ORIGINAL RESEARCH

Antimuscarinic Discontinuation in Patients with Overactive Bladder in Nursing Homes: A Retrospective Study of Medicare Beneficiaries

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ABSTRACT

Introduction: Although antimuscarinics form the first-line therapy in overactive bladder (OAB), little is known regarding antimuscarinic discontinuation among OAB patients in nursing homes. This study examined treatment patterns and predictors of antimuscarinic discontinuation among long-term nursing home (LTNH) residents with OAB.

Methods: The study cohort included LTNH residents (defined as residents staying ≥ 101 consecutive days) from the Minimum Data Set linked 2013–2015 Medicare claims data. Patients with OAB were defined by OAB-related claims and medication codes. Treatment patterns and discontinuation (medication gap ≥ 30 days) were characterized by

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examining OAB-specific antimuscarinics prescribed during LTNH stays. The Andersen Behavioral Model was used to identify predisposing, enabling and need factors that predict discontinuation. Kaplan-Meier curves and multivariable Cox proportional hazards regression model were used to assess the unadjusted and adjusted times to discontinuation, respectively, among different antimuscarinics.

Results: The mean age of the study cohort ($n = 11,012$) was 81.6 years (± 8.5), 74.6% were female, and 89.8% were non-Hispanic White. The mean duration of nursing home stay was 530.1 (± 268.4) days. The most commonly prescribed OAB-specific antimuscarinic was oxybutynin (69.8%). Overall, 66.5% of the study cohort discontinued the index antimuscarinic. Multivariable Cox PH regression analysis revealed that compared to LTNH residents who initiated treatment with oxybutynin, treatment discontinuation was lower with solifenacin or fesoterodin and discontinuation was more frequent when treatment was initiated with tolterodine, darifenacin or trospium compared with oxybutynin. In addition, several need factors (comorbidities, medication use and anticholinergic burden, etc.) were associated with antimuscarinic discontinuation.

Conclusion: About two-thirds of LTNH residents with OAB discontinued their index antimuscarinic during their nursing home stay. There was significant variation in discontinuation based on the index antimuscarinic agent

with lowest risk of discontiuation with solifenacin and fesoterodin. Concerted efforts to optimize antimuscarinic use are needed to improve the management of OAB in nursing homes.

Keywords: Adherence; Antimuscarinic; Overactive bladder; Nursing home; Urology

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Key Summary Points

Why carry out this study?

Antimuscarinics are the front-line pharmacotherapy for overactive bladder (OAB), but there is a paucity of data on treatment persistence in this setting.

The objective of the present study was to examine treatment patterns and to assess the medication discontinuation among different antimuscarinics in long-term nursing home (LTNH) residents with OAB.

What was learned from the study?

A low proportion of LTNH residents with OAB under the fee-for-service Medicare plan is prescribed antimuscarinics.

Antimuscarinic discontinuation during nursing home stay was high among LTNH residents with OAB.

Discontinuation varied based on the index antimuscarinic agent, with the lowest risk of discontinuation among LTNH residents who were prescribed solifenacin and fesoterodin.

INTRODUCTION

In 2014, there were an estimated 1.4 million nursing homes residents in the USA [1]. Although nursing home residents may vary in terms of their physical and mental ability and capacity for self-care, residents on average have a higher disease burden compared with community-dwelling individuals [2]. Urinary incontinence (UI) is a symptom accompanying many conditions common among older adults, affecting as many as 50–70% of nursing home residents [3, 4]. Many cases of UI are associated with overactive bladder (OAB), a clinically defined symptom complex characterized by urgency with or without incontinence, often accompanied by frequency and nocturia [5, 6]. In a large claims-based study, nursing home residents with OAB and/or UI had a higher prevalence of depression (47.7% vs. 32.4%), cerebrovascular accidents (20.4% vs. 10.4%) and dementia (40.8% vs. 35.4%) compared with those without OAB and/or UI [7]. In addition to the clinical burden associated with OAB among nursing home residents, the economic burden is substantial. Although recent data are lacking, in 2000, the total direct cost of OAB in nursing homes, including diagnostic, treatment, routine care and health-related consequences (i.e., falls, skin conditions and urinary tract infections), was estimated at 3.5 billion (year 2000 USD) [8].

Antimuscarinics such as oxybutynin, tolterodine, solifenacin, darifenacin, fesoterodine and trospium are approved as a first-line pharmacotherapy for OAB in the US, and, when used appropriately, are an effective and well-tolerated treatment that improves quality of life in patients with OAB [9]. Although there are limited data on pharmacotherapy treatments for OAB in nursing homes, antimuscarinics appear to be widely used [7]. In a retrospective analysis of nursing home residents, almost 80% of those with OAB were treated with an antimuscarinic (primarily oxybutynin extended-release) [7]. Despite their effectiveness at managing OAB symptoms, adherence (often defined as patients who take at least 80% of their prescribed medication or a medication possession ratio [MPR] ≥ 0.8) [10] to antimuscarinics is low [11, 12]. Among community-dwelling OAB patients, estimates of antimuscarinic adherence range from 14 to 35% [11, 12]. In a national survey, dissatisfaction with treatment effectiveness and side effects, which can include dry mouth, blurred vision, headache and constipation, have been cited as reasons for OAB treatment discontinuation [13]. Based on a systematic review, the treatment discontinuation rate among OAB patients was reported in the range of 43–83% [14].

To date, most studies on antimuscarinics have focused on adherence and have been conducted among community-dwelling individuals [11, 12, 15]; there is thus a paucity of data regarding antimuscarinic discontinuation among nursing home residents with OAB. Only one study examined discontinuation in US outpatient settings and found that 72% discontinued their antimuscarinics, suggesting a significant need to improve adherence [16]. Although it would seem likely that persistence and/or adherence to OAB medications among nursing home residents would be high, given the extensive nursing and supportive care, discontinuation of antimuscarinics and the factors associated with antimuscarinic discontinuation have not been examined in this setting.

Given the high frequency of UI/OAB in nursing home populations and the associated high clinical and economic burden, understanding treatment discontinuation in nursing homes may help improve adherence and quality of care for patients with OAB. Therefore, the objective of the present study was to examine treatment patterns and to characterize antimuscarinic discontinuation in long-term nursing home (LTNH) residents with OAB.

