




A 12-Year Retrospective Study of the Prevalence of Anticholinergic Polypharmacy and Associated Outcomes Among Medicare Patients with Overactive Bladder in the USA

Noll L. Campbell^{1,2} · Lisa Hines³ · Andrew J. Epstein⁴ · David Walker⁵ · Amy Lockefer⁵ · Aki Shiozawa⁵ 

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Abstract

Background and Objective Antimuscarinics, drugs with anticholinergic properties, are frequently prescribed for overactive bladder, and anticholinergic burden is associated with adverse events. The “Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults” (Poly-ACH) measure was developed by the Pharmacy Quality Alliance and is used by the Centers for Medicare and Medicaid Services. Using the Poly-ACH measure, we assessed the prevalence of anticholinergic polypharmacy among Medicare patients in the USA with overactive bladder and determined associations between polypharmacy and medical conditions, care, and spending.

Methods This was a retrospective cohort study of Medicare beneficiaries with overactive bladder (coverage period: 2006–2017). Anticholinergic polypharmacy, measured by the Poly-ACH, was defined as concurrent use of two or more anticholinergics, each with two or more prescription claims on different dates of service for ≥ 30 cumulative days. Change in annual frequency of anticholinergic polypharmacy was assessed using logistic regression. Associations between anticholinergic polypharmacy over 3 years and falls, fractures, mental status, and medical care spending were assessed with longitudinal regression models.

Results In total, 226,712 patients contributed 940,201 person-years of follow-up after overactive bladder diagnosis. The share of patients meeting the Poly-ACH definition was 3.3% in 2006 and 1.7% in 2017. Women and nursing home residents had higher risks of anticholinergic polypharmacy. Having 1 year or more of positive Poly-ACH status in the 3 years prior was associated with higher rates of all outcomes.

Conclusions Anticholinergic polypharmacy was uncommon among older adults with overactive bladder. Prevalence was higher among women and nursing home residents, and it was associated with negative outcomes, highlighting potential longitudinal implications of anticholinergic burden.

✉ Aki Shiozawa
aki.shiozawa@astellas.com

¹ Purdue University College of Pharmacy, West Lafayette, IN, USA

² Indiana University Center for Aging Research, Indianapolis, IN, USA

³ Pharmacy Quality Alliance, Alexandria, VA, USA

⁴ Medicus Economics, Milton, MA, USA

⁵ Medical Affairs, U.S., Astellas Pharma Global Development, Inc., 1 Astellas Way, Northbrook, IL 60062, USA

Key Points

Anticholinergic polypharmacy, as defined by the “Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults” measure, was uncommon among Medicare beneficiaries with overactive bladder. Prevalence was higher among women and long-term nursing home residents.

Positive anticholinergic polypharmacy status was significantly associated with a greater number of negative outcomes, including falls, fractures, and altered mental status, as well as higher medical spending compared with negative status, drawing attention to the longitudinal implications of anticholinergic burden.

1 Introduction

Overactive bladder (OAB) comprises a constellation of urinary symptoms typically characterized by urgency, with or without urge urinary incontinence, and accompanied by frequency and nocturia [1, 2]. A review of the epidemiological literature indicates that the estimated overall prevalence of OAB in the USA is between 16.5 and 23.3%, with women and minorities accounting for the majority of cases [3]. Currently, the total costs associated with OAB management in the USA, including all medical (direct and indirect) and indirect non-medical costs, are US\$82.6 billion [4].

Antimuscarinic agents are the current mainstay of OAB pharmacotherapy [5]. Among older adults (those aged 65 years and older), previous research using Medicare claims has shown that 75% of Medicare patients with OAB use at least one antimuscarinic drug [6]. However, antimuscarinic agents are part of the class of oral anticholinergic medications, which are associated with numerous central and peripheral adverse events [7–9]. Among older adults, anticholinergic use has been linked to impairments in physical performance, the reduced ability to perform activities of daily living, and an increased risk of dementia [10–12]; cumulative exposure to anticholinergic medications increases the risk of these events [10–12]. As a result, the most recent version of the American Geriatrics Society Beers Criteria includes the recommendation to avoid drugs with strong anticholinergic properties [13]. Notably, all antimuscarinics approved for the treatment of OAB in the USA are considered strong anticholinergics and have been listed as medications to avoid in certain circumstances [13].

Currently, the prevalence and economic implications of anticholinergic burden are largely derived from studies conducted among community-dwelling populations and include individuals across a broad age range. One study found that among commercially insured patients with OAB in the USA, approximately 65% had some level of anticholinergic burden. Furthermore, healthcare resource utilization and costs directly increased with a higher level of anticholinergic burden [14]. Likewise, a study of 3344 community-dwelling older adults found that increasing levels of anticholinergic burden were also associated with higher costs [15]. However, given the lack of studies conducted specifically among older individuals with OAB, the prevalence and economic consequences of anticholinergic burden among this population are not understood.

