

Omalizumab Treatment Patterns Among Patients with Asthma in the US Medicare Population



Pengxiang Li, PhD^{a,b}, Abhishek Kavati, PhD^c, Justin T. Puckett, BA^a, Jordan Jahnke, MS^a, Paula Busse, MD^d, Nicola A. Hanania, MD^e, Benjamin Ortiz, MD^c, and Jalpa A. Doshi, PhD^{a,b} Philadelphia, Pa; East Hanover, NJ; New York, NY; and Houston, Tex

What is already known about this topic? Older patients and patients with disabilities have unique problems (eg, comorbidities, polypharmacy, poorer cognition, and lower incomes) that make management of their asthma more challenging versus younger patients; older age and increased disease severity are associated with worse asthma outcomes.

What does this article add to our knowledge? In US Medicare patients with asthma initiating omalizumab, patient age, low-income subsidy status, and the number of physician visits for evaluation and management were factors associated with discontinuation and adherence to omalizumab.

How does this study impact current management guidelines? Understanding the reasons for omalizumab treatment discontinuation and adherence in the Medicare population may provide insights that may guide the management of omalizumab in patients with asthma treated with this biologic.

BACKGROUND: Asthma in older adults is associated with high rates of morbidity and mortality; similarly, asthma can be severe enough among younger adults to warrant disability benefits. Reasons for poor outcomes in both groups of patients may include discontinuation and lack of adherence to controller therapies.

OBJECTIVE: To examine characteristics and treatment patterns of US Medicare patients initiating omalizumab for asthma, and factors associated with its discontinuation and adherence.

METHODS: A retrospective claims database analysis of Medicare beneficiaries with asthma initiating omalizumab treatment was carried out. The primary outcomes were omalizumab discontinuation (gap in use ≥ 90 days) and

adherence (proportion of days covered ≥ 0.8) over a 12-month follow-up. Multivariable regressions were used to examine factors associated with omalizumab discontinuation and adherence. **RESULTS:** Of the 3058 Medicare patients initiating omalizumab for asthma (mean age, 62.7 years), 36.9% discontinued omalizumab and 60.6% were adherent. Discontinuation rates were 32.7% and 42.8%, and adherence rates were 65.4% and 53.9%, for disabled and older Medicare patients, respectively. Patients aged 65 to 69 years and 70 to 74 years had significantly lower odds of discontinuation (odds ratios [95% CI], 0.66 [0.46-0.93] and 0.62 [0.43-0.89], respectively) and higher odds of adherence than did patients aged 80 years or older. Compared with patients receiving low-income subsidy, patients not

^aDivision of General Internal Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pa

^bLeonard Davis Institute of Health Economics, Philadelphia, Pa

^cNovartis Pharmaceuticals Corporation, East Hanover, NJ

^dDivision of Allergy and Clinical Immunology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

^eSection of Pulmonary and Critical Care Medicine, Baylor College of Medicine, Houston, Tex

Financial support for the conduct of the research and preparation of this article was provided by Novartis Pharmaceuticals Corporation, East Hanover, NJ. Authors employed by Novartis Pharmaceutical Corporation were involved in the study design, interpretation of data, writing of the report, and the decision to submit the article for publication. Authors received editorial support for this article from Claire Lavin and Jessica Donaldson-Jones of Fishawack Communications Ltd., funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

Conflicts of interest: P. Li has received consulting fees from Avalon Health Economics, Bob Ohsfeldt LLC, and HealthStatistics, all unrelated to the content of this article. A. Kavati and B. Ortiz are employees and stockholders of Novartis Pharmaceuticals Corporation. P. Busse has received honorarium/consulting fees from Biocryst, CSL Behring, CVS Health, Novartis, Pearl Therapeutics, AstraZeneca, Pharming, and Shire; has acted as a legal expert for the law offices of Levin, Riback, Adelman, and Flangel; and their institution has received grant monies from Shire, all unrelated to the content of this article. N. A. Hanania has received consulting fees from AstraZeneca, Boehringer Ingelheim, Genentech,

GlaxoSmithKline (GSK), Novartis, and Sanofi Genzyme; and their institution has received grant monies from AstraZeneca, Boehringer Ingelheim, and GSK, all unrelated to the content of this article. J. A. Doshi has received grant monies from Novartis for activities related to the work under consideration for publication; reports serving as an advisory board member or consultant for Allergan, Ironwood Pharmaceuticals, Janssen, Kite Pharma, Merck, Otsuka, Regeneron, Sarepta, Sage Therapeutics, Sanofi, and Vertex; has received research funding from Abbvie, Biogen, Humana, Janssen, Novartis, Pfizer, PhRMA, Regeneron, Sanofi, and Valeant; and reports her spouse holding stock in Merck and Pfizer, all unrelated to the content of this article. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication February 21, 2019; revised manuscript received and accepted for publication July 12, 2019.

Available online July 20, 2019.

Corresponding author: Jalpa A. Doshi, PhD, Division of General Internal Medicine, University of Pennsylvania Perelman School of Medicine, 1223 Blockley Hall, 423 Guardian Dr, Philadelphia, PA 19104. E-mail: jdoshi@pennmedicine.upenn.edu.

2213-2198

© 2019 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). <https://doi.org/10.1016/j.jaip.2019.07.011>

*Abbreviations used**ICS- Inhaled corticosteroid**LIS- Low-income subsidy**OR- Odds ratio**PDC- Proportion of days covered*

receiving low-income subsidy had lower odds of discontinuation (0.66 [0.52-0.83]) and higher odds of adherence (1.52 [1.20-1.93]). Greater numbers of preindex evaluation and management physician visits and comorbid rhinitis were associated with lower odds of discontinuation and higher odds of adherence.

CONCLUSIONS: More than 60% of Medicare patients with asthma continued and were adherent to omalizumab over a 12-month follow-up. Patient age, low-income subsidy status, and the numbers of evaluation and management physician visits were among factors associated with treatment adherence and discontinuation. © 2019 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). (J Allergy Clin Immunol Pract 2020;8:507-15)

Key words: Omalizumab; Asthma; Treatment patterns; Discontinuation; Adherence; Medicare; Older adults; Disabled

INTRODUCTION

The prevalence of current asthma among older adults (aged ≥ 65 years) in the United States is significant, estimated at 7.4% of the population (>3.5 million people).¹ However, this number is likely larger because asthma is frequently underdiagnosed in this age group.^{2,3} Asthma can also be severe enough among younger patients (aged <65 years) to warrant disability benefits, though the number of patients with asthma currently classified as disabled is difficult to ascertain.⁴ In addition, given that asthma impacts approximately 10.9 million adults between the ages of 35 and 64 years (8.8% of the population),¹ it is possible that asthma is a comorbidity in patients who are receiving disability benefits for another condition. Importantly, older age and more severe asthma are often associated with increased mortality and morbidity in patients with asthma. This includes higher rates of hospitalization after an emergency department visit, longer hospital stays, higher rates of readmission, and poorer lung function.^{2,3,5-9} This trend is likely secondary to multiple factors including undertreatment, poor adherence, delayed recognition of symptoms, multiple comorbidities and associated concomitant medications, lack of treatment response, reduced mobility, and possible differences in airway inflammation with aging.^{8,10,11} Consequently, older patients and disabled patients with severe asthma have increased health care usage and cost associated with their disease,^{9,11,12} and poorly controlled asthma can significantly reduce quality of life, compared with their younger and healthier counterparts.^{2,3} Despite a growing population of older people with asthma,^{1,13,14} this group is often underrepresented in clinical trials.^{2,15} Similarly, the exclusion of adults with a disability from clinical trials is well documented.^{16,17} Therefore, there are limited evidence-based guidelines and data on treatment patterns and effectiveness for such patients.^{2,15,18} Efforts to

better understand treatment patterns in older adults with asthma and adults with a disability with asthma could ultimately help alleviate the burden of disease in these populations.

