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Insights from the AQUA Registry: a retrospective study of anticholinergic polypharmacy in the United States

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Abstract

Background: Anticholinergic (ACH) burden is a risk factor for negative health outcomes among older adults. Several medications contribute to ACH burden, including antimuscarinics used to manage overactive bladder (OAB).

Objectives: This study aimed to understand the extent of ACH burden in an OAB population in the United States.

Design: Non-interventional retrospective analysis.

Methods: Adults with OAB whose care providers participated in the American Urological Association Quality (AQUA) Registry between 2014 and 2020 were included in this study. An adapted version of the Pharmacy Quality Alliance (PQA) measure of anticholinergic polypharmacy (poly-ACH) was used to assess ACH burden. The primary outcome was the annual prevalence of poly-ACH, and a secondary outcome was the percentage of patients taking 0, 1, 2, 3, 4, or ≥ 5 ACH medications by calendar year. Analyses were stratified by age category at diagnosis and sex.

Results: The sample comprised 552,840 patients with OAB. The mean age at initial OAB diagnosis was 65.7 years (58.2% male; 57.4% white). Prevalence of poly-ACH was highest in 2015 (3.7%) and lowest in 2020 (1.9%). Patients prescribed no ACH medications made up the largest proportion of each cohort, while those prescribed five or more comprised the smallest. The trend of decreasing proportions of patients taking increasing numbers of ACH medications was consistent. The proportion of patients prescribed no ACH medications increased from 63.3% in 2014 to 74.6% in 2020. The percentage of those prescribed three or more ACHs remained largely unchanged. Poly-ACH was highest among younger individuals (< 65 years of age) and females; temporal trends were similar overall and within each age and sex stratum.

Conclusion: In this study, poly-ACH in patients with OAB was relatively infrequent and decreased over the study period. Further evaluation of poly-ACH is needed to assess whether the study findings reflect increased awareness of the negative effects of poly-ACH.

Keywords: anticholinergic burden, observational study, overactive bladder, polypharmacy

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Introduction

Overactive bladder (OAB) is a chronic urologic condition typically characterized by urgency, with or without urge urinary incontinence (UI), and accompanied by frequency and nocturia.^{1,2} The current epidemiological literature suggests that

the overall prevalence of OAB in the United States is between 16.5% and 23.3%, as assessed by self-reported symptoms.³ The burden of OAB is greatest among older adults (aged 65 years and older), with 40% reported to experience symptoms.^{4–6} However, an analysis of Medicare

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fee-for-service claims found that only 7.2% of Medicare beneficiaries had a formal diagnosis of OAB.⁷

Following behavioral intervention, antimuscarinic agents, members of the broader class of anticholinergic (ACH) medications, are the most frequently used form of OAB pharmacotherapy.⁸ However, caution is advised in their use, as cumulative anticholinergic polypharmacy (poly-ACH) is associated with numerous central and peripheral consequences that can lead to negative outcomes, such as xerostomia, constipation, and cognitive decline.^{8–11} Among older adults, ACH use has been linked to impairments in physical performance and the ability to perform activities of daily living (ADLs), and an increased risk of dementia.^{12–14} Furthermore, cumulative exposure to ACH medications ('ACH burden') increases the risk of these events.^{12–14} As a result, the most recent version of the American Geriatrics Society Beers Criteria recommends drugs with strong ACH properties being avoided,¹⁵ a recommendation which includes all antimuscarinics used for treating OAB. Despite this, analyses using Medicare claims have shown that 75% of Medicare patients aged 65 years and older with OAB have used at least one antimuscarinic drug.¹⁶

Efforts to understand the degree of ACH burden among older adults with OAB are currently evolving. The Pharmacy Quality Alliance (PQA) defines poly-ACH as 'concurrent use for ≥ 30 cumulative days of ≥ 2 unique ACH medications, each with ≥ 2 prescription claims on different dates of service during the measurement year'.¹⁷

While administrative claims provide relevant information from the insurer's perspective, data are limited to codes associated with medical encounters and pharmacy claims. Understanding poly-ACH in real-world settings can provide further understanding of the magnitude of burden that can be offset through alternative treatment selection. Therefore, the objectives of this study are (1) to describe the overall prevalence of poly-ACH use among patients with OAB within the American Urological Association Quality (AQUA) Registry over time (by calendar year), stratified by patients' age (< 65 , ≥ 65 years); (2) to describe the percentage of patients according to number of ACHs (0, 1, 2, 3, 4, and 5 or more) by calendar year; and (3) to describe the percentage of OAB patients with any ACH use or

poly-ACH use summarized by calendar year and stratified by age and sex.