METHODS

Data Source

The Minimum Data Set (MDS) linking 2013–2015 Medicare claims data involving Part A, B and D claims [17, 18] was used to examine treatment patterns and predictors of antimuscarinic discontinuation among LTNH residents with OAB. The MDS is a federally mandated nursing home health assessment tool for all residents in Medicare/Medicaid-certified nursing facilities. It is administered to all nursing home residents within 14 days of admission and at quarterly intervals thereafter. It captures detailed information on physical, psychologic and psychosocial functioning and active clinical diagnosis, health conditions, treatments and services. It also provides information on patient's cognitive functioning and behavioral problems. Medicare Part A covers hospital care,

initial care in skilled nursing facilities, hospice care and home health care. Part B covers services such as laboratory, ambulance, outpatient mental health and other physician services that are not included in Part A. Each Part A and Part B record contains up to ten diagnoses recorded according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Part D, launched in 2006, covers prescription benefits for Medicare beneficiaries. Each Part D Prescription Drug Event claim comprises information on prescription drug fills, including drug name, fill date, days of supply and quantity.

The study protocol was approved by the University of Houston Committee for the Protection of Human Subjects. Informed consent was not required given the deidentified nature of the data and feasibility considerations for a large retrospective database such as Medicare.

Study Design and Population

The retrospective cohort consisted of LTNH residents diagnosed with OAB. LTNH residents were defined based on a previously validated MDS/Skilled Nursing Facility algorithm as residents with at least one nursing home episode lasting at least 101 consecutive days [19]. Patients were included in the cohort using a step-wise process if they met the following criteria: (1) ≥ 65 years of age at index date, which was defined as the first long-stay nursing home admission date; (2) at least one claim with an OAB diagnosis either during the nursing home episode or prior (identified based on previously published lists of ICD-9-CM codes) [12, 20, 21] or at least one prescription claim for OAB-specific medication (antimuscarinics, mirabegron or onabotulinumtoxinA specific for bladder usage) during nursing home stay (Supplementary Table 1); (3) Parts A, B and D coverage in the 3 months before the nursing home admission and until the end of the nursing home stay; (4) newly initiated antimuscarinic medication claims lasting at least 30 days continuously during nursing home stay.

Outcome Measures

Antimuscarinics initiated during the nursing home stay were used to examine treatment patterns. Antimuscarinic medications were operationally defined using the American Hospital Formulary Service classification system and identified using National Drug Codes (NDC) [22]. Antimuscarinic medications included darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine and trospium. Treatment discontinuation was defined as the treatment gap of ≥ 30 days between prescription refills prior to nursing home discharge date [23, 24]. Accordingly, patients were categorized into two groups: those who discontinued the index antimuscarinic medication and those who did not discontinue the index antimuscarinic medication [25].

Conceptual Framework

A multivariable Cox proportional hazards (PH) regression analysis was performed to assess the time to discontinuation of antimuscarinic medication among OAB patients. The Andersen Behavioral Model (ABM) was used to guide selection of independent variables in the analysis [26, 27]. This model postulates that an individual's use of health services is a function of predisposing, enabling and need characteristics [26, 27]. Variables corresponding to these factors were selected based on the published literature and data available in the Medicare claims and the MDS [11, 28]. Predisposing factors are the characteristics of an individual that were in existence before the illness and included age, gender, race/ethnicity and marital status. Enabling factors are related to the ability of an individual to secure the healthcare services and included region, Medicare-Medicaid dual eligibility and urban/rural area. Urban/rural area was captured using MDS as the data source. The urban/rural distinction was based on the location of nursing home facility. The need factors describe the perceived and actual health status of an individual. The need variables were captured from both the Medicare claims and the MDS. These included index antimuscarinic

agent, comorbidities measured using the Elixhauser comorbidity scores [29] and falls, prescription medication use (such as antidepressants, diuretics, beta-blockers, calcium channel blockers, anticonvulsants, angiotensin converting enzyme [ACE] inhibitors, antipsychotics, antiparkinson agents and alpha-blockers), anticholinergic burden (measured using the Anticholinergic Cognitive Burden [ACB] scale [30]) and body mass index (BMI). All variables were measured 3 months prior to the first long-stay nursing home admission date. Need characteristics for the ABM were also determined based on the MDS assessment recorded at nursing home admission. These included the presence of urinary or bowel incontinence (defined as always continent, occasionally incontinent, frequently incontinent, always incontinent or not rated, the former of which has been used to characterize patients with urinary incontinence in several studies [31]), bladder continence management (i.e., use of an indwelling/external catheter, ostomy and/or intermittent catheterization), urinary toileting program, response to toileting program, current toileting program or trial, depressed mood indicator and scores on the Cognitive Performance Scale (CPS) [32] and Activities of Daily Living (ADL) scale [33]. Using the CPS, a higher score is indicative of greater impairment, ranging from 0 (intact cognition) to 6 (severe cognitive impairment). Mild cognitive impairment is associated with a score of 2. A higher score on the ADL is indicative of greater impairment/dependence [33]. Using the ADL, an individual's independence is graded as dependent [4–6], limited/extensive assistance [7–9] and independent [10–18]. Due to the higher number of missing values, UI-specific measures (i.e., use of an indwelling/external catheter, ostomy, intermittent catheterization) were not included in the multivariable Cox PH regression model.

Statistical Analysis

Descriptive statistics were used to characterize LTNH residents with OAB and antimuscarinic use. For the study cohort, the discontinuation

rate based on the index antimuscarinic medication was reported. Categorical and continuous patient characteristics were compared among patients who discontinued the index antimuscarinic medication versus those who did not discontinue, using chi-square and student's t-tests, respectively. Time to discontinuation between different antimuscarinic users was compared using Kaplan-Meier curves and log-rank test. Proportionality hazards assumption was confirmed using the Schoenfeld test. Multivariable Cox proportional hazards regression analysis was performed to assess the risk of discontinuation among different antimuscarinic medications with time to discontinuation as the dependent variable. Independent variables were predisposing, enabling and need characteristics based on the ABM framework. Death and loss to follow-up due to lack of insurance coverage were considered as censoring criteria. All relevant variables available in the data set were included in the model.

All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC) with statistical significance set at an a priori- specified level of 0.05.