Omalizumab (anti-IgE) is a biologic therapy approved by the US Food and Drug Administration in 2003.¹⁹ Omalizumab treatment has been shown to reduce the number of asthma exacerbations, dosing of inhaled corticosteroid (ICS), and rescue medication use in adults and children with moderate to severe persistent allergic asthma.¹⁹⁻²⁴ Evidence suggests that omalizumab is also effective and well tolerated in people aged 50 years or older.²⁵⁻²⁹ To our knowledge, no study to date has examined treatment patterns with omalizumab for asthma among older patients (>65 years) or patients with a disability (<65 years) covered under Medicare, a federal government program that offers health insurance to approximately 60 million older adults and/or individuals with a disability in the United States.³⁰ To address this question, we performed a retrospective claims database analysis to examine the characteristics and factors associated with treatment patterns (adherence and discontinuation) in a national sample of US Medicare patients initiating omalizumab for asthma.

METHODS

Data source

This study was a retrospective claims database analysis using the 2011 to 2015 Chronic Condition Data Warehouse 100% Medicare files available from the Centers for Medicare & Medicaid Services. The Chronic Condition Data Warehouse includes Medicare Part A (hospital, skilled nursing facility, and limited home health services) and Part B (outpatient hospital, physician, physician-administered drugs, other outpatient, durable medical equipment, hospice, and home health services) medical claims and Medicare Part D prescription claims (outpatient prescription drug events). These files were linked to personal summary files that contained patients' demographic characteristics and eligibility information as well as Part D plan characteristics files.

Sample

The study population consisted of Medicare beneficiaries initiating omalizumab treatment between January 1, 2012, and December 31, 2014 (intake period). The first medical/pharmacy claim date for omalizumab during the intake period was defined as the index date; patients were followed for 12 months from this date. Patients were required to have continuous eligibility of Medicare fee-for-service and stand-alone Part D coverage for 12 months before and 12 months after the index date to ensure completeness of data during the study period. In addition, patients were required to have 1 or more claims with diagnosis of asthma (*International Classification of Diseases, Ninth Revision* code 493.x) in the 12 months before or on the index date. To ensure that the sample included new initiators of omalizumab treatment, patients with 1 or more omalizumab claims during the 12 months before the index period were excluded. Finally, patients with missing values on any covariates were excluded (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org).

This study was approved by the University of Pennsylvania's Institutional Review Board.

Outcomes

The primary outcomes included adherence to and discontinuation of omalizumab. Adherence was captured using the proportion

of days covered (PDC) measure, which has a range from 0 to 1. PDC was calculated as the number of days covered with omalizumab during a fixed time interval, divided by the length of the fixed time interval (ie, 365 days) from the omalizumab initiation date.³¹ For example, a patient with omalizumab coverage available for 292 days during the 365-day post-index date period would have a PDC of $292/365 = 0.80$. Patients with a PDC of 0.80 or more were classified as adherent. Additional information on how the PDC was calculated from Medicare Part D pharmacy claims and Part B medical claims is available in [Appendix E1](#) in this article's Online Repository at www.jaci-inpractice.org.

Discontinuation was defined as a continuous gap in availability of treatment after a prespecified permitted gap between refills.³² In this study, discontinuation was captured via a dichotomous measure indicating the presence of a continuous 90-day or more period without omalizumab during the 12-month follow-up period (ie, if another prescription fill or administration for omalizumab did not occur for ≥ 90 consecutive days after the final day covered by the previous days' supply [or assigned days' supply] of a fill or administration, then this was coded as discontinuation).

Finally, we measured whether patients who discontinued omalizumab (1) switched to another asthma therapy, defined as the first occurrence of a prescription fill of a different asthma therapy within 90 days after the last days' supply of omalizumab, or (2) restarted omalizumab or another asthma therapy, defined as a prescription fill of omalizumab or another asthma therapy after a continuous 90-day period without omalizumab but within 1 year after the index date. Patients who had neither switched nor restarted before the end of the follow-up period were categorized as other discontinuers. In addition, nondiscontinuers (patients who did not discontinue omalizumab) were grouped on the basis of whether there was augmentation (add-on of a new asthma medication during continuous use of omalizumab) or nonaugmentation.

Statistical analyses

Descriptive statistics including mean $\pm$ SD and absolute/relative frequencies for continuous and categorical data, respectively, were reported. Multivariable logistic regression was used to examine discontinuation of, and adherence to, omalizumab over a 12-month follow-up period; odds ratios (ORs) and 95% CIs were generated for all variables. A multivariable Cox regression analysis of time to omalizumab discontinuation was also performed. A multinomial logistic regression was conducted to examine factors associated with omalizumab treatment patterns (ie, continuous users without augmentation [reference group], continuous users with augmentation, switchers, restarters, and other discontinuers).

Covariates in the regression analyses included sociodemographic characteristics (age, sex, and race/ethnicity), clinical characteristics in the 12 months before omalizumab initiation (resource use in the 12 months before the index date with primary asthma diagnosis, prescription drug hierarchical condition category score [a risk adjustment method³³ that has been used to adjust for potential selection biases in drug use studies among Medicare patients³⁴⁻³⁶], relevant comorbidities, asthma medications, baseline oral systemic corticosteroid use, and the number of other medications), Medicare Part D–related variables (Part D plan characteristics, Part D low-income subsidy [LIS] status, index omalizumab claim received under Part D benefit or not), county-level characteristics and census region, and year and season of index date.

Subgroup analyses of discontinuation were conducted on the basis of patient age (ie, age < 65 years [adults with a disability] or age

≥ 65 years [older adults]). In addition, sensitivity analyses on the sample selection criteria and outcome definitions were conducted. First, because urticaria is also a Food and Drug Administration–approved indication for omalizumab,^{19,20} we reran our analyses after the exclusion of patients with a diagnosis of urticaria during the preindex period. Second, sensitivity analyses were also performed to assess factors associated with adherence on the basis of alternative cutoff points (PDC ≥ 0.70 and PDC ≥ 0.90).

Analyses were performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement,³⁷ where descriptive statistical analyses were reported only for demographic and clinical characteristics (item 14[a] of the statement), and inferential statistical analyses for outcome variables were limited to reporting CIs for the differences between the 2 groups.

Statistical analyses were performed using Stata 15.0 software (StataCorp, College Station, Texas). To ensure data quality and integrity, all data analyses, initially performed by a biostatistician from the University of Pennsylvania, were archived. A senior investigator then separately assessed the methodology and data to ensure validity.

RESULTS

Study population

A total of 13,364 Medicare beneficiaries initiated omalizumab during the intake period (January 1, 2012, to December 31, 2014). After applying the inclusion and exclusion criteria, the final sample included 3058 patients; sample attrition is summarized in [Figure E1](#). Patients had a mean age of 62.7 ± 13.4 years, of whom 58.6% were 65 years or older, and 67.0% were women ([Table I](#)). The mean age of patients with a disability (age < 65 years) was 49.6 ± 9.8 years, and that of older patients (age ≥ 65 years) was 72.0 ± 5.3 years. During the 12 months before the index date, the mean number of hospitalizations, evaluation and management physician visits, and emergency department visits with asthma as the primary diagnosis were 0.3 ± 0.8 , 3.7 ± 3.5 , and 0.7 ± 2.0 per patient, respectively. The most common comorbid conditions were rhinitis (71.6%); upper respiratory tract infection, laryngitis, or nasopharyngitis (71.0%); and chronic obstructive pulmonary disease or emphysema (63.8%). Rates of anxiety or depression were also high (42.1%). An individual may have reported 1 or more of the listed comorbidities. The mean prescription drug hierarchical condition category score was 1.1 ± 0.4 . During the preindex period, 98.3% of patients were receiving some asthma medication (data not shown). Most patients were receiving ICS + long-acting β_2 agonist (69%), leukotriene receptor antagonist (70%), or short-acting β_2 agonist (78%). Approximately one-third of patients received ICS, long-acting muscarinic antagonist, and/or short-acting β_2 agonist + short-acting muscarinic antagonist. Only 8.4% of patients were receiving short-acting muscarinic antagonist as one of their asthma medications ([Table I](#)). The mean number of 30-day supply equivalent prescriptions for nonasthma medications was 6.5 ± 5.3 . Approximately half of all patients were receiving LIS (49.8%). Most patients received omalizumab under Part B (only 6.6% under Part D). Distribution of omalizumab initiation was similar when categorized according to the season of the index date ([Table I](#)).

