)	42 (14%)
Other fellowship-trained	73 (38%)	38 (34%)	111 (37%)
Not-fellowship-trained	68 (36%)	61 (55%)	129 (43%)

Note: 19 physicians (6%) did not fill out the demographic part of the questionnaire.



**Fig. 1.** Distribution of answers to the questions: *When do you wish to see your patients after starting their treatment?* and *When do you realistically see your patients after starting their treatment?*

lowed by “as needed basis” (21, 22%), “one month” (18, 19%), “six months” (12, 13%), “one year” (6, 6%) and “immediately” (6, 6%). The remaining physicians who treat OAB for a defined time period do not see patients or ask them to contact their family doctor if needed (35, 27%).

## Discussion

Pharmacotherapy has been at the centre of treatment regimens for OAB management. The efficacy of anti-muscarinics and mirabegron in OAB patients is well-documented.<sup>7-9</sup> Whereas significant therapeutic effects are expected from most of these drugs seven days from the start of treatment,<sup>10</sup> data on treatment duration are sparse, although many clinical studies on OAB pharmacotherapy have been published.

The resolution of bothersome symptoms has been given as one of the most common reasons for termination of treatment and may be achieved in more than one-third of OAB cases.<sup>11-15</sup> Other common reasons for medication discontinuation are adverse effects and/or failure of expected clinical outcome. There is no consensus regarding the optimal duration of OAB treatment, as in the vast majority of available clinical trials, time periods of drug administration have been reported to range from two weeks to 12 months.<sup>16</sup> It could be speculated that these studies may underestimate drug efficacy with short time periods of drug administration,<sup>17-19</sup> whereas treatment duration may be lengthier than necessary.<sup>20,21</sup> To make matters even more complex, a specific

**Table 2. Demographic characteristics of respondents who answered the question: Do you start treatment with the lowest or highest recommended medication dose?**

	Lowest dose	Highest recommended dose
Number of answers	202 (81% of physicians treating OAB)	40 (16% of physicians treating OAB)
Specialization (p=0.04)		
Urology	140 (77% of urologists treating OAB)	34 (19% of urologists treating OAB)
Gynecology	62 (56% of gynecologists treating OAB)	6 (5% of gynecologists treating OAB)
Gender (p=0.0007)		
Male	122 (78% of male physicians treating OAB)	35 (22% of male physicians treating OAB)
Female	76 (95% of female physicians treating OAB)	4 (5% of female physicians treating OAB)
Number of years of practice (p=0.23)		
<5	55 (92% of those practicing <5 years and treating OAB)	5 (8% of those practicing <5 years and treating OAB)
5–10	36 (78% of those practicing 5–10 years and treating OAB)	10 (22% of those practicing 5–10 years and treating OAB)
11–20	57 (83% of those practicing 11–20 years and treating OAB)	12 (17% of those practicing 11–20 years and treating OAB)
>20	50 (81% of those practicing >20 years and treating OAB)	12 (19% of those practicing >20 years and treating OAB)
Practice (p=0.15)		
Academic	67 (91% of academics treating OAB)	7 (9% of academics treating OAB)
Community	86 (80% of those working at community hospitals and treating OAB)	21 (20% of those working at community hospitals and treating OAB)
Academic and community	45 (80% of those working at either academic or community hospitals and treating OAB)	11 (20% of those working at either academic or community hospitals and treating OAB)
Fellowship (p=0.41)		
Functional urology/neurourology-trained	38 (90% of functional urology-trained physicians)	4 (10% of functional urology-trained physicians)
Other fellowship-trained	74 (82% of other fellowship-trained physicians treating OAB)	16 (18% of other fellowship-trained physicians treating OAB)
Not-fellowship-trained	86 (82% of not-fellowship-trained physicians treating OAB)	19 (18% of not-fellowship-trained physicians treating OAB)

OAB: overactive bladder.