RESULTS

Study Population

Figure 1 describes the process of cohort derivation. A total of 250,016 LTNH residents ≥ 65 years of age with evidence of OAB and continuous enrollment were initially identified. From this group, 11,012 (4.4%) LTNH residents were newly initiated with antimuscarinic prescription for OAB and had continuous supply of medication for at least 30 days dispensed during the LTNH stay. The mean (± SD) age of the cohort was 81.6 (± 8.5) years. The cohort consisted of 74.6% women and 89.8% non-Hispanic whites. Most of the patients were from South (37.4%) and Midwest (33.5%) regions and resided in urban areas (70.2%). Frequently reported comorbidities included hypertension (80.4%), cardiac arrhythmias (40.7%), diabetes (37.6%) and fluid and electrolyte disturbances (33.4%). The most

frequently prescribed medications were antidepressants (47.4%), beta-blockers (41.5%) and diuretics (36.3%). The mean (± SD) ACB score of the cohort pre-index was 0.7 (± 1.4). This was a pre-index measure of anticholinergic burden. Additional characteristics of the study cohort are summarized in Table 1. The mean duration of nursing home stay was 530.1 (± 268.4) days.

Admission MDS assessments of LTNH residents with OAB revealed that 23.5% had UI frequently (i.e., incontinent seven or more episodes over a 7-day look-back period) and 37.1% had bowel continence constantly. Data on UI were missing for 22.2%. Approximately two-thirds (66.8%) of patients did not require any bladder continence management and 11.1% required some kind of continence management—including an indwelling/external catheter (9.7%), ostomy (1.9%) and intermittent catheterization (0.3%). Approximately 10.1% of the patients required a urinary toileting program (i.e., scheduled training, prompted voiding and bladder training). However, only 1.1% were completely dry (i.e., continent) or showed decreased wetness (i.e., whereby urinary incontinence frequently decreased) following the toileting program. The majority of patients had intact cognition (88.3%) but just over half (51.1%) were dependent on their ADLs (Table 1).

OAB Treatment and Antimuscarinic Discontinuation

About 4.4% (n = 11,012) of the LTNH residents were newly initiated with antimuscarinics with supply lasting at least 30 days continuously. Oxybutynin (69.8%) was the most commonly prescribed antimuscarinic, followed by tolterodine (13.0%) and solifenacin (12.3%) (Table 2). About 67% (n = 7319) of the study cohort was identified to have discontinued the index antimuscarinic medication during their nursing home stay, and while the median days to discontinuation was 61 (interquartile range [IQR]: 31–121) days, the mean (standard deviation) days to discontinuation was 99.9 (± 105.8) days. Discontinuation rate based on the index medication in the order were darifenacin
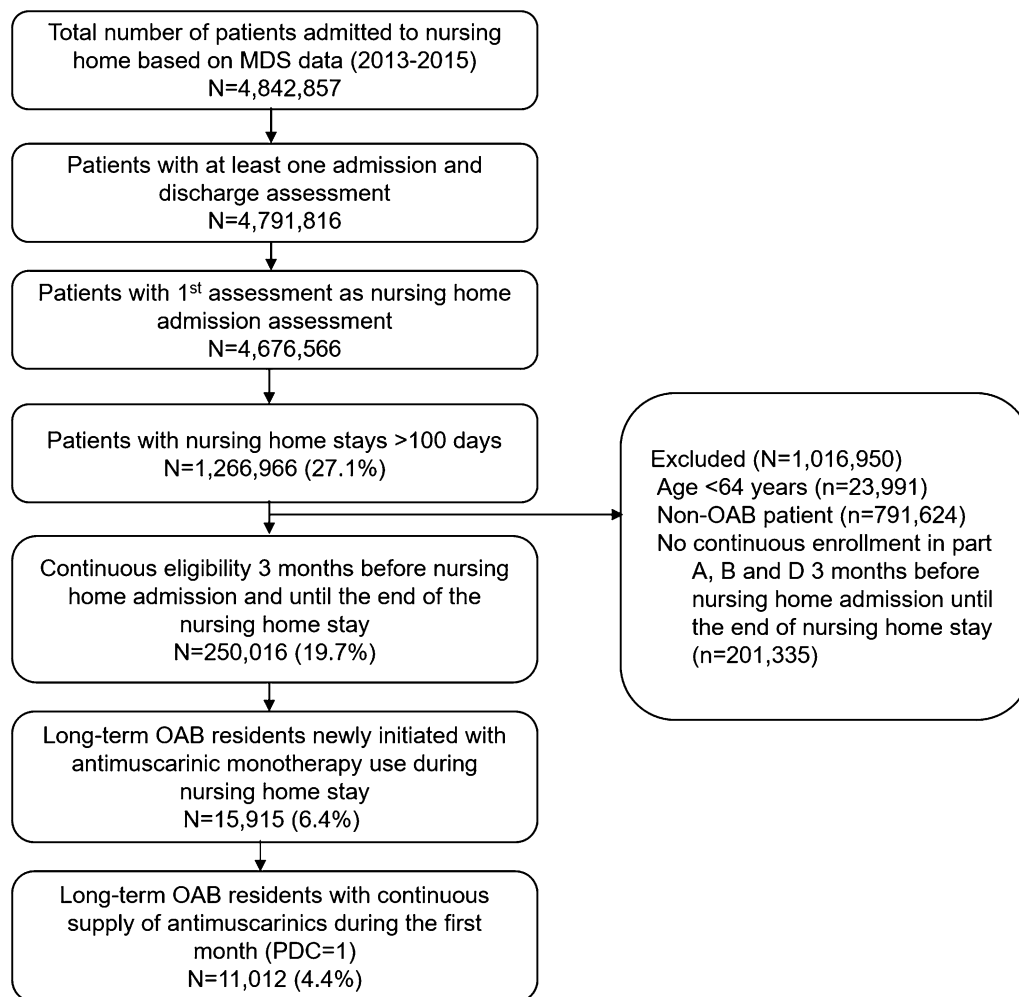
Fig. 1 Study cohort derivation. *MDS* minimum data set, *OAB* overactive bladder, *PDC* Proportion Days Covered

(78.8%), trospium (78.2%), tolterodine (70.8%), oxybutynin (66.4%), fesoterodine (61.4%) and solifenacin (59.8%) (Table 2).

