Effect of Potentially Inappropriate Use of Antimuscarinic Medications on Healthcare Use and Cost in Individuals with Overactive Bladder

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OBJECTIVES: To examine potentially inappropriate medication (PIM) use in older adults initiating an antimuscarinic medication for the treatment of overactive bladder (OAB).

DESIGN: Retrospective database analysis.

SETTING: Medical and pharmacy claims data.

PARTICIPANTS: Medicare Advantage Prescription Drug Plan members aged 65 and older newly initiated on an antimuscarinic OAB treatment were identified and assigned to PIM and non-PIM comparison groups based on 2012 American Geriatrics Society Beers Criteria and/or the presence of an anticholinergic medication interaction at the time of initiation of treatment (N = 66,275).

MEASUREMENTS: Healthcare costs and OAB medication use.

RESULTS: Of members initiated on an antimuscarinic OAB medication, 31.1% had a drug–drug or drug–disease or syndrome interaction. Dementia was the most common disease or syndrome interaction (11.3%), followed by constipation (8.6%) and delirium (2.9%). Paroxetine (2.6%), amitriptyline (2.2%), cyclobenzaprine (1.7%), and meclizine (1.6%) were the most common interacting medications. Subjects in the PIM group had greater healthcare costs over 12 months of follow-up ($12,001) than those in the non-PIM group ($9,373) after controlling for baseline characteristics ($P < .001$). There was no difference between the PIM and the non-PIM groups in odds of discontinuing OAB treatment at 12 months after controlling for baseline characteristics (odds ratio = 0.98, 95% confidence interval = 0.89–1.07, $P = .63$).

CONCLUSION: Potentially inappropriate medication use was highly prevalent and was associated with greater total healthcare costs. Providers should carefully consider medical history and concurrent medication use when initiating antimuscarinic medication for the treatment of OAB. Development of interventions to reduce potentially inappropriate use of antimuscarinics in individuals with OAB is warranted. **J Am Geriatr Soc 2015.**

Key words: overactive bladder; potentially inappropriate medication use; healthcare costs

Older adults generally have a greater risk of medication-related adverse events than younger individuals because they use more medications and because of age-related physiological changes. Inappropriate prescribing of medication in elderly adults is common and can lead to higher healthcare costs, adverse drug reactions, hospitalization, and mortality.[1–9] The economic burden of potentially inappropriate medication (PIM) use is substantial, estimated at $7.2 billion in 2001.[10] Owing to the substantial clinical and economic consequences of PIM, explicit PIM criteria such as the 2012 American Geriatrics Society (AGS) Beers Criteria[11] have been incorporated into a number of healthcare quality initiatives, including Centers for Medicare and Medicaid Services Star Ratings measures.

Antimuscarinic medications are a type of anticholinergic that block the activity of acetylcholine at muscarinic receptors. Muscarinic receptors are distributed throughout the body, including the urinary bladder, bowel, salivary glands, ciliary muscle of the eye, and central nervous system.[12] The distribution of muscarinic receptors gives rise to the potential for a broad range of anticholinergic side effects, such as dry mouth, blurred vision, constipation, and impaired cognition.[13] Antimuscarinic side effects can be related to anticholinergic burden resulting from exposure to multiple medications with anticholinergic properties (pharmacodynamic drug–drug interaction) or related

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to the use of antimuscarinic medications in individuals with predisposing medical conditions (drug–disease or syndrome interaction).

Potentially inappropriate anticholinergic use in elderly adults has been documented in a number of previous studies.[9,14–16] Research has demonstrated that exposure to anticholinergic medications in older adults is associated with poorer cognitive performance, greater cognitive decline, and greater mortality.[17,18] According to the 2012 AGS Beers Criteria, strong anticholinergic medications such as antihistamines, tertiary tricyclic antidepressants, scopolamine, and benztropine should be categorically avoided in older adults.[11] It is recommended that other anticholinergics, such as antimuscarinics for treatment of overactive bladder (OAB), be avoided in older adults with certain medical conditions or syndromes. Antimuscarinics used to treat urinary incontinence are specifically recommended against in individuals with dementia, chronic constipation, or delirium.[11]