**Table 3. Demographic characteristic of respondents who answered the question: Do you think that OAB pharmacotherapy (medications) needs to be given lifelong or for a defined time period?**

	Lifelong	Time period
Number of answers	112 (45% of physicians treating OAB)	130 (52% of physicians treating OAB)
Specialization (p=0.03)		
Urology	73 (40% of urologists treating OAB)	101 (56% of urologists treating OAB)
Gynecology	39 (57% of gynecologists treating OAB)	29 (42% of gynecologists treating OAB)
Gender (p=0.43)		
Male	70 (45% of male physicians treating OAB)	87 (55% of male physicians treating OAB)
Female	40 (50% of female physicians treating OAB)	40 (50% of female physicians treating OAB)
Number of years of practice (p=0.08)		
<5	31 (52% of those practicing <5 years and treating OAB)	29 (48% of those practicing <5 years and treating OAB)
5–10	15 (33% of those practicing 5–10 years and treating OAB)	31 (67% of those practicing 5–10 years and treating OAB)
11–20	38 (55% of those practicing 11–20 years and treating OAB)	31 (45% of those practicing 11–20 years and treating OAB)
>20	26 (42% of those practicing >20 years and treating OAB)	36 (58% of those practicing >20 years and treating OAB)
Practice (p=0.52)		
Academic	32 (43% of academics treating OAB)	42 (57% of academics treating OAB)
Community	54 (50% of those working at community hospitals and treating OAB)	53 (50% of those working at community hospitals and treating OAB)
Academic and community	24 (43% of those working at either academic or community hospitals and treating OAB)	32 (57% of those working at either academic or community hospitals and treating OAB)
Fellowship (p=0.08)		
Functional urology/neurourology-trained	24 (57% of functional urology-trained physicians)	18 (43% of functional urology-trained physicians)
Other fellowship-trained	34 (38% of other fellowship-trained physicians treating OAB)	56 (62% of other fellowship-trained physicians treating OAB)
Not-fellowship-trained	52 (50% of not-fellowship-trained physicians treating OAB)	53 (50% of not-fellowship-trained physicians treating OAB)

OAB: overactive bladder.

definition of refractory OAB has not yet been established, resulting in different initiation time points with other medications or treatment modalities.<sup>22</sup>

Canadian urologists and gynecologists generally agree that OAB treatment should be started with the lowest recommended medication dose. Our survey revealed that a slim majority of respondents (52% vs. 45%) recommend OAB pharmacotherapy for a defined time period rather than lifelong. Interestingly, practice patterns of limited treatment duration are more typical for urologists than for gynecologists, who prefer lifelong management. Furthermore, a higher percentage of urologists are more inclined to start treatment with the highest recommended medication dose. Six-month and one-year time periods of OAB pharmacotherapy are the most commonly chosen answers by physicians who treat their patients for a defined time period (41% and 25%, respectively).

In the current literature, the point at which to discontinue OAB pharmacotherapy and the time during which therapeutic efficacy is sustained after discontinuation of drug administration still remain in dispute. Hsiao et al,<sup>16</sup> in their prospective study, proposed that minimal duration

of anti-muscarinic administration for OAB control should be three months. Enrolled patients (n=164) were prescribed 5 mg of solifenacin or 4 mg of tolterodine extended-release capsules daily and then monitored for a mean follow up of one month during a six-month period in order to investigate treatment efficacy and discontinuation patterns.

Other researchers have assessed the effects of drug cessation after different treatment periods. Choo et al<sup>23</sup> measured changes in OAB symptoms in patients (n=68) after discontinuation of successful three-month treatment with 20 mg of propiverine hydrochloride daily. Four weeks after the cessation of anti-muscarinic medication, the retreatment rate of 35.3% was due to worsening symptoms. Patients in the retreatment group were significantly older and had higher initial urgency scores than those requiring no further treatment. Patients who underwent urodynamic study (n=23) and demonstrated detrusor overactivity experienced more rapid symptom recurrence after medication discontinuation than those without detrusor overactivity. However, this correlation was not statistically significant. The authors concluded that, although three months of OAB pharmacotherapy was effective, it could not sustain symptom improvement for one month after discontinuation.



These results line up with those reported by a British group with exactly the same time periods in patients (n=251) treated with flexible-dose fesoterodine (4 and 8 mg).<sup>24</sup> OAB symptoms were significantly improved after the 12-week treatment period but, at four weeks after fesoterodine discontinuation, 61% of patients showed increased micturition frequency, added severity of bladder-related problems, and reduced health-related QoL. Dose escalation from 4 to 8 mg at week four did not appear to influence the level of deterioration. In view of these findings, it can be stated that the beneficial effects on OAB symptoms and patient-reported outcomes after 12 weeks of treatment with an anti-muscarinic drug are not maintained as early as four weeks after treatment stoppage.