Treatment patterns

The distribution of patients across omalizumab utilization groups at 12 months is presented in [Table II](#). On the basis of a

TABLE I. Patients' baseline characteristics

Characteristic	All patients (N = 3058)
Age (y), mean $\pm$ SD	62.7 $\pm$ 13.4
Age category (y), n (%)	
<65	1267 (41.4)
65-69	701 (22.9)
70-74	588 (19.2)
75-79	319 (10.4)
≥ 80	183 (6.0)
Sex: female, n (%)	2049 (67.0)
Race, n (%)	
White	2386 (78.0)
Black	455 (14.9)
Hispanic	87 (2.8)
Other/unknown	130 (4.3)
Resource use in the 12 mo before the index date with primary asthma diagnosis, mean $\pm$ SD	
No. of ED visits	0.7 $\pm$ 2.0
No. of evaluation and management physician visits	3.7 $\pm$ 3.5
No. of hospitalizations	0.3 $\pm$ 0.8
RxHCC score, mean $\pm$ SD	1.1 $\pm$ 0.4
Comorbid conditions, n (%)	
Anxiety or depression	1287 (42.1)
Bronchitis	1146 (37.5)
Chronic obstructive pulmonary disease or emphysema	1951 (63.8)
LRTI excluding pneumonia	1167 (38.2)
Pneumonia	714 (23.3)
Rhinitis	2189 (71.6)
Sinusitis	1381 (45.2)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	2171 (71.0)
Use of asthma medication in the 12 mo before the index date, n (%) [*]	
ICS + LABA	2120 (69.3)
ICS	992 (32.4)
LAMA	932 (30.5)
LTRA	2128 (69.6)
SABA + SAMA	768 (25.1)
SABA	2396 (78.4)
SAMA	257 (8.4)
Oral systemic corticosteroid claims, mean $\pm$ SD	4.5 $\pm$ 4.2
No. of 30-d supply equivalent prescriptions for nonasthma medications, mean $\pm$ SD	6.5 $\pm$ 5.3
Part D drug benefit type [†]	
Defined standard	91 (3.0)
Actuarially equivalent standard	1229 (40.2)
Basic alternative	563 (18.4)
Enhanced alternative	1175 (38.4)
Part D LIS status, n (%)	
Full-year LIS, partial-year LIS, or plan switch	1523 (49.8)
None	1535 (50.2)
Received omalizumab under Part D, n (%)	203 (6.6)

(continued)

TABLE I. (Continued)

Characteristic	All patients (N = 3058)
County-level characteristics, mean $\pm$ SD	
Income, per capita, \$10,000s	5.3 $\pm$ 1.4
Allergy or immunology physicians per 10,000 residents	14.8 $\pm$ 29.5
Pulmonologists per 10,000 residents	39.6 $\pm$ 75.3
Census region, n (%)	
Northeast	545 (17.8)
Midwest	719 (23.5)
South	1202 (39.3)
West	592 (19.4)
Year of index date, n (%)	
2012	871 (28.5)
2013	961 (31.4)
2014	1226 (40.1)
Season of index date, n (%)	
Fall	782 (25.6)
Winter	645 (21.1)
Spring	765 (25.0)
Summer	866 (28.3)

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

*An individual may be receiving ≥ 1 of the listed preindex asthma medications.

†Plan D drug benefit definitions: "Defined standard" benefits have an annual deductible with 25% coinsurance in the initial coverage phase (the beneficiary is responsible for costs in any coverage gap); "actuarially equivalent standard" benefits have an annual deductible and may substitute certain cost-sharing requirements in "defined standard" benefit coverage; "basic alternative" benefits may have a reduced or zero-dollar deductible, can use tiered co-payments or coinsurance, and may have a modification to the initial coverage limit (remains actuarially equivalent to the standard benefit); "enhanced alternative" coverage exceeds the value of the "defined standard" benefit and includes prescription drug coverage and supplemental benefits (ie, reduction in cost-sharing in the "coverage gap"; a reduction in, or elimination of, the initial deductible; a reduction in the coinsurance or co-payments applicable during the initial coverage phase; an increase in the initial coverage limit).³⁸

definition of PDC greater than or equal to 0.8, 60.6% of patients were adherent to omalizumab treatment. In total, 36.9% of patients discontinued omalizumab within 12 months after treatment initiation (primary end point). Most patients who discontinued did not resume treatment before the end of the follow-up period (61.3% of discontinuers; 22.6% of the overall sample); 26.3% of discontinuers (9.7% of the overall sample) switched to a new asthma medication, and 12.3% of discontinuers (4.5% of the overall sample) used a new drug or resumed omalizumab therapy after a gap of 90 or more consecutive days. Among the continuers, 32.8% (20.7% of the overall sample) augmented their omalizumab treatment with another asthma medication. Discontinuation rates were 32.7% and 42.8%, and adherence rates were 65.4% and 53.9%, for disabled and older Medicare patients, respectively (data not shown).

Factors associated with omalizumab discontinuation and adherence

Results from the multivariable logistic regression analysis are presented in Figure 1. Patients aged 65 to 69 years and 70 to 74 years had significantly lower odds of omalizumab discontinuation (OR [95% CI], 0.66 [0.46-0.93] and 0.62 [0.43-0.89],

TABLE II. Distribution of omalizumab treatment utilization groups at 12 mo

Characteristic	All patients (N = 3058)		
PDC, mean $\pm$ SD	0.74 $\pm$ 0.31		
Adherence (PDC $\geq$ 0.8), n (%)	1854 (60.6)		
Subgroup	Patients, n	Percentage of all patients, %	Percentage of subgroup, %
Continuous omalizumab use	1930	63.1	100.0*
Nonaugmentation	1297	42.4	67.2*
Augmentation†	633	20.7	32.8*
Discontinuation‡	1128	36.9	100.0§
Switch	297	9.7	26.3§
Restart¶	139	4.5	12.3§
Other discontinuation#	692	22.6	61.3§

*Percentage of continuous omalizumab users (n = 1930).

†Patient received add-on of another asthma medication during continuous use of omalizumab.

‡Defined as a continuous gap of $\geq$ 90 d.

§Percentage of discontinuers (n = 1128).

||Patients started treatment with a new drug within 90 d of discontinuing the index biologic.

¶Patients used a new drug or resumed omalizumab therapy after a gap of $\geq$ 90 consecutive days; restart occurred within 1 y after the index date.

#Patients did not resume treatment before the end of the follow-up period.

respectively) and higher odds of adherence (OR [95% CI], 1.45 [1.02-2.07] and 1.50 [1.05-2.15], respectively) than did patients 80 years or older (reference group) at the 12-month follow-up (Figure 1). There were no significant differences between patients younger than 65 years and patients 80 years or older with respect to adherence and discontinuation rates (OR [95% CI], 1.03 [0.71-1.49] and 0.87 [0.61-1.26], respectively). However, when analyses were run with a binary age variable (<65 years vs ≥ 65 years), patients younger than 65 years (ie, patients with a disability) had significantly poorer adherence (OR [95% CI], 0.77 [0.63-0.95]) and higher discontinuation (OR [95% CI], 1.25 [1.02-1.55]) than adults 65 years or older (data not shown). Men had significantly greater odds of adherence than women (OR [95% CI], 1.20 [1.02-1.43]), even though the odds for discontinuation were not significantly different (OR [95% CI], 0.99 [0.83-1.17]). Compared with patients receiving LIS, patients not receiving LIS had higher odds of adherence (OR [95% CI], 1.52 [1.20-1.93]) and lower odds of discontinuation (OR [95% CI], 0.66 [0.52-0.83]). Patients receiving their index omalizumab via the Part D benefit were significantly less likely to be adherent than those receiving it via the Part B benefit (OR [95% CI], 0.52 [0.36-0.74]), although the odds for discontinuation were not significantly different. A higher number of all-cause patient evaluation and management physician visits in the 12 months before the index date was associated with lower odds of discontinuation (OR [95% CI], 0.96 [0.94-0.99]) and higher odds of adherence (OR [95% CI], 1.03 [1.00-1.05]). Rhinitis was the only comorbidity associated with significantly lower odds of omalizumab discontinuation (OR [95% CI], 0.82 [0.69-0.97]) and higher odds of omalizumab adherence (OR [95% CI], 1.23 [1.03-1.46]) versus patients without rhinitis in the 12 months before the index date. Patients using ICS with or without a long-acting β_2 agonist in the preindex period had significantly higher odds of omalizumab adherence 12 months after the index date (OR [95% CI], ICS + long-acting β_2 agonist, 1.29 [1.08-1.55]; ICS, 1.19 [1.00-1.40]) versus those not receiving these medications (Figure 1). The use of oral systemic corticosteroids during the preindex period did not have a significant association with omalizumab discontinuation and adherence.