Overactive bladder is a urological condition characterized by the presence of bothersome urinary problems such as urinary urgency, frequent urination, nocturia, and urinary incontinence. Antimuscarinic medications such as oxybutynin, tolterodine, and solifenacin are traditional pharmacological treatments for OAB. Nonpharmacological interventions and medications with alternate mechanism of action (e.g., beta-3 agonist) are also appropriate treatments for OAB. The American Urological Association guidelines for diagnosis and treatment of OAB in adults recommends antimuscarinics or beta-3 agonist as pharmacological treatment after or in conjunction with first-line interventions involving behavioral therapies such as bladder and pelvic floor training.[19] The guidelines caution that individuals who are taking other medications with anticholinergic effects and frail individuals should not take antimuscarinic OAB medications.

Within the context of evolving options for the treatment of OAB and concerns regarding the use of antimuscarinics in high-risk older adults, this study was undertaken to examine the prevalence of PIM in Medicare beneficiaries aged 65 and older newly initiating antimuscarinic treatment for OAB. In addition to the prevalence of PIMs related to OAB antimuscarinic use in older adults, this study sought to determine the relationship between potentially inappropriate prescribing of antimuscarinic OAB medications and healthcare costs and OAB medication use.

METHODS

Design

This was a retrospective, observational, longitudinal cohort study. Administrative claims data from Humana Inc., from January 1, 2007, to July 31, 2013, were used. Enrollment data were used to determine demographic characteristics including age, sex, and race and ethnicity. Pharmacy claims data included prescription fill dates, National Drug Code numbers, quantity dispensed, days' supply, and drug cost data. Medical claims included *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes associated with medical encounters, service dates, and financial data. An independent institutional review board reviewed and approved the research protocol before study initiation.

Study Population

Individuals aged 65 to 89 enrolled in a Medicare Advantage Prescription Drug plan and newly prescribed antimuscarinic OAB medication between January 1, 2008, and July 31, 2012, were identified. The date of first prescription claim for an antimuscarinic OAB medication was treated as the index date, and all subjects were required to have 12 months of preindex and 12-months of postindex continuous enrollment. To ensure that all subjects were newly initiated on antimuscarinic OAB medication, a 12-month antimuscarinic OAB medication-free preindex period was required.

PIM Use

Potentially inappropriate medication use was identified based on subjects having a drug–disease or syndrome interaction or indication of significant anticholinergic medication burden at the time of initiation of an antimuscarinic OAB treatment. PIM-qualifying drug-disease or syndrome interactions were determined based on medical conditions included in the 2012 AGS Beers Criteria list of conditions in which anticholinergic medication use is deemed potentially inappropriate.[11] If an individual receiving a new prescription for an antimuscarinic OAB medication had one or more medical claims with an ICD-9-CM diagnosis code for dementia, delirium, or constipation during the 12-month preindex period, that member was identified as having a PIM-qualifying drug–disease or syndrome interaction. A medication proxy was also used to identify subjects with dementia. Subjects with one or more prescription claims for medications indicated for treatment of Alzheimer's disease (acetylcholinesterase inhibitor or memantine) were identified as having dementia.[20,21]

In addition to identifying PIMs based on the presence of a drug–disease or syndrome interaction, PIM use was also identified based on assessment of anticholinergic burden when OAB treatment was initiated. Health plan members taking non-OAB medications with high anticholinergic burden were identified based on Anticholinergic Cognitive Burden Scale (ACB) classifications. The ACB classifies medications as drugs with possible anticholinergic effects (ACB score 1) or drugs with established and clinically relevant anticholinergic activity (ACB score 2 or 3). The ACB has been used in a variety of clinical and research settings to identify and quantify anticholinergic exposure.[18,22,23] Individuals receiving one or more anticholinergic medications with an ACB score of 2 or 3 and with anticholinergic medication coverage that overlapped the index date or within 30 days after the index date were identified.