The Kaplan-Meier curve with discontinuation probabilities of antimuscarinic medication over time is shown in Fig. 2. Discontinuation of antimuscarinics varied solely based on the need characteristics (Table 3). Results from the multivariable Cox PH regression model revealed that LTNH residents who initiated with solifenacin (Hazards Ratio (HR) 0.79, 95% CI 0.73–0.85) and darifenacin (HR 0.82, 95% CI 0.68–0.99) were less likely to discontinue medication, while patients who started with tolterodine (HR 1.11, 95% CI 1.03–1.18), darifenacin (HR 1.33, 95% CI 1.06–1.67) and trospium (HR

1.44, 95% CI 1.24–1.66) were more likely to discontinue medication compared to those who were started with oxybutynin. Patients who had liver disease (HR 0.82, 95% CI 0.71–0.94), antipsychotic use (HR 0.93, 95% CI 0.86–0.99) and participated in a urinary toileting program (HR 0.75, 95% CI 0.58–0.97) were less likely to discontinue antimuscarinics than their counterparts, whereas LTNH residents with severe cognitive impairment (HR 1.25, 95% CI 1.10–1.42), dependent on ADL (HR 1.13, 95% CI 1.04–1.23) and occasionally bowel incontinent (HR 1.09, 95% CI 1.01–1.19) were more likely to discontinue antimuscarinics compared to their counterparts. For every unit increase in the pre-index ACB burden, there was a 4%

Table 1 Demographics of long-term nursing home residents with OAB, overall and by discontinuation status

Characteristic	Total (11,012)		Discontinued (7,319, 66.46%)		Not discontinued (3,693, 33.54%)		P value
	n	Percent (%)	*n*	Percent (%)	*n*	Percent (%)	
Predisposing factors							
Age (mean ± SD)	81.57	± 8.52	81.5	± 8.49	81.7	± 8.56	0.313
65–75 years	2621	23.80%	1764	24.10%	857	23.21%	0.568
75–85 years	3875	35.19%	2570	35.11%	1305	35.34%	
≥ 85 years	4516	41.01%	2985	40.78%	1531	41.46%	
Gender							
Male	2799	25.42%	1877	25.65%	922	24.97%	0.44
Female	8213	74.58%	5442	74.35%	2771	75.03%	
Race/ethnicity							
Non-Hispanic White	9891	89.82%	6540	89.36%	3351	90.74%	0.139
Non-Hispanic Black	734	6.67%	514	7.02%	220	5.96%	
Hispanics	123	1.12%	83	1.13%	40	1.08%	
Others	264	2.40%	182	2.49%	82	2.22%	
Marital status							0.82
Unmarried (single/widowed)	8415	76.42%	5580	76.24%	2,835	76.77%	
Married	2529	22.97%	1694	23.15%	835	22.61%	
Others	68	0.62%	45	0.61%	23	0.62%	
Enabling factors							
Medicare/Medicaid dual eligible	5077	46.10%	3462	47.30%	1615	43.73%	**0.004**
Region							0.39
South	4123	37.44%	2778	37.96%	1345	36.42%	
Northeast	2057	18.68%	1369	18.70%	688	18.63%	
Midwest	3688	33.49%	2420	33.06%	1268	34.34%	
West	1144	10.39%	752	10.27%	392	10.61%	
Urban–rural							0.377
Rural	3283	29.81%	2,162	29.54%	1121	30.35%	
Urban	7729	70.19%	5157	70.46%	2572	69.65%	

Table 1 continued

Characteristic	Total (11,012)		Discontinued (7,319, 66.46%)		Not discontinued (3,693, 33.54%)		*P* value
	n	Percent (%)	*n*	Percent (%)	*n*	Percent (%)	
Need factors							
Index antimuscarinic prescription¥							< 0.0001
Solifenacin	1353	12.29%	809	11.05%	544	14.73%	
Fesoterodin	189	1.72%	116	1.58%	73	1.98%	
Tolterodine	1437	13.05%	1017	13.90%	420	11.37%	
Trospium	243	2.21%	190	2.60%	53	1.44%	
Darifenacin	99	0.90%	78	1.07%	21	0.57%	
Oxybutinine	7691	69.84%	5109	69.80%	2582	69.92%	
Elixhauser comorbidities							
Elixhauser Index Score (mean ± SD)	10.12	± 8.77	9.8	± 8.67	10.7	± 8.95	< 0.0001
Prior history of falls	2858	25.95%	1833	25.04%	1025	27.76%	0.003
Congestive heart failure	3171	28.80%	2040	27.87%	1131	30.63%	0.0001
Cardiac arrhythmias	4477	40.66%	2,882	39.38%	1595	43.19%	< 0.0001
Valvular disease	1715	15.57%	1068	14.59%	647	17.52%	0.001
Pulmonary circulation disorders	683	6.20%	414	5.66%	269	7.28%	0.407
Peripheral vascular disorders	2747	24.95%	1808	24.70%	939	25.43%	0.788
Hypertension	8851	80.38%	5888	80.45%	2963	80.23%	0.732
Paralysis	635	5.77%	426	5.82%	209	5.66%	0.568
Other neurologic disorders	2780	25.25%	1860	25.41%	920	24.91%	0.248
Chronic pulmonary disease	3404	30.91%	2236	30.55%	1168	31.63%	0.469
Diabetes	4137	37.57%	2767	37.81%	1370	37.10%	0.615
Hypothyroidism	2643	24.00%	1746	23.86%	897	24.29%	0.195
Renal failure	2031	18.44%	1325	18.10%	706	19.12%	0.003
Liver disease	357	3.24%	211	2.88%	146	3.95%	0.505
Peptic ulcer	164	1.49%	105	1.43%	59	1.60%	0.127
AIDS/HIV	14	0.13%	***	***	***	***	0.58
Lymphoma	91	0.83%	58	0.79%	33	0.89%	0.0002
Metastatic cancer	163	1.48%	86	1.18%	77	2.09%	0.141
Solid tumor without metastasis	782	7.10%	501	6.85%	281	7.61%	0.576
Rheumatoid arthritis	622	5.65%	407	5.56%	215	5.82%	0.339
Coagulopathy	510	4.63%	329	4.50%	181	4.90%	0.943