Multivariable Cox regression analysis of the factors associated with time to omalizumab discontinuation (see Table E1 in this article's Online Repository at www.jaci-inpractice.org) showed qualitatively similar findings to those from the multivariable logistic regression analysis of omalizumab discontinuation. The multinomial logistic regression analysis of the factors associated with varying omalizumab treatment patterns of augmentation, switching, restarting, and other discontinuation (relative to nondiscontinuation) is presented in Table E2 in this article's Online Repository at www.jaci-inpractice.org. This analysis found that patients aged 70 to 74 years were less likely to reinstate treatment than those 80 years or older, and those aged 65 to 69 years were the only group of patients (vs those aged ≥ 80 years) significantly more likely to resume treatment after a gap of 90 or more consecutive days and before the end of the study follow-up period. Patients with anxiety or depression were significantly more likely to switch to a new treatment within 90 days of discontinuing omalizumab (OR [95% CI], 1.39 [1.03-1.86]) (Table E2). Patients with comorbid upper respiratory tract infection, laryngitis, or nasopharyngitis were significantly more likely to restart therapy after a period of discontinuation than those without these comorbidities (OR [95% CI], 2.20 [1.26-3.85]), whereas patients with bronchitis were significantly less likely to restart (OR [95% CI], 0.31 [0.11-0.85]) (Table E2).

Subgroup analysis in older patients (≥ 65 years) found similar results to the main sample in terms of the trends for associations of the age groups of 65 to 69 and 70 to 74 years, number of evaluation and management physician visits, rhinitis, non-LIS status, and receipt of omalizumab under Part D, with adherence and discontinuation (see Table E3 in this article's Online Repository at www.jaci-inpractice.org). In a subgroup analysis among patients with a disability younger than 65 years, patients younger than 45 years were significantly more likely to discontinue omalizumab therapy compared with patients aged 55 to 64 years (OR [95% CI], 1.66 [1.22-2.27]) (Table E3). Although not significant in the main sample, anxiety or depression was significantly associated with lower adherence rates among the population with a disability (Table E3). The directions of the

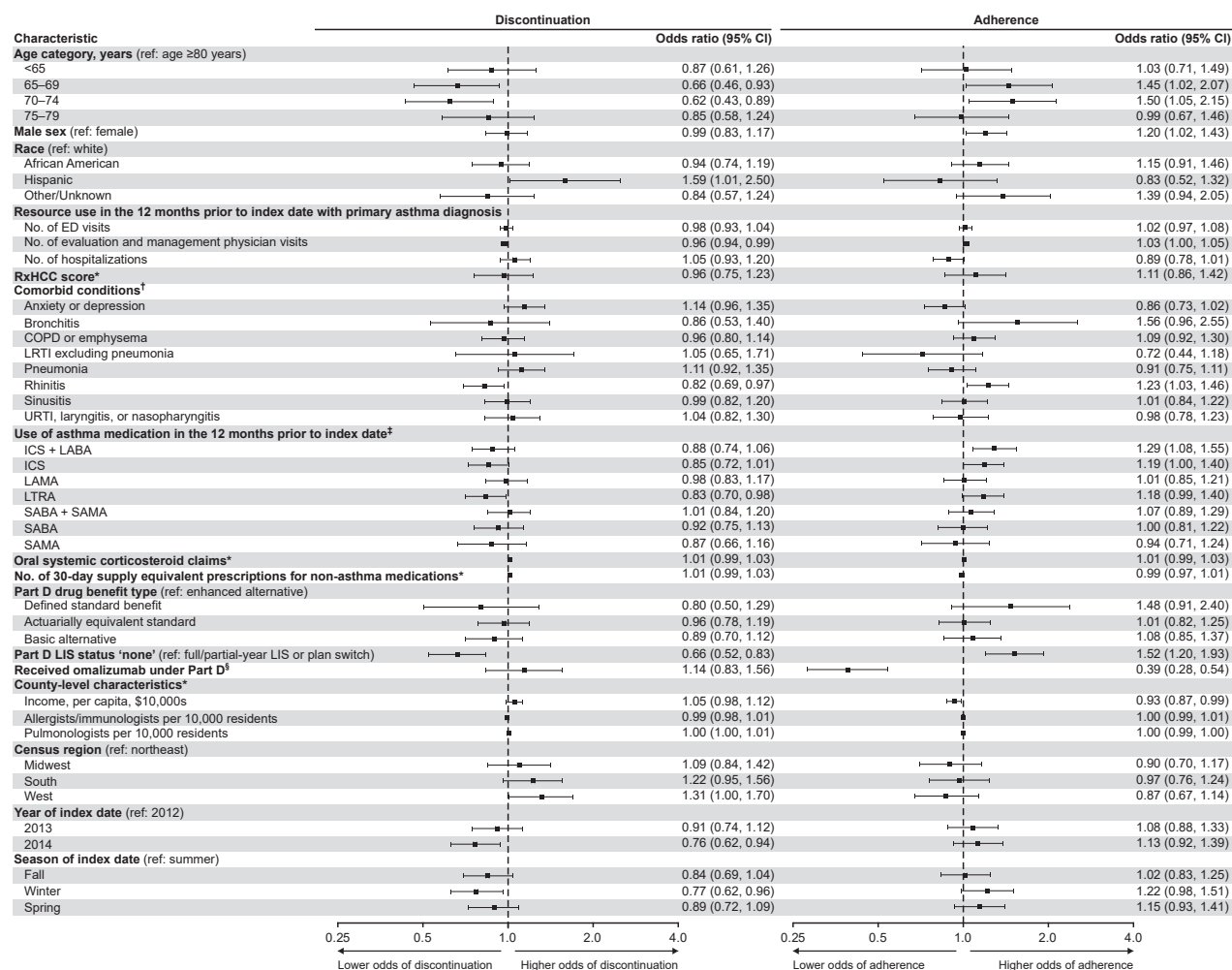


FIGURE 1. Factors associated with omalizumab discontinuation and adherence during the 12-month follow-up period. ORs were adjusted for the covariates listed. Ref indicates the reference group against which other factors within that group were compared. *COPD*, Chronic obstructive pulmonary disease; *ED*, emergency department; *LABA*, long-acting β_2 agonist; *LAMA*, long-acting muscarinic antagonist; *LRTI*, lower respiratory tract infection; *LTRA*, leukotriene receptor antagonist; *RxHCC*, prescription drug hierarchical condition category; *SABA*, short-acting β_2 agonist; *SAMA*, short-acting muscarinic antagonist; *URTI*, upper respiratory tract infection. *ORs indicate how odds of the outcome change if the mean value increases by 1. †Reference group contains those patients without the asthma-related comorbidity in the preindex period. ‡Reference group contains those patients not using the specified drug in the preindex period. §Reference group contains those patients who did not receive omalizumab under Part D.

association of the various factors associated with discontinuation and adherence were quite similar in sensitivity analyses conducted among patients without urticaria (see Table E4 in this article's Online Repository at www.jaci-inpractice.org), and when defining adherence on the basis of alternative cutoff points ($PDC \geq 0.70$ and $PDC \geq 0.90$; see Table E5 in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

This study is among the first to investigate omalizumab treatment patterns and associated factors among a national sample of fee-for-service Medicare beneficiaries with moderate to severe persistent allergic asthma. Because patients are eligible for Medicare at age 65 years, or can become eligible due to disability, Medicare claims offer an ideal data set to study discontinuation

and adherence among both older adults and adults with a disability. Among patients initiating omalizumab during the study period, we found that approximately 60% were adherent to treatment over a 12-month follow-up period. More than one-third of the patients discontinued omalizumab. Some of these patients switched therapies (~25% of discontinuers) or eventually restarted omalizumab or another therapy (>10% of discontinuers), whereas the remainder did not have evidence of resuming treatment before the end of the study period. Among patients who were continuous users of omalizumab, approximately one-third augmented their omalizumab treatment with another asthma therapy. Our study identified several factors associated with these treatment patterns.