After members with PIM at the time of antimuscarinic OAB treatment initiation were identified, a non-PIM comparison group was identified. To be included in the non-PIM comparison group, members were required to have no 2012 AGS Beers Criteria diagnosis (dementia, delirium, constipation) and no prescription claim for any medication

with an ACB score of 2 or 3 during the pre- or postindex period (index OAB medication not included).

ACB Score

In addition to using the ACB to identify PIMs, ACB scores were used to quantify general anticholinergic burden in study subjects. An ACB score was calculated for each member based on summing the ACB score contributed by each antimuscarinic medication for that member, including all medications with ACB scores of 1, 2, or 3. Multiple exposures to the same anticholinergic ingredient were counted only once.

Medical Conditions

Elixhauser medical conditions were identified using diagnosis codes associated with inpatient and outpatient medical claims during the preindex measurement period and based on the enhanced ICD-9-CM implementation of Quan et al.[24–26] Elixhauser comorbidities were counted if the condition was coded on an inpatient medical claim or on two or more outpatient claims observed at least 30 days apart.[27,28] In addition to the Elixhauser conditions, diagnosis of OAB or neurogenic bladder and use of OAB-related medical procedures (sacral nerve stimulation, percutaneous tibial nerve stimulation, botulinum toxin administration, other surgical or invasive procedures) were measured during the preindex period.

Healthcare Costs

All-cause and OAB-related healthcare costs were based on actual paid amounts, including member and plan share, as recorded on adjudicated medical and pharmacy claims. OAB-related medical and pharmacy costs were measured as the cumulative costs associated with medical when an ICD-9-CM code for OAB was found in the primary diagnosis position or pharmacy claims for OAB medications. Preindex costs were measured during a fixed 12-month period before the index date, and postindex costs were measured during a fixed 12-month period after the index date. All healthcare costs were adjusted to 2013 dollars based on the medical care component of the consumer price index.

OAB Medication Adherence and Persistence

Overactive bladder medication use was examined in terms of medication adherence and persistence.[29] OAB treatment persistence was assessed as time in days from the index date to discontinuation of index antimuscarinic treatment. Treatment discontinuation was identified using the permissible gap method.[30] For the purposes of this study, the predetermined period of permissible gap time allowed between refills was 15 days. A 30-day permissible gap was also used as a sensitivity analysis.

Antimuscarinic medication adherence was assessed as proportion of days covered (PDC) with the index OAB treatment over three predefined postindex observation periods: 3, 6, and 12 months. Multiple observation periods for the PDC calculation were used to examine the effect of PIM use on medication adherence over short- and long-term measurement periods. The numerator for the PDC calculation was total number of days for which the member had medication coverage with the index therapy supplied; the denominator was total number of days in the given observation period.[31,32] Subjects with a PDC of 0.80 or greater were defined as adherent. In addition to medication adherence and persistence, number of prescription claims for index OAB medication, cumulative days' supply for index OAB medication, and preindex cumulative days' supply of any anticholinergic medication were measured.

Statistical Analysis

Means and standard deviations were calculated for continuous variables and frequency counts and percentages for categorical variables. *T*-tests were used to compare normally distributed continuous data between the PIM and non-PIM comparison groups, chi-square tests for categorical or dichotomous data, log-rank tests for time-to-event data, and Wilcoxon rank-sum tests for nonnormal continuous data.

Multivariable-adjusted analyses were used to examine the relationship between PIM status and outcome measures after controlling for preindex differences in demographic, healthcare spending, and clinical characteristics between the two groups. Three outcomes were modeled: postindex all-cause total healthcare cost, 12-month PDC, and 12-month treatment persistence. Multivariable generalized linear models (GLMs) were used for all adjusted analysis. Healthcare cost was log-transformed and modeled as a continuous variable using the identity link. The model for PDC was fit using the identity link and a gamma distribution. Twelve-month treatment persistence status was modeled using the logit link and a binary distribution. All three models included age, sex, race and ethnicity, geographic region, indicators for each Elixhauser condition category, an indicator for neurogenic bladder status, and an indicator for OAB-related procedure status as covariates. Preindex all-cause healthcare cost was also included as a covariate in the cost model. A constant of 1 was added to each value of pre- and postindex costs to ensure no zero values before cost data were log-transformed or modeled.[33] Mean adjusted total healthcare cost and 95% confidence intervals (CIs) were calculated using smeared estimates.[34] As a sensitivity analysis, cost data were alternatively modeled with GLM using a log-link and gamma distribution. All analyses were conducted using SAS Enterprise Guide 5.1 (SAS Institute, Inc., Cary, NC). The a priori alpha level for all inferential analyses was set at 0.05, and all statistical tests were two-sided.