The Pharmacy Quality Alliance developed a health plan performance measure, titled “Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults” (Poly-ACH). Poly-ACH is a medication safety measure to identify co-prescribing of strong anticholinergic medications in older adults because of an associated risk of

cognitive decline [15]. The measure defines anticholinergic polypharmacy as the use of at least two anticholinergic medications that overlap for at least 30 days in the measurement year [16]. While there are several scales to measure anticholinergic burden, Poly-ACH is especially important because of its policy relevance. Recently, the Centers for Medicare and Medicaid Services has adopted it for use in its Medicare Part D plan reporting efforts (Patient Safety Reports). The Centers for Medicare and Medicaid Services intends to include health-plan-specific Poly-ACH scores in its publicly available Display Pages in 2021 (using 2019 data) and is evaluating whether to include the Poly-ACH measure as part of their publicly available health-plan-specific Star Ratings in the future [17]. However, anticholinergic burden, as defined by the Poly-ACH measure, has not yet been widely studied.

Therefore, there is a need to understand the extent of anticholinergic burden and the associated clinical and economic outcomes among older adults with OAB, particularly across a broader range of residential settings that includes both community-dwelling and institutionalized individuals. Our study had two objectives. We first sought to characterize secular trends in the annual frequency of anticholinergic polypharmacy as measured by the Poly-ACH, overall and by important beneficiary attributes. We also assessed the associations between positive Poly-ACH status and clinical and economic outcomes, including the risk of falls, fractures, altered mental status (AMS; chosen as AMS/delirium is a shorter term outcome and appropriate to the timeframe of this work [11, 18]), and medical care spending.

2 Methods

2.1 Study Design and Data

This was a retrospective cohort study using Medicare enrollment and claims data for individuals covered under traditional Medicare from 1 January, 2006 through 31 December, 2017. Enrollment files contain monthly information on individuals’ enrollment in each part of Medicare, including Part D (pharmacy) coverage, in addition to demographic information, residential location (at the 5-digit ZIP code level), and date of death (from Medicare administrative files). Claims data are available for all medical services and outpatient prescription drugs covered by the program and are organized into data files based on the nature and source of the claim. MedPAR and outpatient files include institutional claims from hospitals for inpatient and outpatient services and from nursing homes for short-stay “skilled” admissions. The Carrier file includes fee-for-service claims submitted by professional providers,

including physicians, physician assistants, clinical social workers, and nurse practitioners. The Part D files include all information on all transactions covered by a beneficiary's Medicare prescription drug plan. This study was reviewed and approved by the New England Institutional Review Board (#1-6735-1).

2.2 Core Study Sample

The core study sample included beneficiaries with OAB who were US residents, aged ≥ 65 years, and had continuous enrollment in Medicare Parts A, B, and D and no enrollment in Medicare Part C (Medicare Advantage). The presence of OAB was determined by one or more inpatient or outpatient facility claims or at least two Carrier file claims on separate dates with an OAB diagnosis code (Table 1 of the Electronic Supplementary Material [ESM]) [19, 20]. Enrollment and medical claims data from 2005 were used to assess an individual's earliest medical claim with an OAB diagnosis code for those who enrolled in Medicare prior to the start of Part D (1 January, 2006). Individuals were excluded if they had a diagnosis code for any of the following conditions on at least one medical claim at any time during the study period: neurogenic bladder/neurogenic detrusor overactivity, pregnancy, malignant neoplasm, renal impairment, hepatic insufficiency, trauma, or organ transplantation, as these conditions have similar symptomatology to OAB but unique pathology that may incorrectly influence associations being evaluated. A procedure code for any of the following was also exclusionary: non-indwelling bladder catheter, sterile intermittent catheter kit, indwelling bladder catheter, or transplant. For both study objectives, the unit of analysis was the person-year; thus, incomplete calendar years (i.e., when a patient entered after 1 January or exited before 31 December) were excluded.

2.3 Anticholinergic Polypharmacy as Measured by the Poly-ACH

The National Drug Code lists required to calculate the Poly-ACH measure as specified were obtained from the Pharmacy Quality Alliance. The anticholinergic medications targeted for the measure are Drugs with Strong Anticholinergic Properties from the 2019 American Geriatrics Society Beers Criteria [13]. A binary indicator was used to indicate whether beneficiaries had Poly-ACH in a given calendar year (yes/no; positive/negative) based on the Pharmacy Quality Alliance definition. This definition included the following four components:

1. An individual had positive evidence of Poly-ACH when the individual had concurrent use for ≥ 30 cumulative days of two or more unique anticholinergic medications, each with two or more prescription claims on different dates of service during the measurement year.
2. Concurrent use was identified using the dates of an individual's prescription claims and corresponding days' supply. The days of concurrent use were calculated as the count of days during the measurement year with overlapping days' supply for two or more unique anticholinergic medications. Days' supply or overlap that occurred after the end of the measurement year were excluded.
3. If multiple prescription claims for the same anticholinergic medication (active ingredient) were filled on the same day, the number of days covered by the anticholinergic medication were calculated using the prescriptions with the longest days' supply.
4. If multiple prescription claims of the same anticholinergic medication (active ingredient) were filled on different days with overlapping days' supply, each day in the measurement year was counted only once toward the Poly-ACH status determination. There was no adjustment for early fills or overlapping days' supply.