Methods

Data source and study design

A non-interventional retrospective analysis using electronic health record (EHR) data from the AQUA Registry from January 1, 2014 through December 31, 2020 was conducted. The AQUA Registry is a national registry of urologic care providers, designed to measure, report, and improve healthcare quality and attendant patient outcomes. Participating practices include solo practices, large private group practices, and academic medical centers, representing all geographic regions in the United States.¹⁸ Data are automatically extracted from EHR systems and subsequently de-identified. Structured data are directly extracted, and written notes and other data are analyzed for additional data using regular expression searches.¹⁸ Between 2014 and 2020, there were 3019 urologic care providers across the United States actively registering their patients in the database, resulting in nearly 7.5 million unique patients by the end of 2022.

To be included in this study, patients in the AQUA Registry were required to be aged ≥ 18 years, have ≥ 1 International Classification of Diseases (ICD)-9 or ICD-10 code for OAB (Supplementary Table 1) or ≥ 1 prescription for OAB medication (mirabegron, darifenacin, fesoterodine, solifenacin, tolterodine, trospium, or oxybutynin; see Supplementary Table 2 for complete list of codes), and ≥ 1 year of continuous enrollment in the AQUA Registry. Patients were excluded from this study if they were pregnant, had record of a malignant neoplasm, renal impairment, hepatic insufficiency, trauma, (Supplementary Table 3), or had ≥ 1 ICD-9 or ICD-10 code indicative of neurogenic OAB, to avoid incorrect categorization of those with conditions with similar symptoms to those of idiopathic OAB. This practice is standard in studies using claims data in OAB.¹⁹

Definition of poly-ACH

The PQA definition of poly-ACH was used to address the study objectives, with some modifications to account for limitations within the AQUA Registry. Specifically, the original PQA definition

requires that there be ≥ 2 prescription claims for each unique ACH medication on different dates of service during the measurement year. However, medication refills are not captured by most practices within the AQUA Registry; therefore, the definition was adjusted so that patients were required to have only one prescription record during the measurement year. In addition, the list of medications associated with the Anticholinergic Cognitive Burden (ACB) scale was used in lieu of that of the American Geriatric Society (AGS) Beers criteria, on which the PQA was based.²⁰ The ACB scale was used as it comprises a more comprehensive list of ACH medications and facilitates an estimate of quantitative burden. The four components used to define poly-ACH in this study were as follows:

1. An individual had positive evidence of Poly-ACH when they had concurrent prescriptions for ≥ 30 cumulative days of ≥ 2 unique ACH medications, each with ≥ 1 prescription claims on different dates of service during the measurement year (for the purposes of this study, the list of medications in the ACB scale was used to identify ACH medications; Supplementary table 4).²¹
2. Concurrent prescription was identified using the dates of service and days' supply of an individual's prescription claims. The days of concurrent prescription were calculated as the count of days during the measurement year with overlapping days' supply for ≥ 2 unique ACH medications. Days' supply or overlap that occurred after the end of the measurement year was excluded.
3. If multiple prescription claims for the same ACH medication (active ingredient) were recorded on the same day, the number of days covered by the ACH medication was calculated using the prescriptions with the longest days' supply.
4. If multiple prescription claims of the same ACH medication (active ingredient) were recorded on different days with overlapping days' supply, each day in the measurement year was counted only once toward the poly-ACH determination. There was no adjustment for early fills or overlapping days' supply.

Statistical analyses

Data were available from the AQUA database for the period between January 1, 2014 and December

Table 1. Annual analytic cohorts.

Cohort	Time frame
2014	January 1, 2014–December 31, 2014
2015	January 1, 2015–December 31, 2015
2016	January 1, 2016–December 31, 2016
2017	January 1, 2017–December 31, 2017
2018	January 1, 2018–December 31, 2018
2019	January 1, 2019–December 31, 2019
2020	January 1, 2020–December 31, 2020

31, 2020. Analysis was conducted on a calendar year basis, using cohorts constructed for each year. In total, seven cohorts were constructed (Table 1).

To be included in the analysis for a given year, patients were required to contribute data for the full year. The baseline year for any patient was the year of first observation; patients continued to be included in the analyses for subsequent years as long as follow-up data were available.

Prevalence of poly-ACH. Within each annual cohort, a binary outcome variable for poly-ACH status (Yes/No) was constructed based on the core definition of poly-ACH (concurrent use for ≥ 30 cumulative days of ≥ 2 unique ACH medications, each with ≥ 1 prescription record during the measurement year). The prevalence of poly-ACH in each year was determined by the number of patients with poly-ACH status in a given year divided by the number of eligible patients with OAB in that same year. Analysis was conducted for each annual cohort and stratified by age (< 65 and ≥ 65 years). To explore the impact of the poly-ACH definition on prevalence, an analysis using a broader definition was also conducted that did not require the medications to be used concurrently.

Yearly distribution of patients according to the number of ACHs prescribed. To estimate the prevalence of patients on each of 0, 1, 2, 3, 4, and ≥ 5 ACH medications, the number of patients within each of these ACH categories in a given year was divided by the total number of eligible patients with OAB in that year. Analysis was conducted for each annual cohort. Stratified analyses of the prevalence of patients with poly-ACH use in each year were also performed by age and sex.