One of the key factors identified in our study was patient age. Previous studies have documented that older patients have low adherence to asthma medications, which may be linked to a

number of factors, including comorbidities, polypharmacy, and limited health literacy.³⁹⁻⁴¹ We found that among older Medicare patients, being older than 80 years was associated with higher odds of discontinuation, consistent with existing literature. Of note, we found that more than 40% of our sample comprised patients with a disability younger than 65 years, significantly higher than the wider Medicare population.⁴² Although some studies have shown that omalizumab treatment is associated with good rates of adherence in relatively younger patient populations (mean age, <50 years),^{38,43,44} our subgroup analysis found that patients younger than 45 years were more likely to discontinue treatment compared with patients aged 55 to 64 years. This might suggest that patients with a disability are at a greater risk for discontinuation than other younger patients.

Interestingly, we also discovered that nearly half of omalizumab users were receiving LIS. Those patients receiving LIS were less likely to be adherent to omalizumab and more likely to discontinue this treatment than non-LIS patients. Part D LIS status likely serves as a general proxy measure for socioeconomic status (eg, patients receiving LIS may have lower income, have lower education attainment, and are more likely to be of a racial/ethnic minority vs patients without LIS), which may contribute to the lower adherence and compliance to omalizumab of LIS versus non-LIS patients.⁴⁵ In addition, because omalizumab should be administered by a health care provider in a health care setting,¹⁹ patient access to transport and associated travel time and costs related to visiting a physician office or administration center may create additional barriers for patients receiving LIS. Previous studies have shown that despite these issues, LIS patients are more likely to use Part D—covered specialty and biologic drugs than non-LIS patients because their otherwise high out-of-pocket costs are subsidized to minimal amounts under Part D.⁴⁶⁻⁵⁰ In contrast, most patients in this study received omalizumab through the Part B medical benefit wherein a majority of both LIS and non-LIS patients are shielded from the cost-sharing burden owing to the presence of Medicare supplemental insurance. However, post hoc analysis did find that patients who received omalizumab under Medicare Part D, especially non-LIS patients, were significantly more likely than LIS patients to be nonadherent to omalizumab treatment. These findings suggest that, to the extent possible, physicians should consider administering omalizumab via the Part B benefit to non-LIS patients.

Our study also suggested potential clinical factors associated with adherence to omalizumab in Medicare patients with asthma. Those with concomitant rhinitis were more likely to be adherent to omalizumab compared with patients without rhinitis. Treatment with omalizumab targets a common underlying disease mechanism in both allergic rhinitis and allergic asthma, and has been shown to provide significant clinical benefits in a study of patients with these concomitant diseases.⁵¹ In experiencing an improvement in symptoms relating to both conditions, this may explain the greater odds of adherence in patients with this concomitant rhinitis in the present study. In addition, patients with recurrent upper respiratory tract infection, laryngitis, or nasopharyngitis were significantly more likely to restart therapy (a new drug or resume omalizumab therapy) after a period of discontinuation than those individuals without these comorbidities. Notably, high rates of anxiety or depression were also observed in the study population. Anxiety and depression are known barriers to adherence to medication in chronic disease, including asthma,^{40,52,53} and this was corroborated in our subgroup of patients with a disability

(age <65 years) in which these comorbidities were associated with lower adherence rates.

Patients with more frequent physician visits for evaluation and management of asthma in the year before the index date (ie, 1 year before their first claim for omalizumab) were less likely to discontinue omalizumab treatment. We did not capture resource use data after the index date because this was outside the scope of our study, but this finding may suggest that patients who had more frequent physician visits before initiating omalizumab had greater severity of disease and may have been more informed about their condition and treatment options, resulting in them being less likely to discontinue treatment. Thus, physician visits provide an opportunity to provide education about asthma and to discuss any patient concerns regarding treatment, which may relate to adherence and compliance. The hypothesis that more physician contact and visits will increase adherence to omalizumab should be explored in future research.

Our study had some potential limitations worth noting. As a retrospective claims-based study, details on treatment response, adverse events, and reasons for nonadherence or gaps in treatment were unavailable. Therefore, we were unable to determine whether omalizumab discontinuation was deliberate and appropriate (eg, due to lack of efficacy or adverse events) or otherwise (eg, related to factors such as age, treatment cost, or patient burden/inconvenience). Although we performed adjusted regression analyses for a number of covariates, we acknowledge the potential for possible confounding due to unobserved covariates. Our data may also have been affected by limitations relating to the measures used (eg, proxies of comorbidity status), possible coding errors, and the possibility of patients receiving medication outside of Part D not being captured. In addition, Medicare medical claims do not include dosing information for omalizumab received under Medicare Part B; as a result, we cannot determine whether patients were prescribed omalizumab for 2 weeks or 4 weeks. As outlined in the Methods section, we opted to assume a 28 days' supply to minimize underestimation of adherence among those patients receiving a 28-day supply. However, this might have resulted in a slight overestimation of adherence for patients receiving a 14-day supply. Because Medicare beneficiaries are generally older and/or have a disability, our findings may not be representative of the broader population with asthma; although approximately 40% of patients in this study were younger than 65 years, they were likely to have had more comorbidities than people not covered by Medicare. The generalizability of our results to patients in other countries (with different health care systems) is also unknown, although higher discontinuation rates have also been observed in older versus younger patients with asthma in a German study (≥50 years vs <50 years).^{26,28}

CONCLUSIONS

This study is the first to provide new national data regarding treatment patterns of disabled and older Medicare patients with asthma initiating omalizumab. We found that 60% of patients newly starting omalizumab were adherent to the treatment over a 1-year follow-up. More than one-third of the patients initiating omalizumab discontinued treatment over the same time frame. We have identified at-risk groups and modifiable factors that can potentially be targeted to increase adherence to omalizumab with a goal to improve outcomes in these vulnerable patients with asthma.