It should be noted that the Poly-ACH measure denominator excludes individuals in hospice care (during the measurement year) though this exclusion was not applied for the study.

2.4 Statistical Analysis: Trends in Poly-ACH

To characterize secular trends in the annual frequency of positive Poly-ACH status overall and by important beneficiary attributes, the following covariates were considered: age category (65–74, 75–84, 85+ years), female sex, Census region (Northeast, South, Midwest, West), and nursing home use category (none, short term, or long term). Regarding the classification of nursing home use, individuals were characterized according to their highest level of nursing home use during each calendar year (e.g., individuals who switched from a short-term to long-term status were classified as long term).

Counts and percentages were calculated for all covariates stratified by Poly-ACH status (yes/no) and compared with χ^2 tests. Logistic regression was used to model Poly-ACH as predicted by a vector of indicator variables for the calendar year. Stratified trends were calculated for each stratification variable one at a time.

Adjusted overall trends were calculated by controlling for the stratification variables (in addition to calendar year) as main effects in the logistic regression. Predictive margins

on the probability scale and their 95% confidence intervals (CIs) were calculated from each logistic regression model. Estimated standard errors were adjusted to be robust to heteroskedasticity of unknown form and for multiple yearly observations per person.

2.5 Statistical Analysis: Associations between Poly-ACH Status and Outcomes

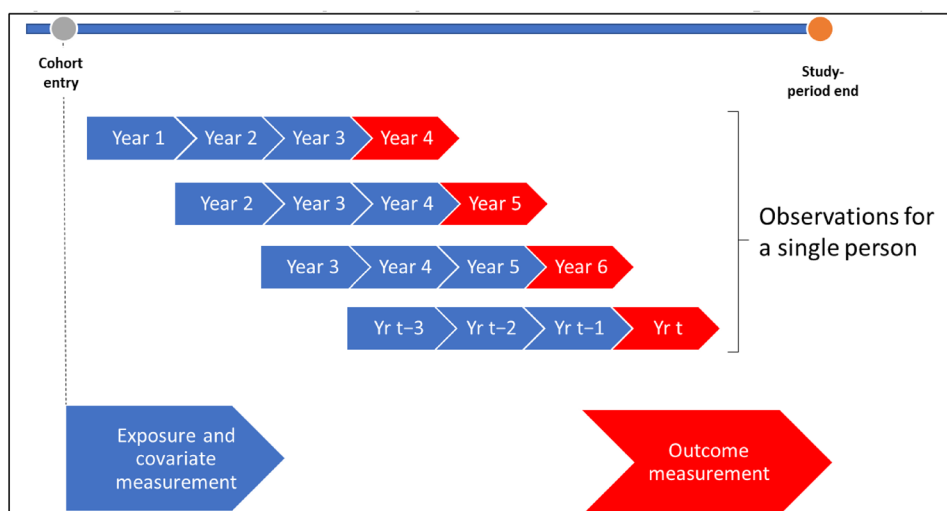
The association between lagged Poly-ACH and current outcomes were estimated using longitudinal regression analyses; this approach, also known as panel regression modeling, has previously been applied to similar efforts [21]. As shown in Fig. 1, for each year “ t ” during which an outcome was measured, the exposure was the count over the prior 3 years ($t-1$, $t-2$, and $t-3$) that a beneficiary experienced Poly-ACH (i.e., between zero and three). Control variables were measured during year $t-1$. As a result of this design, the sample was limited to individuals who met the additional criterion of having at least 4 consecutive years of enrollment (3 years of baseline/lagged Poly-ACH and 1 year of follow-up). Thus, the subset of individuals within the core sample who met this additional criterion formed the analytic sample for the second study objective. Beneficiaries contributed observations to the analytic dataset in a rolling manner; for example, a beneficiary with 6 consecutive years of data contributed three observations, starting with their fourth year.

Clinical and economic outcomes assessed for this analysis included fall, fracture, AMS, and total medical spending. The first three were specified as binary variables (yes/no) indicating whether an individual had a medical claim with a relevant diagnosis (International Classification of Diseases, 9th Revision, Clinical Modification and International

Classification of Diseases, 10th Revision, Clinical Modification or service code [Current Procedural Terminology Code]) for a given outcome during each calendar year (Table 2 of the ESM). Total medical spending was calculated as the sum of total dollars paid by Medicare, other payers, and patients on yearly medical care as found on inpatient, skilled nursing facility, outpatient, and Carrier claim files and was inflated to 2017 US dollars using the Gross Domestic Product Price Index [22]. Patient-year-level observations were compared based on their distribution of lagged 3 years with Poly-ACH two ways: any years with Poly-ACH during the prior 3 years vs no Poly-ACH (1 = any, 0 = none), and number of years with Poly-ACH (1, 2 or 3) vs no Poly-ACH (0).