RESULTS

Of 66,275 individuals who met the study inclusion and exclusion criteria (Table 1), 31.1% (n = 20,629) initiated on an OAB medication were identified as having a drug–drug or drug–disease or syndrome interaction, and 3.8% (n = 2,543) were identified as having both a drug–drug and drug–disease or syndrome interaction at the index date (Table 2). Dementia (according to ICD-9-CM code) (11.3%, n = 7,455) was the most common drug–disease or

syndrome interaction observed, followed by constipation (8.6%, n = 5,713) and delirium (2.9%, n = 1,915). Dementia was observed according to medication proxy in 6.3% (n = 4,152) of subjects. An anticholinergic drug–drug interaction was present in 14.3% (n = 9,501) of members at the time of initiation of a new antimuscarinic OAB treatment. Paroxetine, amitriptyline, cyclobenzaprine, and meclizine were the most common potentially interacting antimuscarinic medications observed at the index date (data not shown).

Of the 45,646 members who did not meet the study definition for PIM use at the time of initiation of a new OAB medication, 30.2% (n = 13,802) had a newly identified antimuscarinic or drug–disease or syndrome interaction during the postindex period. In addition, 6,333 members were identified who had a prescription claim for an antimuscarinic medication during the preindex period but did not meet the requirement for overlap in days coverage to be classified in the PIM group at index. The primary analysis, therefore, involved comparisons of healthcare costs and medication use for 20,629 members flagged with PIM use at the index date and 25,511 non-PIM members.

Table 1. Subject Selection and Attrition Flow Summary

Selection Criteria	n
Medicare Advantage Prescription Drug beneficiary with prescription claim for antimuscarinic OAB medication between January 1, 2008, and July 31, 2012	543,960
Age ≥65 and <90 years at index	397,105
No OAB medication claim observed during 12-month preindex period	297,091
≥12 months of continuous preindex enrollment	146,621
≥12 months of continuous postindex enrollment	66,697
Complete demographic data[a]	66,275
Final cohort	66,275

[a]Complete demographic data include sex, geographic region, and race and ethnicity.
OAB = overactive bladder.

Table 2. Prevalence of Potentially Inappropriate Medication (PIM) Use, Drug–Disease or Syndrome Interactions, and Antimuscarinic Medication Interactions in Subjects Newly Initiated on Antimuscarinic Medication for Overactive Bladder (N = 66,275)

PIM Type	n (%)
Any drug–disease or syndrome interaction or antimuscarinic medication interaction at index	20,629 (31.1)
Any drug–disease or syndrome interaction at index	13,671 (20.6)
Dementia according to ICD-9-CM code	7,455 (11.3)
Dementia according to medication proxy	4,152 (6.3)
Delirium	1,915 (2.9)
Constipation	5,713 (8.6)
Anticholinergic medication interaction present at index date[a]	9,501 (14.3)
Drug–disease or syndrome and anticholinergic medication interaction present at index	2,543 (3.8)

Drug–disease or syndrome categories are not mutually exclusive. Dementia according to medication proxy is not mutually exclusive from dementia according to *International Classification of Disease, Ninth Edition, Clinical Modification* (ICD-9-CM) diagnosis code.
[a]Medication coverage that overlaps the index date or prescription filled within 30 days after the index date.

The demographic and clinical characteristics of the PIM and non-PIM comparison groups are summarized in Table 3. The PIM and non-PIM groups differed in age, sex, geographic region, race and ethnicity, and health plan type (all $P < .001$). Oxybutynin was the most frequently observed index OAB medication in both groups, followed by tolterodine and solifenacin. Mean cumulative days' supply ± standard deviation of antimuscarinic medications during the preindex period was 92.9 ± 130.9 for the PIM group. The preindex ACB cumulative score was greater in the PIM group (3.9 ± 3.3) than the non-PIM group (1.0 ± 1.1) ($P < .001$). Mean number of Elixhauser conditions was 3.3 ± 2.8 in the PIM group and 2.1 ± 2.0 in the non-PIM group ($P < .001$).