Table 1 continued

Characteristic	Total (11,012)		Discontinued (7,319, 66.46%)		Not discontinued (3,693, 33.54%)		P value
	n	Percent (%)	*n*	Percent (%)	*n*	Percent (%)	
Obesity	847	7.69%	562	7.68%	285	7.72%	0.214
Weight loss	962	8.74%	622	8.50%	340	9.21%	0.102
Fluid and electrolyte disorders	3682	33.44%	2,409	32.91%	1273	34.47%	0.937
Blood loss anemias	222	2.02%	147	2.01%	75	2.03%	0.299
Deficiency anemias	1020	9.26%	663	9.06%	357	9.67%	0.349
Alcohol abuse	185	1.68%	117	1.60%	68	1.84%	0.953
Drug abuse	189	1.72%	126	1.72%	63	1.71%	0.266
Psychoses	1905	17.30%	1287	17.58%	618	16.73%	**0.005**
Depression	3171	28.80%	2171	29.66%	1000	27.08%	**0.018**
Medication use							
Alpha-blockers	228	2.07%	155	2.12%	73	1.98%	0.624
Beta-blockers	4564	41.45%	3030	41.40%	1534	41.54%	0.889
Calcium channel blockers	2984	27.10%	2034	27.79%	950	25.72%	**0.021**
ACE inhibitors	2985	27.11%	1991	27.20%	994	26.92%	0.749
Diuretics	3996	36.29%	2632	35.96%	1364	36.93%	0.316
Antidepressants	5219	47.39%	3543	48.41%	1676	45.38%	**0.003**
Antipsychotics	1716	15.58%	1,170	15.99%	546	14.78%	**0.101**
Anticonvulsants	2742	24.90%	1,884	25.74%	858	23.23%	**0.004**
Antiparkinson agents	1130	10.26%	759	10.37%	371	10.05%	0.597
ACB scale (mean ± SD)	0.65	± 1.35	0.72	± 1.42	0.53	± 1.18	**< 0.0001**
Body mass index*							0.426
Underweight	2878	26.14%	1940	26.51%	938	25.40%	
Normal weight	482	4.38%	323	4.41%	159	4.31%	
Overweight	2385	21.66%	1600	21.86%	785	21.26%	
Obese	2686	24.39%	1750	23.91%	936	25.35%	
Missing/unknown	2581	23.44%	1706	23.31%	875	23.69%	
Urinary continence*†							**< 0.0001**
Always continent	1835	16.66%	1153	15.75%	682	18.47%	
Occasionally incontinent	1932	17.54%	1216	16.61%	716	19.39%	
Frequently incontinent	2583	23.46%	1755	23.98%	828	22.42%	
Always incontinent	1,241	11.27%	941	12.86%	300	8.12%	

Table 1 continued

Characteristic	Total (11,012)		Discontinued (7,319, 66.46%)		Not discontinued (3,693, 33.54%)		*P* value
	n	Percent (%)	*n*	Percent (%)	*n*	Percent (%)	
Not rated	975	8.85%	644	8.80%	331	8.96%	
Missing/unknown	2446	22.21%	1610	22.00%	836	22.64%	
Bladder continence management*							
Indwelling/external catheter							0.663
Yes	1068	9.70%	703	9.61%	365	9.88%	
No	7514	68.23%	5015	68.52%	2499	67.67%	
Missing/unknown	2430	22.07%	1601	21.87%	829	22.45%	
Ostomy							0.321
Yes	210	1.91%	149	2.04%	61	1.65%	
No	8372	76.03%	5569	76.09%	2803	75.90%	
Missing/unknown	2,430	22.07%	1601	21.87%	829	22.45%	
Intermittent catheterization							0.327
Yes	34	0.31%	19	0.26%	15	0.41%	
No	8548	77.62%	5699	77.87%	2,849	77.15%	
Missing/unknown	2430	22.07%	1601	21.87%	829	22.45%	
None of the above bladder appliance							0.766
Yes	7359	66.83%	4907	67.04%	2452	66.40%	
No	1223	11.11%	811	11.08%	412	11.16%	
Missing/unknown	2430	22.07%	1601	21.87%	829	22.45%	
Urinary toileting program*							< 0.0001
Yes	1115	10.13%	795	10.86%	320	8.67%	
No	6020	54.67%	4170	56.97%	1850	50.09%	
Missing/unknown	3877	35.21%	2354	32.16%	1,523	41.24%	
Response to toileting program*							0.096
No improvement	151	1.37%	111	1.52%	40	1.08%	
Decreased wetness	81	0.74%	61	0.83%	20	0.54%	
Completely dry (continent)	39	0.35%	26	0.36%	13	0.35%	
Missing/unknown	10,741	97.54%	7121	97.29%	3620	98.02%	
Current toileting program or trial*							0.002
Yes	751	6.82%	528	7.21%	223	6.04%	
No	515	4.68%	368	5.03%	147	3.98%	
Missing/unknown	9746	88.50%	6423	87.76%	3323	89.98%	

Table 1 continued

Characteristic	Total (11,012)		Discontinued (7,319, 66.46%)		Not discontinued (3,693, 33.54%)		P value
	n	Percent (%)	n	Percent (%)	n	Percent (%)	
Bowel continence*							< 0.0001
Always continent	4090	37.14%	2574	35.17%	1516	41.05%	
Occasionally incontinent	1216	11.04%	792	10.82%	424	11.48%	
Frequently incontinent	1638	14.87%	1158	15.82%	480	13.00%	
Always incontinent	1416	12.86%	1046	14.29%	370	10.02%	
Not rated	206	1.87%	138	1.89%	68	1.84%	
Missing/unknown	2446	22.21%	1611	22.01%	835	22.61%	
MDS Cognition Scale*							< 0.0001
Intact	9724	88.30%	6391	87.32%	3333	90.25%	
Mild	146	1.33%	93	1.27%	53	1.44%	
Moderate	370	3.36%	241	3.29%	129	3.49%	
Moderate/severe	93	0.84%	69	0.94%	24	0.65%	
Severe	395	3.59%	311	4.25%	84	2.27%	
Missing/unknown	284	2.58%	214	2.92%	70	1.90%	
Activities of daily living*							< 0.0001
Independent	2708	24.59%	1578	21.56%	1130	30.60%	
Limited/extensive assistance	379	3.44%	258	3.53%	121	3.28%	
Dependent	5624	51.07%	3981	54.39%	1643	44.49%	
Missing/unknown	2301	20.90%	1502	20.52%	799	21.64%	
Depressed mood indicator*							< 0.0001
Yes	245	2.22%	182	2.49%	63	1.71%	
No	7637	69.35%	5,135	70.16%	2,502	67.75%	
Missing/unknown	3130	28.42%	2002	27.35%	1128	30.54%	

ACB anticholinergic burden, *AIDS/HIV* acquired immune deficiency syndrome/human immune deficiency virus, *LTNH* long-term nursing home, *MDS* minimum data set, *OAB* overactive bladder, *SD* standard deviation

Significant values are bolded

*Based on MDS Admission Assessment and includes missing data

**Based on enrollment data and includes missing data

***Cannot report due to small cell size

[†] Categories of urinary incontinence were defined as: always continent (over a 7-day look-back period, resident was continent with urine, with no episodes of incontinence); occasionally incontinent (over a 7-day look-back period, resident was incontinent less than 7 episodes); frequently incontinent (over a 7-day look-back period, resident was incontinent 7 or more episodes); always incontinent (over a 7-day look-back period, resident had no continent episodes); not rated (over a 7-day look-back period the resident had an indwelling catheter, condom catheter, ostomy or no urine output for the entire 7 days)

[¥] Index antimuscarinic prescription refers to antimuscarinic medication that patients were newly started with upon nursing home admission

increased likelihood of discontinuing the antimuscarinic medication.