Regression modeling was used to assess the independent statistical associations between anticholinergic polypharmacy exposures and each outcome. Models were specified as logistic regression for binary outcomes and generalized linear models using a log link and a Poisson family distribution (as determined by the modified Park test) for total medical spending [23]. Controls included covariates (as categorical variables), specifically patient demographics and medical conditions, particularly those that were associated with anticholinergic use. These covariates were measured during the prior year and lagged outcome during the prior 3 years. Demographics were observed during year 1 and included age category, sex, census region, nursing home category, and calendar year. Medical conditions included those associated with a higher risk of falls and fractures from Szabo et al. [19] (e.g., Parkinson’s disease, dementia, hypertension, and diabetes), Elixhauser comorbidities [14, 24], and conditions indicated for treatment with an anticholinergic medication (Fall/fracture-related diagnostic codes: Table 2 of the ESM; Conditions: Table 3 of the ESM).

Fig. 1 Longitudinal data structure: patients were observed for at least 4 consecutive years including three baseline/lagged Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure) years and 1 follow-up year. *Beneficiaries contributed observations to the analytic dataset in a rolling manner; for example, a beneficiary with 6 consecutive years of data contributed three observations, starting with their fourth year



Abbreviations: yr = year

Predictive margins and average marginal effects on the original scale (i.e., probability, dollars) and their 95% CIs as well as relative risks were calculated from each regression model. Estimated standard errors were adjusted to be robust to heteroskedasticity of unknown form and for multiple yearly observations per person.

3 Results

The core sample initially included 226,712 beneficiaries with 1,926,495 calendar years of data. After including only complete person-years that occurred after the first observed OAB diagnosis, the final sample consisted of a total of 940,201 years of data from 226,712 beneficiaries. For the second study objective, the additional requirement of having at least 4 consecutive complete calendar years of data reduced the sample to 405,343 person-year observations from 105,608 beneficiaries.

Person-years with positive Poly-ACH tended to be from individuals who were older, more frequently female, more commonly from the Midwest and South Census regions, and more frequent users of long-term care facilities (Table 1). Regarding anticholinergic use over the entire study period (2006–2017), an average of 26% of all beneficiaries in each year had at least one claim for an anticholinergic medication, 3% had at least two claims for at least two anticholinergic medications, and 3% met the criteria for Poly-ACH. Further details of anticholinergic use in the cohort are available in Table 4 of the ESM.

3.1 Trends in the Annual Frequency of Positive Poly-ACH Status

Overall, Poly-ACH was infrequent and declined over the study period (2006–2017) (Table 2). The percentage of beneficiaries with Poly-ACH was 3.3% in 2006, 1.5% in 2015, and 1.7% in 2017. Specific subgroups of the study population were consistently at a higher risk of anticholinergic polypharmacy, including women and users of nursing home care. Regression adjustment for age, sex, geographic region, and nursing home use had minimal effect on the anticholinergic polypharmacy estimates in the most recent years (Fig. 2).

3.2 Clinical and Economic Outcomes Associated with Positive Poly-ACH Status

Having at least 1 year with positive Poly-ACH status over the prior 3 years was associated with a 1.26 greater risk of any fall (absolute difference of 1.0 percentage points; 95% CI 0.07–1.30; $p < 0.001$), a 1.14 greater risk of fracture (absolute difference of 0.4 percentage points; 95%

CI 0.20–0.7; $p = 0.001$), a 1.31 greater risk of AMS (absolute difference of 0.8 percentage points; 95% CI 0.50–0.10; $p < 0.001$), and 1.13 times higher medical care spending (absolute difference of US\$1116; 95% CI US\$677–US\$1556; $p < 0.001$) (Table 3). The effect of having any anticholinergic polypharmacy in the prior 3 years did not vary systematically by the count of lagged years with Poly-ACH. For the annual medical care spending outcome, relative to no years of Poly-ACH, having 1 year of positive Poly-ACH was associated with US\$1163 higher spending, 2 years with US\$1169 higher spending, and 3 years with US\$964 (Table 3).

4 Discussion

Overall, this study found that anticholinergic polypharmacy is not common among Medicare beneficiaries with OAB. Regarding trends among those with anticholinergic polypharmacy, it was more common among women and those in long-term care settings.