Unadjusted postindex all-cause total healthcare, medical, and pharmacy costs were greater in the PIM group than the non-PIM group (all $P < .001$, Table 4). Likewise, unadjusted OAB-related total healthcare, medical, and pharmacy costs were greater in the PIM group than the non-PIM group (all $P < .001$, Table 4).

Mean number of index OAB medication prescription claims (3.6 ± 3.4 vs 3.1 ± 3.1, $P < .001$) and cumulative days' supply (118.5 ± 108.8 vs 108.8 ± 105.4, $P < .001$) was greater in the PIM group than the non-PIM group. In the non-PIM group, 47.8% (n = 12,202) of subjects did not refill their index medication, compared with 41.4% (n = 8,535) of members in the PIM group ($P < .001$). The PIM group had modest but statistically significant greater mean OAB medication PDC for each of the prespecified follow-up intervals (3 months 0.62 ± 0.31 vs 0.59 ± 0.32, 6 months 0.45 ± 0.32 vs 0.42 ± 0.31, 12 months 0.32 ± 0.30 vs 0.30 ± 0.29; all $P < .001$), and a greater percentage were classified as adherent (PDC ≥0.80) at each follow-up interval (3 months 37.0% vs 35.0%, 6 months 23.3% vs 19.7%, 12 months 12.7% vs 10.7%; all $P < .001$). PIM group members had more days to end of persistent therapy (87.6 ± 94.7 vs 80.9 ± 90.3, log-rank test $P < .001$), and a greater percentage of the PIM group than of non-PIM group was persistent with antimuscarinic OAB treatment at 3 (23.9% vs 20.3%), 6 (13.2% vs 11.4%), and 12 (5.1% vs. 4.5%) months (all $P < .001$). Findings from the sensitivity analysis using a 30-day permissible gap were similar to the primary analysis based on a 15-day permissible gap.

Multivariable Adjusted Analyses

After controlling for between-group differences in baseline demographic and clinical characteristics and preindex costs, subjects with PIM use retained statistically significantly higher 12-month mean total healthcare costs ($12,001, 95% CI = $11,657–12,355) than those without PIM use ($9,373, 95% CI = $9,113–9,641) ($P < .001$). The sensitivity analysis using GLM with log-link and gamma distribution yielded similar hypothesis testing results. After controlling for baseline demographic and

Table 3. Baseline Demographic and Clinical Characteristics of Subjects Assigned to the Potentially Inappropriate Medication (PIM) Use and the Non-PIM Use Comparison Groups