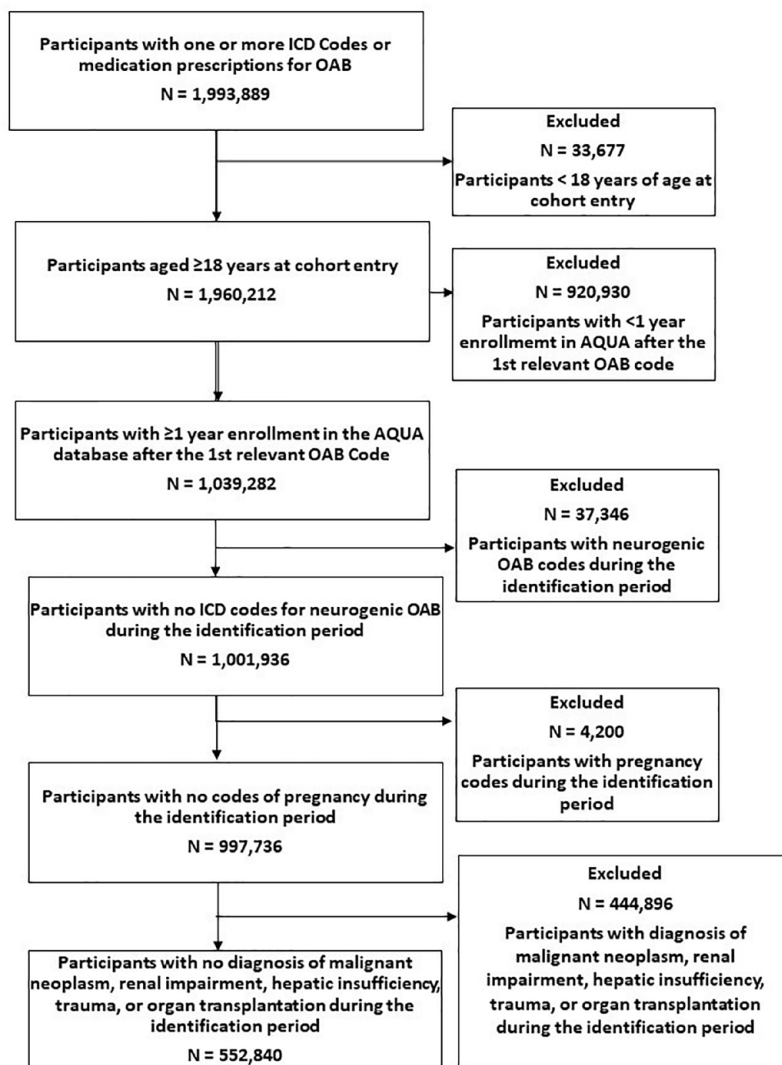


Figure 1. Patient attrition.

Results

Patient demographic and clinical characteristics

The study sample comprised $N=552,840$ OAB patients (Figure 1). The mean age at diagnosis was 65.7 years ($SD=13.8$), 58.2% were male, and 57.4% were white. The most common comorbidity was uncomplicated hypertension (24.0%); other common comorbidities included uncomplicated diabetes (9.5%) and chronic pulmonary disease (4.5%). Comorbidities reported which may be associated with OAB and ACH medications include depression (4.2%), cardiac arrhythmias (2.5%), psychoses (1.1%), and other neurological disorders (1.7%). The majority

(86.5%) lived in an urban area, and commercial insurance was the most common insurance type (46.4%; Table 2).

Baseline participating practice characteristics

Among the physicians seen by the study participants, the majority were part of single-specialty practices (84.0%) which saw high volumes of OAB patients, median [interquartile range (IQR)] number of patients per practice = 8990 (3164, 15,788). Multi-specialty practices were the second most frequent type (12.5%) and had the largest absolute number of OAB patients per practice [median (IQR) = 9179 (2446, 31,528)]. Solo, academic, and other practices were the least

Table 2. Baseline patient characteristics of the overall study cohort.

Category	Overall cohort
No. of patients	552,840
Age at index date (years)	
Mean (SD)	65.7 (13.8)
Median (IQR)	68.0 (58.0, 75.0)
Age group at index date (years), <i>n</i> (%)	
18–39	27,898 (5.0)
40–59	127,764 (23.1)
60–79	314,900 (57.0)
≥80	82,278 (14.9)
Sex, <i>n</i> (%)	
Female	231,026 (41.8)
Male	321,564 (58.2)
Unknown	250 (0.05)
Race/ethnicity, <i>n</i> (%)	
White	317,089 (57.4)
Asian	8130 (1.5)
Black/African American	33,069 (6.0)
Hispanic	216 (0.04)
Other	194,336 (35.2)
Elixhauser comorbidity index score ^{a,b}	
Mean (SD)	–0.2 (2.34)
Median (IQR)	0.0 (0.0, 0.0)
Range (min, max)	63.0 (–20.0, 43.0)
Elixhauser comorbidities (<i>n</i> , %)	
Congestive heart failure	4170 (0.8)
Cardiac arrhythmias	13,702 (2.5)
Valvular disease	2043 (0.4)
Pulmonary circulation disorders	1199 (0.2)
Peripheral vascular disorders	3119 (0.6)
Hypertension, uncomplicated	132,826 (24.0)
Hypertension, complicated	877 (0.2)