Notably, although anticholinergic polypharmacy was infrequent among the chosen study population, a relationship between positive Poly-ACH status and negative outcomes was nonetheless observed. Specifically, patients who experienced anticholinergic polypharmacy in at least one of the prior 3 years had statistically significant and clinically meaningful higher risks of fall, fracture, and AMS, and higher annual medical care spending. These findings highlight the longitudinal nature of the consequences of anticholinergic polypharmacy, the implications of which have to an extent been previously evaluated. Indeed, a number of recent studies have found that exposure to certain anticholinergic medications is associated with an increased risk of negative outcomes, including dementia and falls/fractures, the latter of which has specifically been evaluated among older adults with OAB [11, 18, 19, 25, 26]. Furthermore, even the lowest levels of exposure were associated with an increased risk. While the current study was not designed to determine causality, the findings nonetheless contribute evidence to an association between exposure to multiple anticholinergics and negative long-term consequences, which should be explored further. The insights regarding these associations derived from the Poly-ACH measure have important implications for decision makers and care providers and should be considered when evaluating interventions to reduce exposure. Finally, it is possible that the number of older adults with OAB and positive Poly-ACH status is larger than the current study suggests, given that the estimated proportions of individuals with OAB derived from other studies using Medicare claims data (9–14%) [27] are less than those that have been reported for the general US population (16.5–23.3%) [3].

Table 1 Descriptive statistics (person-years over the entire study period)

Variable name	Overall	No Poly-ACH	Yes Poly-ACH	<i>p</i> value
Sample size (person-years)	940,201	919,963	20,238	
Age category, years, <i>N</i> (%)				< 0.001
65–74	505,045 (54%)	496,468 (54%)	8577 (42%)	
75–84	280,448 (30%)	273,923 (30%)	6525 (32%)	
85+	154,708 (16%)	149,572 (16%)	5136 (25%)	
Sex, <i>N</i> (%)				< 0.001
Male	276,271 (29%)	274,173 (30%)	2098 (10%)	
Female	663,930 (71%)	645,790 (70%)	18,140 (90%)	
Census region, <i>N</i> (%)				< 0.001
Midwest	270,545 (29%)	264,133 (29%)	6412 (32%)	
Northeast	176,798 (19%)	173,855 (19%)	2943 (15%)	
South	335,715 (36%)	328,082 (36%)	7633 (38%)	
West	157,143 (17%)	153,893 (17%)	3250 (16%)	
Annual nursing home use category, <i>N</i> (%)				< 0.001
No NH	852,436 (91%)	837,354 (91%)	15,082 (75%)	
SNF only	16,148 (1.7%)	15,407 (1.7%)	741 (3.7%)	
Long-term NH	71,617 (7.6%)	67,202 (7.3%)	4415 (22%)	
Person-years by calendar year, <i>N</i> (%)				< 0.001
2007	40,092 (4.3%)	37,821 (4.1%)	2271 (11%)	
2008	47,490 (5.1%)	45,321 (4.9%)	2169 (11%)	
2009	53,039 (5.6%)	51,120 (5.6%)	1919 (9.5%)	
2010	58,496 (6.2%)	56,706 (6.2%)	1790 (8.8%)	
2011	63,877 (6.8%)	62,221 (6.8%)	1656 (8.2%)	
2012	70,872 (7.5%)	69,426 (7.5%)	1446 (7.1%)	
2013	80,647 (8.6%)	79,161 (8.6%)	1486 (7.3%)	
2014	94,476 (10%)	93,026 (10%)	1450 (7.2%)	
2015	112,614 (12%)	110,976 (12%)	1638 (8.1%)	
2016	139,997 (15%)	138,125 (15%)	1872 (9.2%)	
2017	178,601 (19%)	176,060 (19%)	2541 (13%)	
Sample size	940,201	919,963	20,238	

Medicare enrollment and claims data, calendar year 2006–2017

NH nursing home, *Poly-ACH* Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure), *SNF* skilled nursing facility

Although differences exist between study populations, the findings from this study are in line with those of previous studies. In the present study, having at least one year with positive Poly-ACH status was associated with higher risks of fall and fracture. Szabo et al. found that cumulative anticholinergic burden was also associated with an increased risk of falls and fractures among patients with OAB in a community setting; those with low, medium, and high levels of burden had a 23%, 30%, and 38% higher risk, respectively, than those with no burden [19]. Additionally, Lozano-Ortega et al. found that healthcare resource utilization among outpatients with OAB increased with the level of anticholinergic burden. Furthermore, costs associated with

falls and fractures also rose as the level of anticholinergic burden increased [14].

Limitations of this analysis included those that are inherent to administrative claims data. Ascertainment of conditions and treatments relied on administrative codes, which are subject to coding error. Furthermore, anticholinergic medications obtained over the counter would not be recorded; thus, the level of exposure observed in this study may be underestimated. Cases of OAB, along with outcomes such as fractures, falls, and AMS, may also be underreported. Furthermore, the denominator of the Poly-ACH measure is meant to exclude individuals in hospice care, but those individuals were not excluded from the current

Table 2 Core counts of beneficiaries with OAB diagnosis with anticholinergic drug claims and Poly-ACH status by calendar year