Characteristic	Non-PIM, n = 25,511	PIM, n = 20,629	*P*-Value
Sex, n (%)			
Female	16,319 (64.0)	14,342 (69.5)	<.001
Male	9,192 (36.0)	6,287 (30.5)	
Age, mean ± SD	74.8 ± 6.2	76.3 ± 6.6	<.001
Age, n (%)			
65–69	6,340 (24.9)	4,069 (19.7)	<.001
70–74	7,073 (27.7)	4,648 (22.5)	
75–79	5,718 (22.4)	4,836 (23.4)	
80–84	4,158 (16.3)	4,302 (20.9)	
85–89	2,222 (8.7)	2,774 (13.4)	
Geographic region, n (%)			
Midwest	6,899 (27.0)	4,692 (22.7)	<.001
Northeast	602 (2.4)	392 (1.9)	
South	15,247 (59.8)	13,649 (66.2)	
West	2,763 (10.8)	1,896 (9.2)	
Race and ethnicity, n (%)			
White	21,573 (84.6)	17,402 (84.4)	<.001
Black	2,636 (10.3)	2,032 (9.9)	
Hispanic	515 (2.0)	568 (2.8)	
Other, missing	787 (3.1)	627 (3.0)	
Health plan type, n (%)			
Health maintenance organization	10,037 (39.3)	8,353 (40.5)	<.001
Private fee for service	6,160 (24.1)	4,545 (22.0)	
Preferred provider organization	5,803 (22.7)	3,947 (19.1)	
Point of service	219 (0.9)	140 (0.7)	
Other, missing	3,292 (12.9)	3,150 (15.3)	
Index drug, n %			
Oxybutynin	11,799 (46.3)	9,046 (43.9)	<.001
Tolterodine	6,502 (25.5)	5,394 (26.1)	.11
Solifenacin	5,826 (22.8)	4,836 (23.4)	.12
Darifenacin	1,342 (5.3)	1,302 (6.3)	<.001
Fesoterodine	42 (0.2)	50 (0.2)	.06
Trospium	0 (0.0)	1 (0.0)	.27
Elixhauser comorbidity score, mean±SD	2.1 ± 2.0	3.3 ± 2.8	<.001
Elixhauser conditions, n (%)			
Congestive heart failure	1,215 (4.8)	2,201 (10.7)	<.001
Cardiac arrhythmia	2,935 (11.5)	4,025 (19.5)	<.001
Valvular disease	1,239 (4.9)	2,006 (9.7)	<.001
Pulmonary circulation disorder	309 (1.2)	521 (2.5)	<.001
Peripheral vascular disease	2,369 (9.3)	3,148 (15.3)	<.001
Hypertension, uncomplicated	14,111 (55.3)	13,941 (67.6)	<.001
Hypertension, complicated	542 (2.1)	719 (3.5)	<.001
Paralysis	148 (0.6)	445 (2.2)	<.001
Other neurologic disorder	439 (1.7)	2,423 (11.7)	<.001
Chronic pulmonary disease	2,960 (11.6)	4,136 (20.0)	<.001
Diabetes mellitus, uncomplicated	6,329 (24.8)	6,012 (29.1)	<.001
Diabetes mellitus, complicated	2,195 (8.6)	2,367 (11.5)	<.001
Hypothyroidism	3,322 (13.0)	3,715 (18.0)	<.001
Renal failure	2,640 (10.3)	3,116 (15.1)	<.001
Liver disease	162 (0.6)	258 (1.3)	<.001
Peptic ulcer disease	129 (0.5)	252 (1.2)	<.001
Acquired immunodeficiency or human immunodeficiency virus	6 (0.0)	6 (0.0)	.71
Lymphoma	141 (0.6)	159 (0.8)	.004
Metastatic cancer	154 (0.6)	223 (1.1)	<.001
Solid tumor without metastasis	4,124 (16.2)	3,219 (15.6)	.10
Rheumatoid arthritis, collagen vascular disease	795 (3.1)	1,019 (4.9)	<.001
Coagulopathy	376 (1.5)	646 (3.1)	<.001
Obesity	1,152 (4.5)	1,263 (6.1)	<.001
Weight loss	110 (0.4)	478 (2.3)	<.001
Fluid, electrolyte disorder	1,135 (4.4)	3,048 (14.8)	<.001
Blood-loss anemia	170 (0.7)	304 (1.5)	<.001

(Continued)

Table 3 (Contd.)

Characteristic	Non-PIM, n = 25,511	PIM, n = 20,629	*P*-Value
Deficiency anemia	2,184 (8.6)	3,635 (17.6)	<.001
Alcohol abuse	115 (0.5)	218 (1.1)	<.001
Drug abuse	148 (0.6)	329 (1.6)	<.001
Psychosis	557 (2.2)	2,162 (10.5)	<.001
Depression	924 (3.6)	2,828 (13.7)	<.001
Days' supply of antimuscarinic medications, mean ± SD	0.0 ± 0.0	92.9 ± 130.9	<.001
Cumulative Anticholinergic Burden Scale score, mean ± SD	1.0 ± 1.1	3.9 ± 3.3	<.001

P-values are from between-group comparison of non-PIM vs PIM. *T*-tests were used for continuous variables and chi-square tests for categorical variables. SD = standard deviation.