*(Continued)***Table 2.** (Continued)

Category	Overall cohort
Paralysis	720 (0.1)
Other neurological disorders	9143 (1.7)
Chronic pulmonary disease	24,840 (4.5)
Diabetes, uncomplicated	52,777 (9.5)
Diabetes, complicated	3603 (0.7)
Hypothyroidism	18,214 (3.3)
Renal failure	797 (0.1)
Liver disease	2012 (0.4)
Peptic ulcer disease excluding bleeding	2177 (0.4)
AIDS/HIV	309 (0.06)
Lymphoma	116 (0.02)
Metastatic cancer	103 (0.02)
Solid tumor without metastasis	5226 (0.9)
Rheumatoid arthritis/collagen vascular diseases	797 (0.1)
Coagulopathy	1352 (0.2)
Obesity	17,206 (3.1)
Weight loss	981 (0.2)
Fluid and electrolyte disorders	1732 (0.3)
Blood loss anemia	103 (0.02)
Deficiency anemia	862 (0.2)
Alcohol abuse	717 (0.1)
Drug abuse	415 (0.8)
Psychoses	5926 (1.1)
Depression	23,041 (4.2)
Census region, <i>n</i> (%) ^b	
Midwest	133,579 (24.2)
Northeast	85,696 (15.5)
South	249,220 (45.1)
West	78,995 (14.3)
Unknown	5350 (1.0)

(Continued)

Table 2. (Continued)

Category	Overall cohort
Community type at index date, <i>n</i> (%)	
Rural	65,600 (11.9)
Urban	478,362 (86.5)
Unknown	8878 (1.6)
Insurance type, <i>n</i> (%) ^b	
Commercial	256,731 (46.4)
Medicare	129,886 (23.4)
Medicaid	10,403 (1.9)
Other	155,820 (28.2)
AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; IQR, interquartile range; SD, standard deviation. ^a Calculated according to the Agency for Healthcare Research Quality (AHRQ) ²² ; this algorithm has negative weights for some comorbidities, which therefore results in a score range of -33 to 99. ^b Several baseline variables (i.e. patients' census region, insurance type, and Elixhauser Comorbidity Index Score) reflected the most recent data rather than the data at the time a patient became eligible for the study. The EHR systems that feed into the AQUA database are designed such that any updates to these specific data fields will overwrite the existing data.	

represented (2.5%, 0.9%, and 0.2%, respectively), with lower volumes of patients (median = 605–982; Table 3).

Prevalence of poly-ACH

The prevalence of poly-ACH for each annual cohort is summarized overall and by age category (< 65, ≥ 65 years) in Figure 2. The overall prevalence was highest in 2015 (3.7%) and lowest in 2020 (1.9%). In the stratified analysis by age, similar trends were observed across strata, with the highest rates of poly-ACH use in 2015 and the lowest rates in 2020. Compared to older patients (≥ 65 years), patients who were relatively younger (< 65 years) consistently had higher rates of poly-ACH use across all years. In addition, when age was further stratified into those 18–39, 40–59, 60–79, and ≥ 80 years, the highest rates of poly-ACH use were observed among the youngest individuals, across all years. Specifically, those aged 18–39 years had the highest rates of poly-ACH use, followed by those aged 40–59 years. Poly-ACH use further decreased with increasing

Table 3. Baseline participating practice characteristics.

Category	Overall cohort
Practice type, <i>n</i> (%)	
Multi-specialty, <i>n</i> (%)	69,228 (12.5)
No. of OAB patients seen by practice	
Mean (SD)	16,578.7 (13,874.9)
Median (IQR)	9179 (2446, 31,528)
Range (min, max)	31,527 (1, 31,528)
Single-specialty, <i>n</i> (%)	464,356 (84.0)
No. of OAB patients seen by practice	
Mean (SD)	10,118.9 (7688.2)
Median (IQR)	8990 (3164, 15,788)
Range (min, max)	26,840 (1, 26,841)
Solo, <i>n</i> (%)	13,556 (2.5)
No. of OAB patients seen by practice	
Mean (SD)	936.9 (835.1)
Median (IQR)	605 (429, 912)
Range (min, max)	2578 (21, 2599)
Academic	4808 (0.9)
No. of OAB patients seen by practice	
Mean (SD)	948.2 (330.3)
Median (IQR)	982 (814, 1271)
Range (min, max)	1262 (9, 1271)
Other, <i>n</i> (%)	892 (0.2)
No. of OAB patients seen by practice	
Mean (SD)	814.9 (171.5)
Median (IQR)	852 (852, 852)
Range (min, max)	841 (11, 852)
Practice region, <i>n</i> (%)	
Midwest	134,126 (24.3)
Northeast	85,205 (15.4)
South	255,981 (46.3)
West	77,528 (14.0)
Unknown	0 (0.0)
IQR, interquartile range; max, maximum; min, minimum; OAB, overactive bladder; SD, standard deviation.	