DISCUSSION

To our knowledge, this is the first study to characterize discontinuation among different antimuscarinics in LTNH residents with OAB. A total of 11,012 (4.4%) residents were newly started with an OAB antimuscarinic prescription during the LTNH stay. Despite the significant impact of OAB on patients' quality of life and the availability of effective pharmacotherapies that can mitigate those symptoms, a small portion elderly LTNH residents in the current study initiated antimuscarinic medications. The low proportion of patients initiating pharmacotherapies for their OAB identified in the present study may be due to several factors including prescription costs and coverage, perceptions around antimuscarinic safety and effectiveness, inclusion of high-level anticholinergics as part of Beers criteria, patient and provider preferences as well as low rates of persistence with OAB medications [24, 34].

Consistent with the previous US-based literature [35–37], the most commonly prescribed antimuscarinics observed in the present study were oxybutynin (69.8%) followed by solifenacin (12.3%) and tolterodine (13.0%). The high percentage of oxybutynin use is consistent with Zarowitz et al. who reported that among US nursing facilities, 61.1% were treated with oxybutynin extended release [7]. The high frequency of oxybutynin prescriptions may likely be because of generic status, formulary coverage and capitated payment for initial nursing home stays. High rates of use of oxybutynin may be another example of potentially inappropriate medication use within nursing homes, especially in older populations with cognitive issues [38, 39]. In fact, according to the FORTA list, oxybutynin is rated as C/D and should be used with caution or even avoided in older populations [40]. Therefore, if behavioral options are not effective and pharmacotherapies are required given the risk of cognitive effects associated with oxybutynin, caution must be exercised prior to prescribing oxybutynin in

older and/or frail adults presenting with OAB [41–44]. The high rates of oxybutynin use combined with relatively longer times to discontinuation identified in this study give reasons for concern. Although physicians were not queried in this study, it may indicate that clinicians are possibly complacent regarding these risks, especially for the older populations with cognitive issues.

As OAB usually requires long-term treatment to achieve symptom control, persistence to prescribed pharmacotherapy is important in achieving the best treatment outcomes. This study found that almost 67% of the study cohort discontinued antimuscarinic medication prior to their nursing home discharge and several need factors were associated with treatment discontinuation. Across other studies, the discontinuation rate of antimuscarinics among individuals with OAB has been estimated to be about 43–83% based on a systematic review [14, 24] and 52% to 89% from a more recent study [16]. Although persistence in nursing homes may naturally be higher compared to community-dwelling individuals because of the active involvement of care providers in medication management, it is still sub-optimal given that adherence to antimuscarinics improves quality of life in patients with OAB [45]. Although patient-reported reasons for antimuscarinic discontinuation and non-adherence could not be evaluated in the present study because of the data limitations, future research on this is needed to explore the common reasons for discontinuation and develop personalized treatment plans to optimize OAB management.

In the current study, the specific type of index antimuscarinic medication was significantly associated with antimuscarinic discontinuation. Compared to oxybutinin users, solifenacin and fesoterodine users had less risk of discontinuation, whereas tolterodine, darifenacin and trospium carried higher risk of discontinuation. However, in a study that assessed antimuscarinic discontinuation among a Medicare elderly population in a community setting, all five agents (solifenacin, fesoterodine, darifenacin, tolterodine and trospium) showed less

Table 2 Overall treatment pattern, discontinuation rate and time to discontinuation based on index antimuscarinic medication during long-term nursing home stays

	Antimuscarinic utilization rate		Antimuscarinic discontinuation rate		Time to discontinuation of index antimuscarinic medication	
Total	**n 11,012**	**Percent (%) 100.00%**	**n 7319**	**Percent (%) 66.46%**	**Mean (SD)**	**Median (IQR)**
Index antimuscarinic medication						
Oxybutinine	7691	69.8	5109	66.4	96.98 (102.19)	61 (31–121)
Tolterodine	1437	13.0	1017	70.8	97.85 (104.01)	61 (31–113)
Solifenacin	1353	12.3	809	59.8	121.82 (124.42)	71 (43–147)
Trospium	243	2.2	190	78.2	80.64 (97.08)	46 (31–91)
Fesoterodin	189	1.7	116	61.4	122.39 (121.58)	75 (43–151)
Darifenacin	99	0.9	78	78.8	100.59 (111.14)	59 (32–114)

IQR interquartile range, *SD* standard deviation
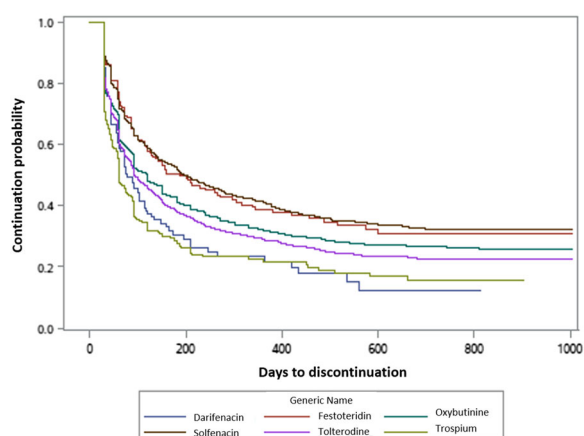
Fig. 2 Kaplan-Meier curve: discontinuation probability by type of antimuscarinic medication

risk of discontinuation compared to oxybutynin [16].

In this study, 67% of LTNH residents discontinued their index antimuscarinic, which is similar to the proportion reported by Vouri et al., among community-based Medicare older adults [16]. An unexpected finding was that none of the predisposing and enabling factors contributed to antimuscarinic discontinuation in LTNH residents, which is in contrast to the aforementioned community-based study.