Table 4. Unadjusted Postindex All-Cause and Overactive Bladder (OAB)-Related Healthcare Expenditures

	$, Mean ± Standard Deviation (Median)		
Expenditure	Non-PIM, n = 25,511	PIM at Index, n = 20,629	*P*-Value
All-cause healthcare expenditures			
Total healthcare	8,930 ± 14,306 (4,580)	17,268 ± 24,614 (8,938)	<.001
Medical	6,515 ± 13,414 (2,162)	13,380 ± 23,513 (4,946)	<.001
Pharmacy	2,415 ± 3,724 (1,662)	3,888 ± 5,031 (2,853)	<.001
OAB-related healthcare expenditures			
Total healthcare	561 ± 1,087 (223)	665 ± 1,173 (324)	<.001
Medical	83 ± 889 (0)	104 ± 964 (0)	<.001
Pharmacy	478 ± 615 (171)	560 ± 654 (270)	<.001

P-values are from between-group comparison for non-potentially inappropriate medication (PIM) vs PIM use at index using Wilcoxon rank sum test. All costs inflated to 2013 dollars based on the Medical Care Component of the Consumer Price Index.

clinical characteristics, PDC was 1.7 percentage points greater in the PIM group than in the non-PIM group (estimate 0.0171, standard error 0.0029, $P < .001$). There was no statistically significant relationship observed between PIM status and OAB treatment discontinuation at 12 months in the multivariable adjusted model based on the primary analysis definition using a 15-day gap or the sensitivity definition using a 30-day gap (15-day definition OR = 0.977, 95% CI = 0.891–1.072, $P = .63$; 30-day definition OR = 0.939, 95% CI = 0.871–1.013, $P = .10$). Detailed reporting of multivariable model results is included in Tables S1 to S4.

DISCUSSION

This study examined the prevalence of OAB antimuscarinic PIM use and the relationship between PIM use and healthcare costs and OAB medication use in older adults. More than 30% of study subjects were identified as having a drug–drug or drug–disease or syndrome interaction at the time of initiation of an antimuscarinic OAB treatment. In addition, approximately 30% of members who did not meet the definition of PIM use at the time of initiation of an antimuscarinic OAB treatment had medication use or a diagnosis that would be considered indicative of PIM use after initiation of OAB antimuscarinic treatment, demonstrating the dynamic nature of medication regimens in and clinical status of this population. The prevalence of antimuscarinic PIM use in this study cohort was high but consistent with other studies of community-dwelling elderly adults, which have identified PIM prevalence ranging from 20% to 40%.[9,14,35–37] In a recent study, the prevalence of PIM use in a general sample of Medicare Advantage Prescription Drug beneficiaries was 31.9%.[37] In general, most studies have examined PIM use on the basis of age criteria (medications that are broadly inappropriate in older individuals). Studies examining PIM use in specific populations and in conditional situations are less common. One study[38] examined PIM use in elderly adults with dementia and found a PIM prevalence of 23.3%; presence of urinary incontinence in adults with dementia was associated with six-fold greater odds of exposure to medications with significant anticholinergic activity.[38] In the current study, focused on individuals initiating antimuscarinic OAB medication, dementia was the most common medical condition associated with PIM use.

To minimize PIM use, providers should consider medical history and concurrent medication use when initiating OAB medication treatment. PIM use is generally associated with more prescribers being involved in an individual's care and more medications being taken.[37,39] In clinical situations in which cognitive impairment may be intrinsic to the presentation, the patient may not be a reliable informant of current or past medication history. Standardized cognitive assessment is warranted before initiating antimuscarinic treatment for OAB in older adults.[19] In addition, research has found that a variety of interventions and care models, ranging from pharmacist interventions to

medical decision-making support tools to geriatric consultation and coordinated care programs, can reduce PIM in frail elderly adults.[40–47]

Consistent with potentially inappropriate use of antimuscarinics in individuals with OAB, healthcare costs were found to be higher in the PIM group than in the non-PIM group in unadjusted and adjusted analyses. Given the potential effect of PIM use on healthcare costs, quality measure performance, and clinical outcomes, health plans may be well situated to encourage and facilitate physician–patient engagement to reduce PIM use in high-risk individuals. Further research to identify specific cost drivers may provide meaningful insights to inform development of interventions designed for providers or patients that modify the prevalence and effect of PIM use in older adults with OAB.