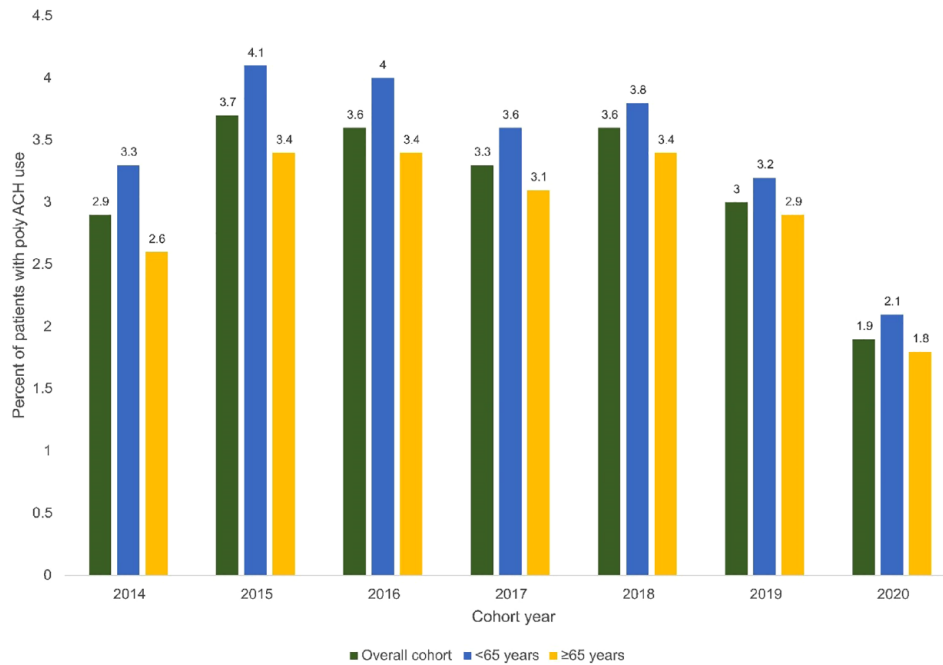


Figure 2. Overall prevalence of poly-ACH use by calendar year. ACH, anticholinergic.

age, although there were no clear temporal trends between those aged 60–79 and ≥ 80 years. Finally, applying a broader definition for poly-ACH, where the requirement for medication use to be concurrent was removed, resulted in an increased prevalence of poly-ACH.

Implementation of varying definitions of poly-ACH (original PQA and the further relaxed) affected the calculated prevalence of poly-ACH. The prevalence was higher at all timepoints under the relaxed definition, and lower at all timepoints under the PQA definition. Temporal trends were similar between the core and PQA definitions; poly-ACH use was highest in 2015 and lowest in 2020 (Figure 3).

Yearly distribution of patients according to number of ACHs prescribed

Within each year, patients receiving no ACH medications made up the largest proportion of the cohort. The proportion receiving each higher number of ACH medications was smaller such that patients receiving ≥ 5 ACH medications made up the smallest proportion of the cohort. The percentage of OAB patients on no ACH medications increased from 63.3% in 2014 to 74.6% in 2020, while the number of OAB patients

on 1 or 2 ACH medications decreased from 24.0% to 14.8% and 7.6% to 5.5%, respectively, in the same time period. The number of OAB patients on ≥ 3 ACH medications decreased slightly over this same time period (5.2–5.1%; Figure 4).

Yearly percentage of patients with poly-ACH stratified by age and sex

When the analysis was stratified by age, similar temporal trends to the overall cohort were observed. Specifically, the highest rates of poly-ACH use were between 2015 and 2018 and the lowest rates were in 2020, across all strata. The youngest patients (18–30 years) consistently had the highest rates of poly-ACH use, and rates steadily declined across the higher age categories until the age of 80 years, where a slight reversal of the trend was observed (Figure 5).

With regard to EHR-identified sex, the prevalence of poly-ACH was consistently higher in females than males, across all years: Rates ranged 3.2–5.7% among females and 1.1–2.3% among males. Similar to the overall cohort, the highest rates for both sexes were observed between 2015 and 2018, and the lowest rates were observed in 2020 (Figure 6).