Furthermore, in the Vouri et al. study patients with congestive heart failure, mild cognitive impairment, depression, diabetes and hypertension were all less likely to discontinue their antimuscarinics [16]. However, in the current study, none of these factors were associated with discontinuation. It is possible that differences between the two studies are due to underlying characteristics of the two populations. The presence of liver failure, obesity and utilization history of antipsychotics were all negatively associated with discontinuation, whereas use of calcium channel blockers/anticonvulsants and severe cognitive decline were positively associated with discontinuation. The current study indicated that a high anticholinergic burden was associated with higher likelihood of discontinuation. Although the overall anticholinergic burden was assessed pre-index in the present study, and therefore relatively low (0.53), it was nevertheless associated with increased discontinuation. As all of the antimuscarinics assessed in the present study would have had an ACB score of 3 had the anticholinergic burden been assessed post-treatment initiation, the results from the present study indicate that even low levels of anticholinergic burden impact persistence among OAB LTNH residents. It is, however, very

Table 3 Factors associated with discontinuation of antimuscarinic drugs in long-term nursing home residents with OAB. Results from multivariable Cox proportional hazards regression model

Characteristic	Adjusted hazards ratio (95% CI)	*P* value
Predisposing factors		
Age (mean ± SD)		
65–75 years	Reference	
75–85 years	0.96 (0.90–1.02)	0.176
≥ 85 years	0.97 (0.90–1.04)	0.391
Gender		
Male	Reference	
Female	0.95 (0.89–1.00)	0.070
Race/ethnicity		
Non-Hispanic White	Reference	
Non-Hispanic Black	1.05 (0.95–1.15)	0.346
Hispanics	0.99 (0.79–1.23)	0.906
Others	1.04 (0.89–1.21)	0.632
Marital status		
Unmarried (single/widowed)		
Married	1.04 (0.98–1.10)	0.214
Others	1.03 (0.76–1.38)	0.867
Enabling factors		
Medicare/Medicaid dual eligible	0.98 (0.93–1.03)	0.460
Region		
South	Reference	
Northeast	0.98 (0.91–1.05)	0.509
Midwest	1.02 (0.96–1.08)	0.558
West	1.05 (0.96–1.14)	0.271
Urban-rural		
Rural	Reference	
Urban	1.03 (0.98–1.09)	0.258
Need factors		
Index antimuscarinic prescription¥		
Solifenacin	**0.79 (0.73–0.85)**	**< 0.0001**
Fesoterodine	**0.82 (0.68–0.99)**	**0.039**
Tolterodine	**1.11 (1.03–1.18)**	**0.004**

Table 3 continued

Characteristic	Adjusted hazards ratio (95% CI)	*P* value
Trospium	**1.44 (1.24–1.66)**	**< 0.0001**
Darifenacin	**1.33 (1.06–1.67)**	**0.012**
Oxybutinin	Reference	
Elixhauser comorbidities		
Elixhauser Index score (mean ± SD)		
Prior history of falls	0.95 (0.90–1.00)	0.050
Congestive heart failure	0.98 (0.93–1.04)	0.518
Cardiac arrhythmias	0.96 (0.92–1.01)	0.141
Valvular disease	0.95 (0.89–1.02)	0.135
Pulmonary circulation disorders	0.92 (0.83–1.02)	0.124
Peripheral vascular disorders	0.97 (0.92–1.02)	0.248
Hypertension	1.00 (0.94–1.06)	0.888
Paralysis	1.01 (0.91–1.11)	0.908
Other neurologic disorders	1.00 (0.94–1.06)	0.979
Chronic pulmonary disease	1.01 (0.95–1.06)	0.829
Diabetes	1.01 (0.96–1.06)	0.833
Hypothyroidism	0.99 (0.93–1.04)	0.650
Renal failure	1.01 (0.95–1.08)	0.653
Liver disease	**0.82 (0.71–0.94)**	**0.005**
Peptic ulcer	0.98 (0.81–1.20)	0.861
AIDS/HIV	1.71 (0.96–3.03)	0.067
Lymphoma	0.85 (0.66–1.11)	0.238
Metastatic cancer	0.80 (0.64–1.01)	0.056
Solid tumor without metastasis	1.03 (0.94–1.14)	0.492
Rheumatoid arthritis	1.02 (0.92–1.13)	0.679
Coagulopathy	1.03 (0.92–1.15)	0.633
Obesity	1.07 (0.98–1.18)	0.134
Weight loss	0.97 (0.89–1.06)	0.494
Fluid and electrolyte disorders	1.00 (0.95–1.05)	0.852
Blood loss anemias	1.06 (0.90–1.25)	0.495
Deficiency anemias	1.00 (0.92–1.08)	0.924
Alcohol abuse	0.97 (0.80–1.17)	0.757

Table 3 continued

Characteristic	Adjusted hazards ratio (95% CI)	*P* value
Drug abuse	0.95 (0.79–1.14)	0.567
Psychoses	0.98 (0.92–1.05)	0.606
Depression	1.06 (1.00–1.12)	0.060
Medication use		
Alpha-blockers	1.01 (0.86–1.18)	0.935
Beta-blockers	1.00 (0.96–1.06)	0.872
Calcium channel blockers	**1.06 (1.01–1.12)**	**0.022**
ACE inhibitors	1.00 (0.95–1.05)	0.931
Diuretics	0.98 (0.93–1.03)	0.379
Antidepressants	1.00 (0.95–1.05)	0.896
Antipsychotics	**0.93 (0.86–0.99)**	**0.032**
Anticonvulsants	**1.07 (1.01–1.13)**	**0.016**
Antiparkinson agents	1.00 (0.92–1.08)	0.945
ACB scale (mean ± SD)	**1.04 (1.03–1.06)**	**< 0.0001**
Body mass index*		
Underweight	Reference	
Normal weight	1.04 (0.92–1.17)	0.554
Overweight	0.97 (0.90–1.03)	0.314
Obese	**0.90 (0.84–0.97)**	**0.006**
Missing/unknown	0.99 (0.82–1.21)	0.960
Urinary continence*†		
Always continent	Reference	
Occasionally incontinent	0.95 (0.87–1.04)	0.258
Frequently incontinent	0.99 (0.90–1.08)	0.800
Always incontinent	1.09 (0.96–1.22)	0.176
Not rated	1.03 (0.83–1.28)	0.809
Missing/unknown	0.65 (0.28–1.51)	0.315
Bladder continence management*		
Indwelling/external catheter		
Yes	Reference	
No	0.86 (0.59–1.24)	0.411
Missing/unknown	1.36 (0.60–3.08)	0.455