Calendar year	Total beneficiaries	1+ claims for 1+ ACH drugs	1+ claims for 2+ ACH drugs	2+ claims for 2+ ACH drugs	Poly-ACH
2006	127,586	44,717 (35%)	13,763 (11%)	7244 (6%)	4750 (4%)
2007	130,977	44,094 (34%)	13,068 (10%)	6564 (5%)	4359 (3%)
2008	132,112	41,057 (31%)	11,001 (8%)	5461 (4%)	3654 (3%)
2009	132,284	38,126 (29%)	9318 (7%)	4458 (3%)	3043 (2%)
2010	134,079	36,933 (28%)	8917 (7%)	4082 (3%)	2692 (2%)
2011	140,243	36,438 (26%)	8378 (6%)	3645 (3%)	2498 (2%)
2012	150,959	35,520 (24%)	7095 (5%)	3125 (2%)	2167 (1%)
2013	164,041	37,061 (23%)	7253 (4%)	3180 (2%)	2216 (1%)
2014	179,873	38,468 (21%)	6779 (4%)	3014 (2%)	2167 (1%)
2015	197,405	41,499 (21%)	7170 (4%)	3199 (2%)	2299 (1%)
2016	214,415	45,680 (21%)	7808 (4%)	3471 (2%)	2500 (1%)
2017	222,521	52,218 (23%)	9354 (4%)	4111 (2%)	3008 (1%)

Source: Medicare enrollment and claims data, calendar year 2006–17

ACH anticholinergic, OAB overactive bladder, Poly-ACH Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure)

study. However, because beneficiaries receiving hospice benefits represent less than 3% of all beneficiaries [28, 29], the impact of their inclusion is expected to be low. Additionally, because data on beneficiaries before their Medicare enrollment were unavailable, it is unknown to what extent any prior exposure to anticholinergic medications or other relevant variables may have affected the outcomes. Similarly, given the nature of the study design, there is the possibility of reverse causality; some of the study outcomes (especially falls and fractures) could have precipitated the prescribing of anticholinergic medications. In addition, the generalizability of study findings is limited to beneficiaries with OAB and continuous enrollment in traditional Medicare, including Part D.

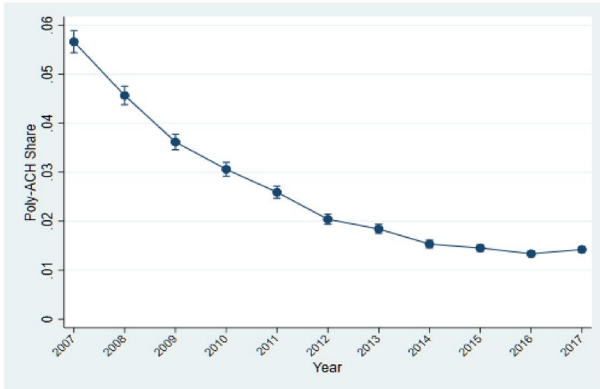
Regarding the Poly-ACH measure, the binary indicator of exposure (yes/no) precludes the consideration of key aspects of cumulative anticholinergic drug use, including the number of days of overlap and total anticholinergic dose. Thus, it is not possible to ascertain the extent to which varying levels of exposure are associated with the current findings. To account for varying exposure times, future research using the Poly-ACH metric could examine cumulative increments (e.g., 30 days) in which Poly-ACH exists and the association with the study outcomes. Next, while positive Poly-ACH status occurred infrequently among the study population, there was nonetheless a correlation with the measured adverse

outcomes. Given that the Poly-ACH measure does not assess characteristics such as medication potency or specific dose, additional research is needed to examine to what extent this relationship is driven by the level of anticholinergic exposure. Finally, this study focused on a sub-population of individuals (those with OAB); the Poly-ACH measure was intended for the broader population of all Medicare beneficiaries. Thus, while the Poly-ACH measure may not be suitable for accountability purposes within specific sub-populations and regarding specific levels of anticholinergic exposure, it appears to have utility as a measure for safety monitoring or quality improvement purposes.

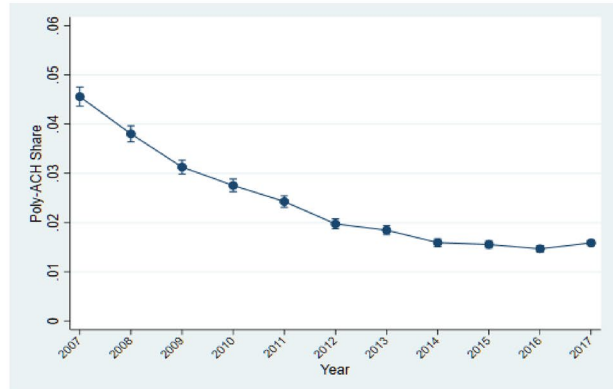
5 Conclusions

These findings contribute to the initial evidence base regarding the extent and implications of anticholinergic burden among older adults with OAB. Anticholinergic burden, as measured by the Poly-ACH metric, was relatively uncommon among Medicare beneficiaries. However, the relationship observed between anticholinergic polypharmacy and adverse outcomes supports the American Geriatrics Society Beers Criteria recommendation [13] that concurrent use of two or more anticholinergic medications should be avoided among older adults.