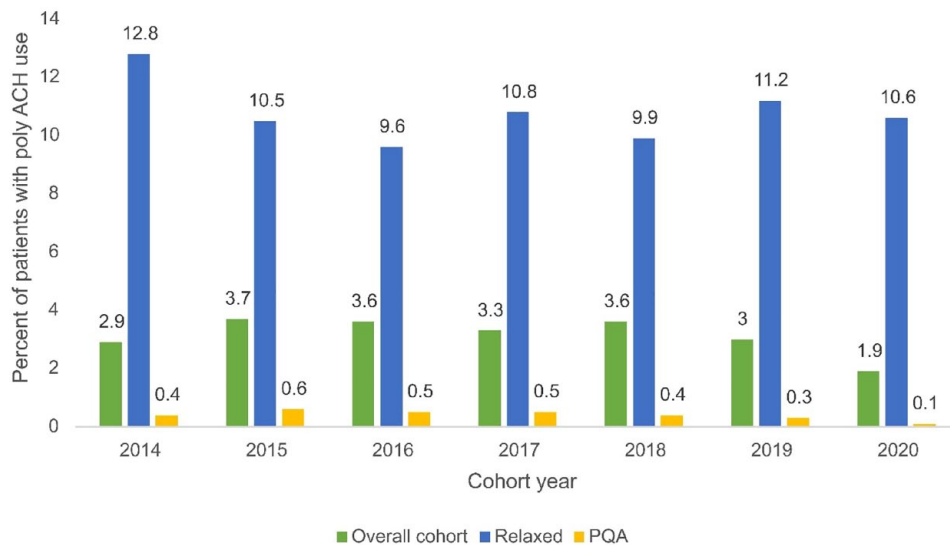


Figure 3. Impact on the calculated prevalence of poly-ACH by varying definitions of poly-ACH. ACH, anticholinergic; PQA, Pharmacy Quality Alliance. The core definition of poly-ACH required the concurrent use for ≥ 30 cumulative days of ≥ 2 unique ACH medications, each with ≥ 1 prescription record during the measurement year; the relaxed definition of poly-ACH required the use of ≥ 2 unique ACH medications, each with ≥ 1 prescription record each year (no requirement for concurrent use); the PQA definition of poly-ACH required the concurrent use for ≥ 30 cumulative days of ≥ 2 unique ACH medications, each with ≥ 2 prescription records on different dates of service during the measurement year.

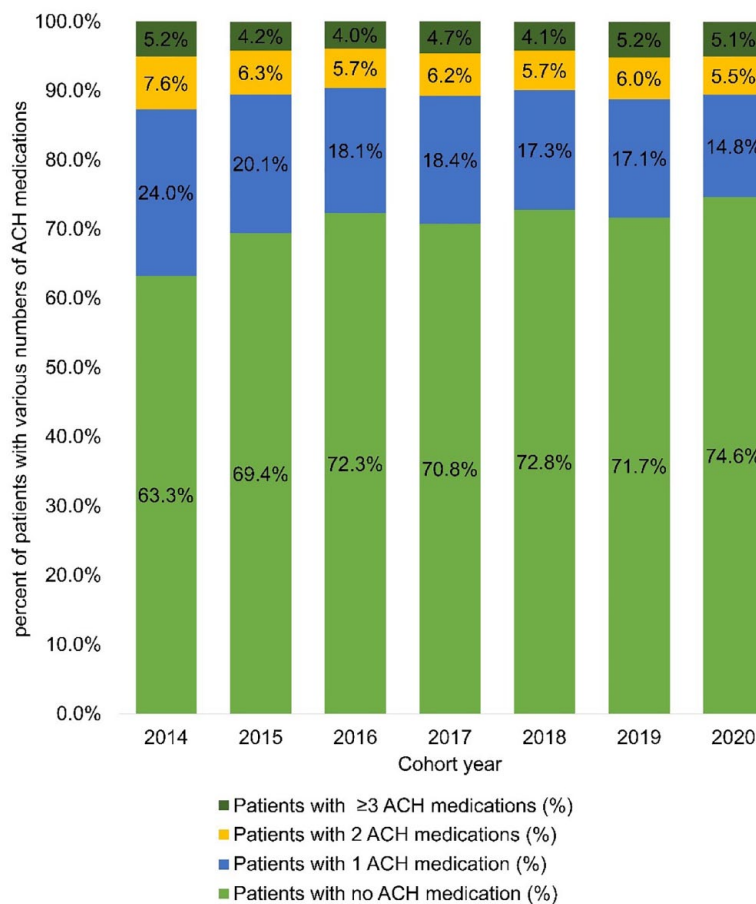


Figure 4. Prevalence of ACH medications use by calendar year. ACH, anticholinergic.