Table 3 continued

Characteristic	Adjusted hazards ratio (95% CI)	*P* value
Ostomy		
Yes	Reference	
No	**1.46 (1.01–2.12)**	**0.044**
Missing/unknown	-	–
Intermittent catheterization		
Yes	Reference	
No	0.68 (0.41–1.13)	0.133
Missing/unknown	-	-–
None of the above bladder appliance		
Yes	Reference	
No	0.96 (0.68–1.34)	0.793
Missing/unknown	-	–
Urinary toileting program*		
Yes	Reference	
No	**0.75 (0.58–0.97)**	**0.027**
Missing/unknown	0.76 (0.66–0.86)	< 0.0001
Response to toileting program*		
No improvement	Reference	
Decreased wetness	1.18 (0.86–1.63)	0.299
Completely dry (continent)	0.93 (0.60–1.43)	0.736
Missing/unknown	1.02 (0.83–1.26)	0.829
Current toileting program or trial*		
Yes	Reference	
No	0.95 (0.83–1.10)	0.510
Missing/unknown	0.72 (0.56–0.91)	0.006
Bowel continence*		
Always continent	Reference	
Occasionally incontinent	1.00 (0.92–1.09)	0.988
Frequently incontinent	**1.09 (1.01–1.19)**	**0.036**
Always incontinent	1.09 (0.98–1.21)	0.125
Not rated	0.78 (0.57–1.08)	0.136
Missing/unknown	1.32 (0.59–2.94)	0.496

Table 3 continued

Characteristic	Adjusted hazards ratio (95% CI)	P value
MDS cognition scale*		
Intact	Reference	
Mild	1.10 (0.89–1.36)	0.387
Moderate	1.04 (0.90–1.20)	0.575
Moderate/severe	1.02 (0.80–1.30)	0.867
Severe	**1.25 (1.10–1.42)**	**0.0001**
Missing/unknown	1.11 (0.97–1.28)	0.132
Activities of daily living*		
Independent	Reference	
Limited/extensive assistance	1.14 (0.99–1.32)	0.061
Dependent	**1.14 (1.05–1.23)**	**0.003**
Missing/unknown	1.00 (0.81–1.25)	0.965
Depressed mood indicator*		
Yes	Reference	
No	1.00 (0.86–1.17)	0.964
Missing/unknown	1.21 (1.05–1.39)	0.010

ACB anticholinergic burden, *AIDS/HIV* acquired immune deficiency syndrome/human immune deficiency virus, *LTNH* long-term nursing home, *MDS* minimum data set, *OAB* overactive bladder, *CI* confidence interval, *SD* standard deviation
All regression models were adjusted for predisposing, enabling and need factors
Significant values are bolded
*Based on MDS Admission Assessment and includes missing data
**Based on enrollment data and includes missing data
[†] Categories of urinary incontinence were defined as: always continent (over a 7-day look-back period, resident was continent with urine, with no episodes of incontinence); occasionally incontinent (over a 7-day look-back period, resident was incontinent less than 7 episodes); frequently incontinent (over a 7-day look-back period, resident was incontinent 7 or more episodes); always incontinent (over a 7-day look-back period, resident had no continent episodes); not rated (over a 7-day look-back period the resident had an indwelling catheter, condom catheter, ostomy or no urine output for the entire 7 days)
[¥] Index antimuscarinic prescription refers to antimuscarinic medication that patients were newly started with upon nursing home admission

likely that the burden was much higher after antimuscarinic initiation and may have been a stronger predictor of discontinuation. Furthermore, patients with participation in a urinary toileting program, those who were dependent on ADL and those with frequent bowel incontinence were associated with higher discontinuation. As this is the first study that assessed antimuscarinic discontinuation among nursing home residents and adjusted for several need variables, comparison and contrast were not possible in the context of these variables.

Although this study provided insights regarding treatment patterns and predictors of antimuscarinic discontinuation, there are several limitations to be acknowledged. First, MDS

measurements are assessed by nursing home providers and are used for resource use and reimbursement purposes rather than research. Therefore, there may be missing data if specific measures are not regarded as relevant, which may explain the high number of missing values for UI-related variables. Second, patients were assumed to have administered the medication-based prescription fills prior to discontinuation. Hence, it should be acknowledged that time to discontinuation could have been much earlier than estimated here in the event that the medications were not taken. However, this would not differentially impact individual antimuscarinic agents. Third, as prescription medication use and discontinuation were based on Part D claims only during the nursing home stay, any medications provided by nursing homes as part of their care under the prospective payment system were not captured. The discontinuation was assessed based on Part D claims only; the issues with Part A coverage were not specifically addressed as Part A covers only the first 100 days and does not include prescription details; also, significant variability exists regarding the coverage source for Part D medications. However, this would not lead to differential bias in adherence/persistence. Fourth, as only antimuscarinics were examined in the present study, more research is needed to evaluate non-antimuscarinics such as mirabegron, sacral neuromodulation, posterior tibial nerve stimulation or the wider category of anticholinergics. As a result, the treatment and discontinuation patterns presented here can only be generalized to LTNH residents with OAB treated with antimuscarinics, and overall treatment rates may actually be higher than those estimated in the current study. Fifth, although the MDS may be a rich data source, several other factors not captured in the data source could not be included. Also, we decided to use a 3-month baseline period to increase the sample size. This could have led to some comorbidities not being captured. Other limitations include that the use of non-pharmacologic treatments (i.e., pads/briefs, or enemas/irrigation) was not captured, and as the data are limited to fee-for-service Medicare beneficiaries, the results cannot be generalized to uninsured nursing home residents or residents insured through Medicare Advantage plans. Lastly, although the ICD codes used here were consistent with those used to identify patients with OAB from other studies, there was the potential for misclassification, as evident by 5% of the study cohort identified with paralysis, which is typically associated with neurogenic detrusor overactivity rather than OAB. Furthermore, although males represented only one-fourth of OAB cases in the present study, it is possible that some of these cases were cases of BPH rather than OAB.

CONCLUSION

This retrospective cohort study found that 67% of LTNH residents with OAB discontinue antimuscarinic medications during nursing home stay, and several need characteristics were associated with discontinuation. Most importantly, the study found significant variation in medication discontinuation based on the index antimuscarinic agent. The study found that oxybutynin is most frequently used in nursing homes and discontinuation risk with oxybutynin is higher than for solifenacin and fesoterodine, but less than for toleterodine, trospium and darifenacin. Therefore, concerted efforts are needed to optimize and improve antimuscarinic medication use to improve quality of care of OAB in nursing homes.

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Compliance with Ethics Guidelines. The study protocol was approved by the University of Houston Committee for the Protection of Human Subjects. Informed consent was not required given the deidentified nature of the data and feasibility considerations for a large retrospective database such as Medicare.

Data Availability. Researchers may request access to anonymized participant-level data, trial-level data and protocols from Astellas-sponsored clinical trials at www.clinicalstudy-datarequest.com. For the Astellas criteria on data sharing see: https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx. The datasets generated during and/or analyzed during the current study are not publicly available as, per government regulations and the data use agreement, data from the Centers for Medicare and Medicaid Services cannot be shared.

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