REFERENCES

- Centers for Disease Control and Prevention. Most recent asthma data (updated May 2018). Available from: https://www.cdc.gov/asthma/most_recent_data.htm. Accessed May 3, 2019.
- Sklout GS, Busse PJ, Braman SS, Kovacs EJ, Dixon AE, Vaz Fragoso CA, et al. An official American Thoracic Society workshop report: evaluation and management of asthma in the elderly. *Ann Am Thoracic Soc* 2016;13:2064-77.
- Yáñez A, Cho S-H, Soriano JB, Rosenwasser LJ, Rodrigo GJ, Rabe KF, et al. Asthma in the elderly: what we know and what we have yet to know. *World Allergy Organ J* 2014;7:1-16.
- Disability Evaluation Under Social Security. 3.00 Respiratory Disorders—Adult. Available from: <https://www.ssa.gov/disability/professionals/bluebook/3.00-Respiratory-Adult.htm#3.02>. Accessed May 3, 2019.
- Hasegawa K, Gibo K, Tsugawa Y, Shimada YJ, Camargo CA Jr. Age-related differences in the rate, timing and diagnosis of 30-day readmissions in hospitalized adults with asthma exacerbation. *Chest* 2016;149:1021-9.
- Tsai C-L, Lee W-Y, Hanania NA, Camargo CA Jr. Age-related differences in clinical outcomes for acute asthma in the United States, 2006-2008. *J Allergy Clin Immunol* 2012;129:1252-1258.e1.
- Tsai C-L, Delclos GL, Huang JS, Hanania NA, Camargo CA Jr. Age-related differences in asthma outcomes in the United States, 1988-2006. *Ann Allergy Asthma Immunol* 2013;110:240-246.e1.
- Porsbjerg C, Menzies-Gow A. Co-morbidities in severe asthma: clinical impact and management. *Respirology* 2017;22:651-61.
- Zeiger RS, Schatz M, Dalal AA, Qian L, Chen W, Ngor EW, et al. Utilization and costs of severe uncontrolled asthma in a managed-care setting. *J Allergy Clin Immunol* 2016;4:120-129.e3.
- Madeo J, Li Z, Frieri M. Asthma in the geriatric population. *Allergy Asthma Proc* 2013;34:427-33.
- Bahadori K, Doyle-Waters MM, Marra C, Lynd L, Alasaly K, Swiston J, et al. Economic burden of asthma: a systematic review. *BMC Pulm Med* 2009;9:24.
- Nunes C, Pereira AM, Morais-Almeida M. Asthma costs and social impact. *Asthma Res Pract* 2017;3:1.
- Centers for Disease Control and Prevention. 2014 Previous most recent asthma data (updated May 2018). Available from: https://www.cdc.gov/asthma/archivedata/2014/2014_data.html. Accessed August 27, 2019.
- Centers for Disease Control and Prevention. 2015 Previous most recent asthma data (updated May 2018). Available from: https://www.cdc.gov/asthma/archivedata/2015/2015_data.html. Accessed August 27, 2019.
- Global Initiative for Asthma. Global strategy for asthma management and prevention (2018 update); 2018. Available from: www.ginasthma.org. Accessed January 17, 2019.
- Rios D, Magasi S, Novak C, Harniss M. Conducting accessible research: including people with disabilities in public health, epidemiological, and outcomes studies. *Am J Public Health* 2016;106:2137-44.
- Spong CY, Bianchi DW. Improving public health requires inclusion of under-represented populations in research. *JAMA* 2018;319:337-8.
- Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343-73.
- US Food and Drug Administration. XOLAIR® (omalizumab). US Prescribing information; 2019. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/103976s5234lbl.pdf. Accessed May 3, 2019.
- European Medicines Agency. XOLAIR® (omalizumab) summary of product characteristics; 2019. Available from: https://www.ema.europa.eu/en/documents/product-information/xolair-epar-product-information_en.pdf. Accessed May 3, 2019.
- Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *J Allergy Clin Immunol* 2001;108:184-90.
- Soler M, Matz J, Townley R, Buhl R, O'Brien J, Fox H, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. *Eur Respir J* 2001;18:254-61.
- Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). *Pediatrics* 2001;108:E36.
- Lanier B, Bridges T, Kulus M, Taylor AF, Berhane I, Vidaurre CF. Omalizumab for the treatment of exacerbations in children with inadequately controlled allergic (IgE-mediated) asthma. *J Allergy Clin Immunol* 2009;124:1210-6.
- Maykut RJ, Kianifard F, Geba GP. Response of older patients with IgE-mediated asthma to omalizumab: a pooled analysis. *J Asthma* 2008;45:173-81.
- Korn S, Schumann C, Kropf C, Stoiber K, Thielen A, Taube C, et al. Effectiveness of omalizumab in patients 50 years and older with severe persistent allergic asthma. *Ann Allergy Asthma Immunol* 2010;105:313-9.
- Adachi M, Kozawa M, Yoshisue H, Lee Milligan K, Nagasaki M, Sasajima T, et al. Real-world safety and efficacy of omalizumab in patients with severe allergic asthma: a long-term post-marketing study in Japan. *Respir Med* 2018;141:56-63.
- Sposato B, Scalese M, Latorre M, Scichilone N, Matucci A, Milanese M, et al. Effects of omalizumab in severe asthmatics across ages: a real life Italian experience. *Respir Med* 2016;119:141-9.
- Tat TS, Cilli A. Evaluation of long-term safety and efficacy of omalizumab in elderly patients with uncontrolled allergic asthma. *Ann Allergy Asthma Immunol* 2016;117:546-9.
- An overview of Medicare. Washington, DC: Henry J. Kaiser Family Foundation; 2019. Available from: <https://www.kff.org/medicare/issue-brief/an-overview-of-medicare/>. Accessed May 3, 2019.
- Peterson AM, Nau DP, Cramer JA, Benner J, Gwady-Sridhar F, Nichol M. A checklist for medication compliance and persistence studies using retrospective databases. *Value Health* 2007;10:3-12.
- Vrijens B, Dima AL, Van Ganse E, van Boven JFM, Eakin MN, Foster JM, et al. What we mean when we talk about adherence in respiratory medicine. *J Allergy Clin Immunol Pract* 2016;4:802-12.
- Robst J, Levy JM, Ingber MJ. Diagnosis-based risk adjustment for Medicare prescription drug plan payments. *Health Care Financ Rev* 2007;28:15-30.
- Donohue JM, Marcum ZA, Gellad WF, Lave JR, Men A, Hanlon JT. Medicare Part D and potentially inappropriate medication use in the elderly. *Am J Manag Care* 2012;18:e315-22.
- Doshi JA, Li P, Puig A. Impact of the Medicare Modernization Act of 2003 on utilization and spending for Medicare part B-covered biologics in rheumatoid arthritis. *Arthritis Care Res* 2010;62:354-61.
- Li P, McElligott S, Bergquist H, Schwartz J, Doshi JA. Effect of the Medicare part D coverage gap on medication use among patients with hypertension and hyperlipidemia. *Ann Intern Med* 2012;156:776-84.
- Vandenbroucke JP, von Elm E, Altman DG, Gotszke PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology* 2007;18:805-35.
- Ke X, Kavati A, Wertz D, Huang Q, Wang L, Willey VJ, et al. Real-world clinical characteristics, treatment patterns, and exacerbations in US patients with asthma newly treated with omalizumab. *Clin Ther* 2018;40:1140-1158.e4.
- Bozek A, Jarzab J. Adherence to asthma therapy in elderly patients. *J Asthma* 2010;47:162-5.
- Krauskopf KA, Sofianou A, Goel MS, Wolf MS, Wilson EAH, Martynenko ME, et al. Depressive symptoms, low adherence, and poor asthma outcomes in the elderly. *J Asthma* 2013;50:260-6.
- Soones TN, Lin JL, Wolf MS, O'Connor R, Martynenko M, Wisnivesky JP, et al. Pathways linking health literacy, health beliefs, and cognition to medication adherence in older adults with asthma. *J Allergy Clin Immunol* 2017;139:804-9.
- Cubanski J, Neuman T, Damico A. Medicare's role for people under age 65 with disabilities. Washington, DC: Henry J. Kaiser Family Foundation; 2016. Available from: <https://www.kff.org/medicare/issue-brief/medicares-role-for-people-under-age-65-with-disabilities/>. Accessed May 3, 2019.
- Broder MS, Chang EY, Ory C, Kamath T, Sapra S. Adherence and persistence with omalizumab and fluticasone/salmeterol within a managed care population. *Allergy Asthma Proc* 2009;30:148-57.
- Janson SL, Solari PG, Trzaskoma B, Chen H, Haselkorn T, Zazzali JL. Omalizumab adherence in an observational study of patients with moderate to severe allergic asthma. *Ann Allergy Asthma Immunol* 2015;114:516-521.e2.
- Mathes T, Jaschinski T, Pieper D. Adherence influencing factors—a systematic review of systematic reviews. *Arch Public Health* 2014;72:37.
- Doshi JA, Hu T, Li P, Pettit AR, Yu X, Blum M. Specialty tier-level cost sharing and biologic agent use in the Medicare part D initial coverage period among beneficiaries with rheumatoid arthritis. *Arthritis Care Res* 2016;68:1624-30.
- Doshi JA, Li P, Pettit AR, Dougherty JS, Flint A, Ladage VP. Reducing out-of-pocket cost barriers to specialty drug use under Medicare Part D: addressing the problem of “too much too soon.” *Am J Manag Care* 2017;23:S39-45.
- Doshi JA, Takeshita J, Pinto L, Li P, Yu X, Rao P, et al. Biologic therapy adherence, discontinuation, switching, and restarting among patients with psoriasis in the US Medicare population. *J Am Acad Dermatol* 2016;74:1057-1065.e4.