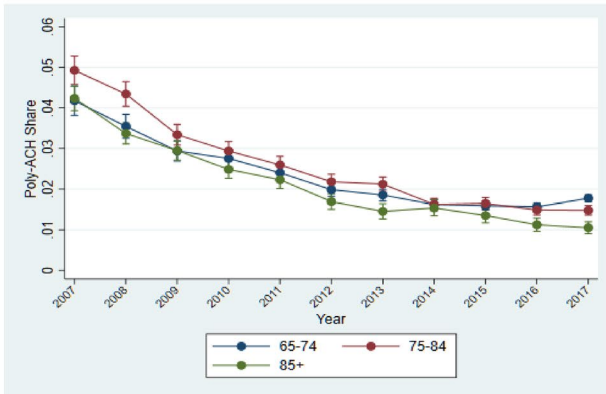
A Overall unadjusted results



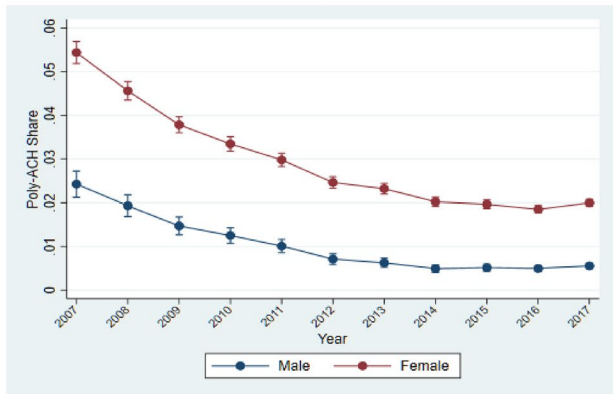
B Overall adjusted results



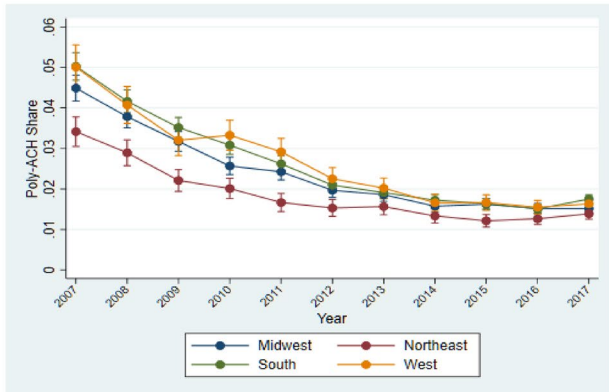
C Results stratified by age category



D Results stratified by sex



E Results stratified by Census Region



F Results stratified by nursing home category

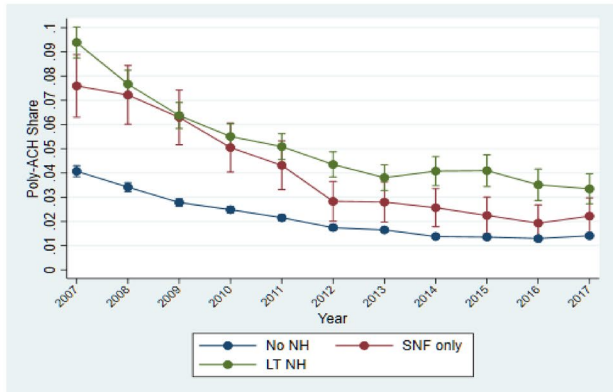


Fig. 2 Trends in Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure) [Poly-ACH] status. Note: figure shows estimates of annual shares and their 95% confidence intervals. Source: Medicare enrollment and claims data, CY 2006–2017.

LT long-term, *NH* nursing home, *Poly-ACH* Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure), *SNF* skilled nursing facility

Table 3 Adjusted clinical outcomes and spending for Medicare beneficiaries with overactive bladder by Poly-ACH status