Another study analyzed retreatment patterns in 108 OAB patients randomized to three different groups with different time periods of OAB pharmacotherapy: tolterodine extended-release 4 mg daily.<sup>14</sup> After the completion of one-, three- or six-month treatment, patients stopped the medication and were followed up for another three months to assess symptom relapse and retreatment rates. Three months after treatment discontinuation, 65% of patients requested retreatment and 62% experienced symptom relapse, including increased micturition frequency, urgency episodes, urgency severity, and incontinence events, compared to these parameters at the end of treatment. Furthermore, longer treatment did not prevent symptom relapse or retreatment. Nevertheless, the authors proposed that, in patients with improved symptoms, it might be possible to discontinue medication after consultation on the risks of symptom relapse and retreatment. They also stressed that physicians need to pay more attention to patients whose baseline QoL has deteriorated severely because of OAB symptoms, as they are at higher risk of retreatment.

A recently published study enrolled 371 OAB patients who took anti-muscarinic agents for more than 12 weeks and responded favourably.<sup>25</sup> They then discontinued anti-muscarinics and were evaluated for recurrence of bothersome symptoms at baseline, one, three, and six months, with a limited number of patients followed up for 12 months. Cumulative recurrence rates at one, three, and six months were concurrent with earlier studies and were 25.6%, 42.3%, and 52.2%, respectively. However, a recurrence rate of 9.7% was seen in patients analyzed at the 12-month period. Patients without symptom recurrence until six months tended to persist with symptom-free status until 12 months of therapy discontinuation. These authors also demonstrated that patients who initially presented with concomitant urinary incontinence had greater risk of symptom recurrence.

A prospective, randomized study of the anti-muscarinics imidafenacin 0.1 mg twice daily and solifenacin 5 mg once daily gave astonishing results, with a 12-month treatment regimen in 109 patients.<sup>21</sup> It disclosed that among those who discontinued treatment because of improvement, three of 12 patients on imidafenacin (25.0%) and seven of 13

patients on solifenacin (53.8%) had recurring OAB symptoms and required medication within 12 months. Thus, it can be hypothesized that required treatment duration may vary between different OAB drugs.

A retrospective study from the U.S., with data from the IMS LifeLink Health Plan Claims Database, showed that 34.6% of 103 250 patients reinitiated treatment by the end of two years, with approximately one-fifth of patients (24.1%) restarting after one year.<sup>26</sup> Of those who reinitiated anticholinergic therapy, 65.6% did so with their index anticholinergic agent, whereas 34.4% went with a different anticholinergic.

A prospective study from Japan (n=73), assessing persistence rates of solifenacin 5 mg daily treatment during a three-year period, demonstrated that 25% of patients required retreatment at an average 10 months after termination.<sup>12</sup>

Until now, there is paucity of data on the impact of physiotherapy on OAB recurrence after treatment cessation. Further research in this area is warranted, as behavioural therapies, including pelvic floor muscle exercises, are relatively non-invasive and could benefit patient health overall.

To sum up, optimal duration of OAB pharmacotherapy and efficacy sustenance have not yet been determined. Based on our survey and literature review, it is proposed that OAB patients can be treated for their symptoms for 6–12 months and persistence to the drug therapy should be encouraged. Then, treatment cessation can be considered. If patients still need medications, lifelong or long-term OAB pharmacotherapy may be required. Thus, the optimal duration of OAB pharmacotherapy should be individualized, as OAB encompasses a heterogeneous patient population with diverse symptoms, severities, and pathophysiologies. Consideration should be given to possible etiologies and improving bladder health through preventive measures to stop OAB progression. The presented approach could help physicians avoid the administration of ineffective medications and potential drug-related adverse effects.

## Conclusion

There is general agreement among Canadian urologists and gynecologists that OAB treatment should be started with the lowest recommended medication dose. A slim majority of respondents think that OAB pharmacotherapy should be given for a defined time period. Practice patterns of limited treatment duration are more typical for urologists than for gynecologists, who prefer lifelong management.

**Competing interests:** Dr. Przydacz has participated in clinical trials supported by Bristol-Myers Squibb. Dr. Campeau has attended advisory boards for Astellas and Pfizer; has been a speaker for Astellas, Duchesnay, and Pfizer; has received payments/grants/honoraria from Astellas and Pfizer; and has participated in clinical trials supported by Pfizer. Dr. Walter has attended advisory boards for Boston Scientific, Kimberly-Clark, and Duchesnay; has received payments/grants/honoraria from Astellas, Duchesnay, Boston Scientific, Kimberly-Clark, and Ethicon GyneCare. Dr. Corcos has attended advisory boards for Allergan, Astellas, Pfizer; has been a speaker for Allergan and Duchesnay; has

received payments/grants/honoraria from Astellas; and has participated in clinical trials supported by Allergan and Ipsen.

This paper has been peer-reviewed.

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