49. Li P, Hu T, Yu X, Chahin S, Dahodwala N, Blum M, et al. Impact of cost-sharing increases on continuity of specialty drug use: a quasi-experimental study. *Health Serv Res* 2018;53:2735-57.
50. Takeshita J, Gelfand JM, Li P, Pinto L, Yu X, Rao P, et al. Psoriasis in the US Medicare population: prevalence, treatment, and factors associated with biologic use. *J Invest Dermatol* 2015;135:2955-63.
51. Vignola AM, Humbert M, Bousquet J, Boulet L-P, Hedgecock S, Blogg M, et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. *Allergy* 2004;59:709-17.
52. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000;160:2101-7.
53. Grenard JL, Munjas BA, Adams JL, Suttorp M, Maglione M, McGlynn EA, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. *J Gen Intern Med* 2011;26:1175-82.

ONLINE REPOSITORY**Appendix E1. Adherence calculation for omalizumab injections covered under Medicare Part B (medical benefit)**

Adherence was captured using the PDC measure, which has a range from 0 to 1. PDC is widely used to evaluate medication adherence in chronic disease. It is calculated as the number of days covered with omalizumab divided by a fixed time interval (ie, 365 days) from the omalizumab initiation date.^{E1} For example, a patient with omalizumab coverage available for 292 days during the 365-day post-index date period would have a PDC of $292/365 = 0.80$. We applied the frequently used threshold of PDC greater than or equal to 0.80 to classify patients as adherent.^{E2-E5} A sensitivity analysis using adherence thresholds of PDC greater than or equal to 0.70 and greater than or equal to 0.90 was also conducted.

Prescription fill date and days' supply information were used from the pharmacy claims to calculate the PDC for patients receiving omalizumab under the Part D prescription drug benefit. For patients receiving omalizumab under the Medicare Part B medical benefit (as would be expected of most patients

given that omalizumab is a physician-administered drug), we did not have access to days' supply or dosing information because this is not contained in Medicare Part B claims. Although omalizumab has 2 possible dosing frequencies (every 2 weeks or every 4 weeks), we opted to assign a 28 days' supply (4 weeks) to all omalizumab Part B claims because this would, at worst, result in an overestimate of adherence for some patients. For example, if both patient A and patient B received omalizumab, that provided coverage for 336 days over the 365-day follow-up. If patient A received 24 administrations of omalizumab every 14 days (ie, 336 days covered) and patient B had 12 administrations of omalizumab every 28 days (ie, 336 days covered), and we assigned 14 days' supply to all omalizumab claims, patient A would have the correct PDC ($[14 \times 24]/365 = 0.92$), but we would substantially underestimate patient B's PDC ($[14 \times 12]/365 = 0.46$). Alternatively, if we assign 28 days' supply for both patients, patient B would have the correct PDC ($[28 \times 12]/365 = 0.92$) and we would slightly overestimate the PDC for patient A ($[336 + 14]/365 = 0.96$; instead of 0.92) given that Part B PDC calculation does not carry over overlap days' supply.

SUPPLEMENTARY DATA

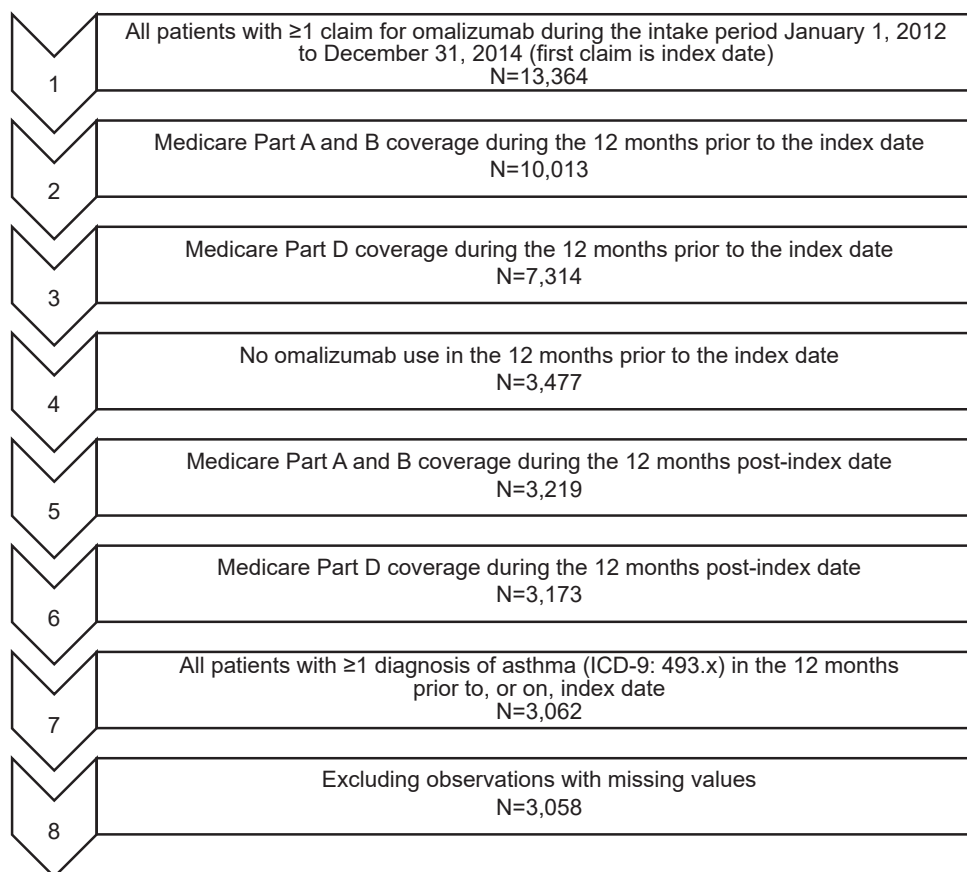


FIGURE E1. Sample selection criteria and sample attrition. *ICD-9, International Classification of Diseases, Ninth Revision.*

TABLE E1. Cox regression analysis of factors associated with time to omalizumab discontinuation