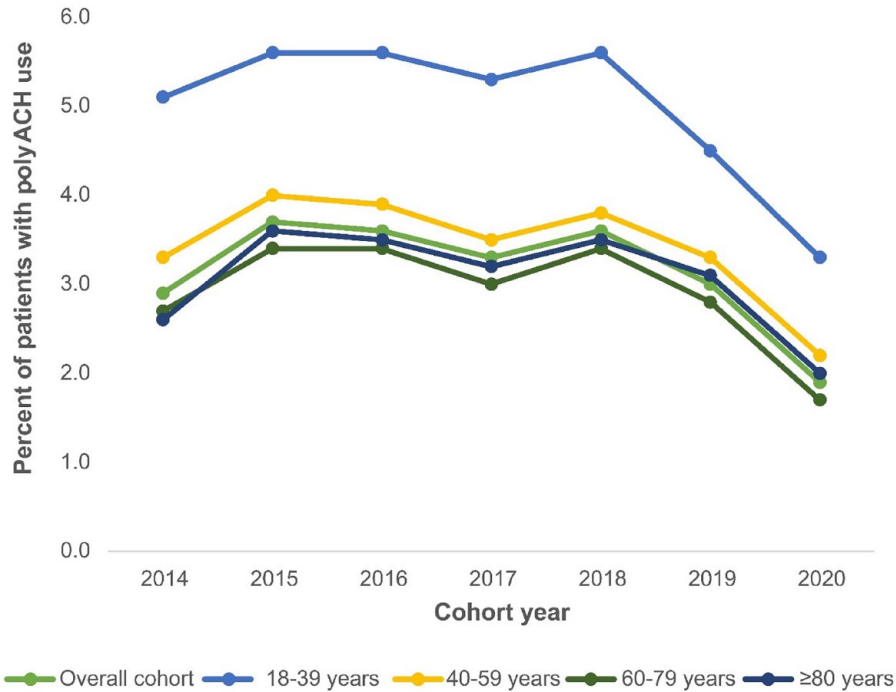


Figure 5. Prevalence of poly-ACH use by calendar year, stratified by patients' age category. ACH, anticholinergic.

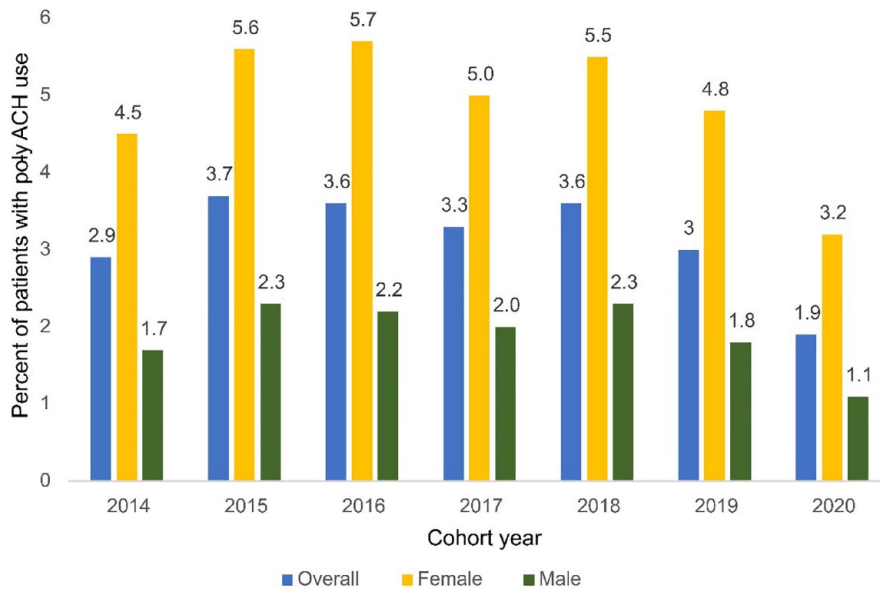


Figure 6. Prevalence of poly-ACH overall and by sex. ACH, anticholinergic.

Discussion

In this retrospective study of urology practice-based EHR data, poly-ACH use was found to be infrequent among adult patients with OAB over

the duration of the study period. The annual prevalence in the cohort ranged 1.9–3.7% and was highest between 2015 and 2018, and lowest in 2020. The proportion of patients taking no

ACH medications increased by just more than 10% between 2014 and 2020, while the proportion of patients taking 1 and 2 ACH medications decreased over the study period. The proportion of those taking 3, 4, and 5 or more ACHs remained largely unchanged. Regarding age, younger patients had higher rates of poly-ACH use than older patients.

Methods for measuring poly-ACH continue to evolve. Lozano-Ortega *et al.*²³ found that among commercially insured adults (18 years of age and older) with OAB in the United States, approximately 65% had some level of ACH burden as assessed by the cumulative ACH burden measure. More recently, however, Campbell *et al.*²⁴ applied the PQA measure of poly-ACH to Medicare claims data and revealed that ACH burden among beneficiaries with OAB was low and had decreased over time (3.3% in 2006 and 1.7% in 2017).