Potentially inappropriate medication status was associated with greater levels of OAB medication adherence in unadjusted analyses and in the regression model controlling for between-group differences in baseline patient characteristics. The clinical significance of the magnitude of difference in OAB medication adherence observed (the 1.7-percentage-point difference in PDC) is not clear. Despite the modestly greater number of days covered with medication for the PIM group, there was no statistically significant difference observed for OAB medication persistence at 12 months in the adjusted analysis. Cognitive impairment is generally associated with poor medication adherence.[48] One potential explanation for the higher rates of adherence in the PIM cohort may be greater caregiver involvement or residential care for older adults with cognitive deficits such as dementia or history of delirium. In previous research in individuals with dementia, reliance on a caregiver has been associated with greater medication adherence.[49] Because the current study did not assess factors such as caregiver involvement, this may warrant further research. Another potential explanation for greater adherence in the PIM group is that these individuals may be experiencing side effects from existing anticholinergic therapies, before initiation of OAB treatment, and may not associate distinct anticholinergic adverse effects with treatment for OAB. In addition, medically complex individuals such as those in the PIM group may have greater interaction with healthcare providers, which may result in greater medication adherence.

The current study was limited in that it examined PIM use related to antimuscarinic OAB medication initiation conditional upon the presence of a drug–disease or syndrome or drug-drug interaction. The rate of overall PIM (use of a broader list of medications that are categorically inappropriate in older adults) was not examined, so the estimate of PIM related to antimuscarinic use is an underestimate of overall PIM use in older adults with OAB. Although this study fills a knowledge gap with regard to potentially inappropriate use of antimuscarinic medications in individuals with OAB, limitations inherent to claims-based research studies, such as inaccuracy of claims data due to coding errors of omission and commission, incomplete claims, unreliable clinical coding, and unobservable factors, may have influenced the observed outcomes. In addition, the ascertainment period used to identify medical conditions of interest such as dementia, delirium, and constipation may have resulted in underdetection in the study population. For example, results from previous claims-based analyses suggest that up to 36 months of claims data may be necessary for optimal identification of dementia using administrative claims data. These factors may result in underestimation of the true prevalence of PIM use based on diagnosis criteria in the study population. This study did not examine clinical outcomes, severity and duration of OAB, whether prior nonpharmacological treatment had been used, or service use such as provider office visits. More broadly, this study was limited in that claims data do not provide insight into rationale or clinical history behind medical decision-making in specific individuals. In addition, interventions aimed at reducing PIM use may not result in reductions in healthcare costs estimated to be associated with PIM use in the current study. Research to determine the effect of interventions to reduce PIM use and the cost-effectiveness of such interventions is necessary. Furthermore, because one health plan provided information for this study, the results may not be generalizable to other plans or other settings.

In conclusion, this study found that potentially inappropriate use of anticholinergic OAB medications was highly prevalent and that PIM use was associated with greater healthcare costs in older adults initiating treatment with an antimuscarinic OAB medication. To minimize PIM use when initiating treatment for OAB, providers should carefully consider medical history and concurrent medication use. Further research to identify cost and quality-of-care drivers may assist in development of interventions that can modify the clinical and economic effect of PIM use in older adults with OAB. Patient and provider interventions should be developed and evaluated to determine whether effective interventions can result in positive outcomes in individuals with OAB.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Results of regression of antimuscarinic overactive bladder medication proportion of days covered on potentially inappropriate medication use status and covariates.

Table S2. Results of logistic regression of antimuscarinic overactive bladder treatment discontinuation (15 day threshold) on potentially inappropriate medication use status and covariates.

Table S3. Results of logistic regression of antimuscarinic overactive bladder treatment discontinuation (30 day threshold) on potentially inappropriate medication use status and covariates.

Table S4. Results of regression of all-cause healthcare costs on potentially inappropriate medication use status and covariates.

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