Outcome name	Comparison vs referent	Mean risk (referent) (%)	Mean risk (comparison) (%)	Absolute risk difference (%)	p value	Lower 95% CL (%)	Upper 95% CL (%)	Risk ratio ^a
Annual indicator for any fall								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	3.8	4.8	1.0	0.000	0.7	1.3	1.26
Count of lagged Poly-ACH	1 yr vs 0 yrs	3.8	4.9	1.0	0.000	0.7	1.4	1.29
	2 yrs vs 0 yrs	3.8	4.6	0.8	0.005	0.2	1.4	1.21
	3 yrs vs 0 yrs	3.8	4.9	1.1	0.000	0.6	1.6	1.29
Annual indicator for ER fall								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	2.8	3.6	0.8	0.000	0.6	1.0	1.29
Count of lagged Poly-ACH	1 yr vs 0 yrs	2.8	3.7	0.9	0.000	0.5	1.2	1.32
	2 yrs vs 0 yrs	2.8	3.4	0.6	0.015	0.1	1.1	1.21
	3 yrs vs 0 yrs	2.8	3.7	0.9	0.000	0.4	1.3	1.32
Annual indicator for inpatient hospital fall								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	0.7	1.0	0.3	0.000	0.2	0.4	1.43
Count of lagged Poly-ACH	1 yr vs 0 yrs	0.7	1.1	0.4	0.000	0.2	0.5	1.57
	2 yrs vs 0 yrs	0.7	1.0	0.3	0.057	0.0	0.5	1.43
	3 yrs vs 0 yrs	0.7	1.0	0.3	0.053	0.0	0.5	1.43
Annual indicator for any fracture								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	3.7	4.2	0.4	0.001	0.2	0.7	1.14
Count of lagged Poly-ACH	1 yr vs 0 yrs	3.7	4.2	0.5	0.008	0.1	0.9	1.14
	2 yrs vs 0 yrs	3.7	3.9	0.2	0.485	-0.4	0.7	1.05
	3 yrs vs 0 yrs	3.7	4.2	0.5	0.063	0.0	1.0	1.14
Annual indicator for ER fracture								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	1.4	1.7	0.3	0.000	0.1	0.5	1.21
Count of lagged Poly-ACH	1 yr vs 0 yrs	1.4	1.8	0.3	0.003	0.1	0.6	1.29
	2 yrs vs 0 yrs	1.4	1.7	0.3	0.131	-0.1	0.6	1.21
	3 yrs vs 0 yrs	1.4	1.7	0.3	0.071	0.0	0.6	1.21
Annual indicator for inpatient hospital fracture								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	1.1	1.4	0.3	0.002	0.1	0.5	1.27
Count of lagged Poly-ACH	1 yr vs 0 yrs	1.1	1.4	0.4	0.004	0.1	0.7	1.27
	2 yrs vs 0 yrs	1.1	1.2	0.1	0.468	-0.2	0.5	1.09
	3 yrs vs 0 yrs	1.1	1.3	0.3	0.166	-0.1	0.7	1.18
Annual indicator for any AMS								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	2.6	3.4	0.8	0.000	0.5	1.0	1.31
Count of lagged Poly-ACH	1 yr vs 0 yrs	2.6	3.2	0.6	0.000	0.3	0.9	1.23
	2 yrs vs 0 yrs	2.6	3.5	0.9	0.000	0.4	1.4	1.35
	3 yrs vs 0 yrs	2.6	3.6	0.9	0.000	0.5	1.4	1.38
Annual indicator for ER AMS								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	1.5	1.9	0.4	0.000	0.2	0.6	1.27
Count of lagged Poly-ACH	1 yr vs 0 yrs	1.5	1.8	0.3	0.006	0.1	0.6	1.20
	2 yrs vs 0 yrs	1.5	1.9	0.5	0.014	0.1	0.8	1.27
	3 yrs vs 0 yrs	1.5	2.0	0.5	0.004	0.2	0.9	1.33
Annual indicator for inpatient hospital AMS								
Any lagged Poly-ACH	1+ yrs vs 0 yrs	0.1	0.2	0.1	0.018	0.0	0.1	2.00
Count of lagged Poly-ACH	1 yr vs 0 yrs	0.1	0.2	0.1	0.041	0.0	0.2	2.00
	2 yrs vs 0 yrs	0.1	0.2	0.1	0.134	0.0	0.2	2.00
	3 yrs vs 0 yrs	0.1	0.2	0.0	0.740	-0.1	0.1	2.00

Table 3 (continued)

Outcome name	Comparison vs referent	Mean spending (referent)	Mean spending (comparison)	Absolute spending difference	<i>p</i> value	Lower 95% CL	Upper 95% CL
Annual medical care spending							
Any lagged Poly-ACH	1+ yrs vs 0 yrs	US\$8645	US\$9762	US\$1116	0.000	US\$677	US\$1556
Count of lagged Poly-ACH	1 yr vs 0 yrs	US\$8645	US\$9808	US\$1163	0.000	US\$560	US\$1766
	2 yrs vs 0 yrs	US\$8645	US\$9815	US\$1169	0.006	US\$327	US\$2011
	3 yrs vs 0 yrs	US\$8645	US\$9610	US\$964	0.029	US\$98	US\$1830

Source: Medicare enrollment and claims data, calendar year 2006–2017

AMS altered mental status, *Poly-ACH* Polypharmacy: Use of Multiple Anticholinergic Medications in Older Adults (measure), *CL* confidence limit, *yrs* years, *ER* emergency room

^aRisk ratio = comparison mean/reference mean

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Declarations

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Availability of data and material Researchers may request access to anonymized participant level data, trial level data, and protocols from Astellas sponsored clinical trials at 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 the Centers for Medicare and Medicaid Services, but restrictions apply to the availability of these data, which were used under license for the current study, and thus are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Centers for Medicare and Medicaid Services.

Code availability Not applicable.

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