It is important to consider the impact of the COVID-19 pandemic when interpreting the study findings. In particular, the greatest decrease in poly-ACH prevalence was observed between 2019 (3.0%) and 2020 (1.9%). However, it should be noted that this is unlikely to be a true decline in poly-ACH prevalence, but rather reflective of a decrease in healthcare resource utilization related to less severe conditions during the pandemic.²⁵ Because prevalence was calculated based on prescription claims, this decrease may be due to challenges accessing healthcare services, or changes in healthcare priorities during that time. Notably, an analysis using the AQUA database found significant declines (>50%) in the number of individuals seeking urological care at the pandemic onset, particularly for non-urgent conditions (up to a 79% decline).²⁶ Therefore, the decline in prevalence observed between 2019 and 2020 in this study may likely be a result of the impact of the COVID-19 pandemic on healthcare utilization. Furthermore, when this data point is omitted, trends are less clear. Future studies should continue to monitor the prevalence of poly-ACH among these patients over time to observe whether a true decrease is occurring, which could indicate an increased awareness of the negative consequences of ACH use.

The findings of this study are in line with those of Campbell *et al.*,²⁴ who reported that the prevalence of poly-ACH (as defined by the PQA) decreased over time (3.3% in 2006 and 1.7% in

2017). These trends remained consistent across age groups. The prevalence of poly-ACH among Medicare beneficiaries tended to be higher among individuals who were older and female; findings regarding sex were similar in this study. Importantly, while poly-ACH was also observed to be infrequent in Campbell *et al.*,²⁴ it was found that having a recent history of poly-ACH was associated with an increased risk of falls, fractures, altered mental status, and increased medical spending. Thus, while the prevalence of poly-ACH was also found to be low in this study, it is still likely to also be associated with higher medical costs and certain negative outcomes.

Although findings between Campbell *et al.*²⁴ and this study are largely similar, differences in study population, setting, and period likely account for variations in the reported estimates of poly-ACH prevalence. The differences between studies in trends by age are likely due to the inclusion of younger adults in this study, while those in the Campbell *et al.*²⁴ study were all aged 65 years or older. The higher prevalence observed in the current study (compared to Campbell *et al.*²⁴) was likely due to the adapted, less restrictive definition of poly-ACH, as the original definition was implemented by Campbell *et al.*²⁴

A key strength of this study is the use of a real-world EHRs database, specifically one that is populated by urologists across the United States. Unlike administrative claims databases, EHR datasets are not limited to only patients with commercial or Medicare health plans and are therefore reflective of a broader patient population. A key limitation of the AQUA database is that most enrolled practices do not capture medication refills. Consequently, our results may underestimate poly-ACH use as defined by the PQA. To mitigate the impact on the study, a less restrictive definition of poly-ACH use was derived, requiring only one prescription record for each medication. As expected, the estimated prevalence of poly-ACH varied according to the definition used, with a less restrictive definition resulting in a higher prevalence and the original definition resulting in a lower prevalence. In addition, the use of the ACB scale, which includes medications with lower ACH properties to estimate burden, may have offset any overestimation of poly-ACH burden.

Other limitations include the potential for medication start and end dates to be missing in some

cases for medications that were started prior to a patient entering the AQUA database, and that certain baseline variables reflect the most recent data rather than the data at the time a patient became eligible for the study. However, given the relatively short study period, significant changes in these variables were not expected for most patients. While this cohort was 58% male, OAB prevalence in the United States is generally estimated to be about equal between the sexes or weighted toward women.^{27,28} The composition of the AQUA Registry (69% of registry patients are male)²⁹ may have affected the weighting of this cohort and thus, to some extent, the generalizability of the results.

Conclusion

Among patients with OAB in the AQUA database, poly-ACH was infrequent and may be decreasing over time. Continued surveillance of the prevalence of poly-ACH is needed to determine whether this trend is due to increasing awareness among physicians regarding the risks of ACH use in older individuals.

Declarations

Ethics approval and consent to participate

As all data from the AQUA Registry used in published reports or articles are de-identified at aggregated levels, requirements for ethical approval and patient consent to participate are not applicable. Further details on the registry can be found here: [https://www.auanet.org/research-and-data/aqa-quality-\(aqua\)-registry/program-information](https://www.auanet.org/research-and-data/aqa-quality-(aqua)-registry/program-information)

Consent for publication

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Author contributions

Matthew R. Cooperberg: Conceptualization; Methodology; Writing – review & editing.

Rachel Mbassa: Conceptualization; Formal analysis; Methodology; Resources; Writing – review & editing.

David Walker: Conceptualization; Methodology; Writing – review & editing.

William Meeks: Conceptualization; Methodology; Resources; Writing – review & editing.

Amy Lockefer: Conceptualization; Methodology; Writing – review & editing.

Baoguo Jiang: Conceptualization; Methodology; Writing – review & editing.

Tina Li: Conceptualization; Formal analysis; Methodology; Writing – review & editing.

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Competing interests

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Availability of data and materials

Researchers may request access to anonymized participant-level data, trial-level data, and protocols from Astellas-sponsored clinical trials at <https://www.clinicalstudydatarequest.com>. For the Astellas criteria on data sharing, see: <https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx>. The data that

support the findings of this study are available from AQUA, but restrictions were applied to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors on reasonable request and with permission from AQUA.

Reporting Guidelines: Study reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Table 5).³⁰

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Supplemental material

Supplemental material for this article is available online.

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