Characteristic	Hazard ratio (95% CI)
Age category (y) (reference age ≥ 80 y)	
<65	0.93 (0.71-1.23)
65-69	0.74 (0.57-0.97)
70-74	0.70 (0.53-0.93)
75-79	0.91 (0.68-1.22)
Male sex (reference female)	0.99 (0.87-1.13)
Race (reference white)	
Black	0.94 (0.78-1.12)
Hispanic	1.29 (0.95-1.77)
Other/unknown	0.86 (0.63-1.17)
Resource use in the 12 mo before the index date with primary asthma diagnosis	
No. of ED visits	0.99 (0.95-1.03)
No. of evaluation and management physician visits	0.97 (0.95-0.99)
No. of hospitalizations	1.05 (0.96-1.15)
RxHCC score*	0.98 (0.81-1.19)
Comorbid conditions†	
Anxiety or depression	1.11 (0.97-1.26)
Bronchitis	0.87 (0.60-1.27)
Chronic obstructive pulmonary disease or emphysema	0.97 (0.85-1.11)
LRTI excluding pneumonia	1.07 (0.74-1.56)
Pneumonia	1.08 (0.93-1.26)
Rhinitis	0.86 (0.75-0.98)
Sinusitis	1.01 (0.87-1.17)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	1.02 (0.85-1.21)
Use of asthma medication in the 12 mo before the index date‡	
ICS + LABA	0.90 (0.78-1.03)
ICS	0.88 (0.77-1.00)
LAMA	0.96 (0.84-1.10)
LTRA	0.86 (0.75-0.98)
SABA + SAMA	1.00 (0.87-1.16)
SABA	0.94 (0.80-1.10)
SAMA	0.93 (0.74-1.16)
Oral systemic corticosteroid claims	1.00 (0.99-1.02)
No. of 30-d supply equivalent prescriptions for nonasthma medications*	1.01 (0.99-1.02)
Part D drug benefit type (reference enhanced alternative)	
Defined standard	0.83 (0.57-1.19)
Actuarially equivalent standard	0.95 (0.81-1.12)
Basic alternative	0.91 (0.75-1.10)
Part D LIS status “none” (reference full-/partial-year LIS or plan switch)	0.70 (0.58-0.85)
Received omalizumab under Part D§	1.12 (0.89-1.41)
County-level characteristics*	
Income, per capita, \$10,000s	1.03 (0.98-1.08)
Allergists/immunologists per 10,000 residents	1.00 (0.99-1.01)
Pulmonologists per 10,000 residents	1.00 (1.00-1.01)

(continued)

TABLE E1. (Continued)

Characteristic	Hazard ratio (95% CI)
Census region (reference Northeast)	
Midwest	1.04 (0.84-1.27)
South	1.13 (0.93-1.38)
West	1.21 (0.99-1.48)
Year of index date (reference 2012)	
2013	0.94 (0.80-1.10)
2014	0.82 (0.70-0.97)
Season of index date (reference summer)	
Fall	0.89 (0.76-1.05)
Winter	0.81 (0.68-0.96)
Spring	0.89 (0.76-1.04)

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

Hazard ratios were adjusted for the covariates listed. Reference indicates the reference group against which other factors within that group are compared.

*Hazard ratios indicate the odds of discontinuing omalizumab at each point in time if the mean value increases by 1.

†Reference group contains those patients without the asthma-related comorbidity in the preindex period.

‡Reference group contains those patients not using the specified drug in the preindex period.

§Reference group contains those patients who did not receive omalizumab under Part D.

TABLE E2. Multinomial logistic regression results for factors associated with augmentation, switching, restart, or other discontinuation of omalizumab treatment (relative to nondiscontinuation)

Factor	OR (95% CI)			
	Augmentation*	Switch†	Restart‡	Other discontinuation§
Age category (y) (reference age ≥80 y)				
<65	1.24 (0.75-2.03)	0.91 (0.48-0.72)	0.95 (0.42-2.13)	0.96 (0.61-1.51)
65-69	1.01 (0.63-1.61)	0.79 (0.43-1.46)	0.65 (0.30-1.44)	0.61 (0.39-0.95)
70-74	1.07 (0.67-1.71)	0.77 (0.41-1.43)	0.23 (0.09-0.58)	0.69 (0.44-1.07)
75-79	0.99 (0.59-1.66)	0.94 (0.48-1.83)	0.55 (0.22-1.38)	0.87 (0.54-1.41)
Male sex (reference female)	0.94 (0.76-1.17)	1.01 (0.75-1.35)	0.79 (0.52-1.20)	0.99 (0.80-1.21)
Race (reference white)				
Black	0.90 (0.66-1.24)	0.89 (0.59-1.35)	1.48 (0.90-2.45)	0.82 (0.61-1.10)
Hispanic	1.64 (0.84-3.20)	1.99 (0.93-4.26)	1.88 (0.70-5.05)	1.85 (1.03-3.33)
Other/unknown	0.80 (0.48-1.34)	0.71 (0.36-1.42)	0.92 (0.37-2.29)	0.79 (0.49-1.28)
Resource use in the 12 mo before the index date with primary asthma diagnosis				
No. of ED visits	0.93 (0.85-1.02)	0.95 (0.85-1.06)	0.81 (0.67-0.98)	0.99 (0.93-1.06)
No. of evaluation and management physician visits	1.00 (0.97-1.03)	0.97 (0.93-1.01)	0.95 (0.89-1.01)	0.96 (0.93-0.99)
No. of hospitalizations	1.21 (1.00-1.45)	1.21 (0.96-1.51)	1.13 (0.79-1.62)	1.09 (0.93-1.28)
RxHCC score	1.14 (0.83-1.58)	0.94 (0.61-1.44)	0.75 (0.41-1.38)	1.09 (0.80-1.49)
Comorbid conditions¶				
Anxiety or depression	0.91 (0.72-1.14)	1.39 (1.03-1.86)	0.81 (0.53-1.22)	1.07 (0.86-1.32)
Bronchitis	0.88 (0.46-1.69)	1.55 (0.68-3.56)	0.31 (0.11-0.85)	0.79 (0.42-1.46)
Chronic obstructive pulmonary disease or emphysema	1.10 (0.88-1.38)	1.25 (0.92-1.68)	0.77 (0.51-1.16)	0.94 (0.76-1.17)
LRTI excluding pneumonia	1.13 (0.59-2.17)	0.71 (0.31-1.63)	2.39 (0.89-6.42)	1.11 (0.60-2.05)
Pneumonia	0.78 (0.61-1.02)	0.93 (0.66-1.30)	1.36 (0.87-2.13)	1.02 (0.80-1.29)
Rhinitis	1.09 (0.86-1.37)	0.93 (0.69-1.25)	0.71 (0.47-1.05)	0.84 (0.67-1.04)
Sinusitis	1.04 (0.81-1.33)	1.36 (0.97-1.91)	0.95 (0.62-1.47)	0.90 (0.71-1.14)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	1.02 (0.76-1.38)	0.76 (0.51-1.14)	2.20 (1.26-3.85)	1.03 (0.78-1.37)
Use of asthma medication in the 12 mo before the index date#				
ICS + LABA	0.60 (0.48-0.75)	0.62 (0.46-0.84)	0.88 (0.56-1.37)	0.76 (0.61-0.96)
ICS	0.76 (0.61-0.94)	0.70 (0.52-0.94)	1.16 (0.79-1.71)	0.75 (0.61-0.92)
LAMA	0.88 (0.70-1.11)	0.91 (0.67-1.23)	1.00 (0.66-1.51)	0.95 (0.77-1.18)
LTRA	0.77 (0.62-0.96)	0.58 (0.44-0.77)	0.68 (0.46-1.03)	0.86 (0.69-1.08)
SABA + SAMA	1.16 (0.92-1.47)	0.82 (0.59-1.14)	1.43 (0.95-2.15)	1.10 (0.87-1.37)
SABA	0.49 (0.38-0.63)	0.56 (0.40-0.79)	0.80 (0.48-1.33)	0.73 (0.56-0.95)
SAMA	0.84 (0.58-1.23)	0.78 (0.47-1.30)	1.27 (0.70-2.32)	0.77 (0.54-1.10)
Oral systemic corticosteroid claims	0.98 (0.95-1.00)	0.98 (0.95-1.02)	1.01 (0.97-1.06)	1.00 (0.98-1.03)
No. of 30-d supply equivalent prescriptions for nonasthma medications	1.01 (0.99-1.04)	1.02 (0.99-1.05)	1.00 (0.96-1.05)	1.01 (0.99-1.04)
Part D drug benefit type (reference enhanced alternative)				
Defined standard	1.65 (0.89-3.05)	1.29 (0.60-2.76)	0.27 (0.06-1.23)	1.04 (0.55-1.93)
Actuarially equivalent standard	0.97 (0.74-1.28)	0.91 (0.64-1.31)	0.64 (0.39-1.05)	1.04 (0.80-1.36)
Basic alternative	0.91 (0.67-1.22)	0.74 (0.49-1.12)	0.65 (0.36-1.17)	0.95 (0.71-1.28)
Part D LIS status “none” (reference full-/partial-year LIS or plan switch)	1.05 (0.77-1.44)	0.61 (0.40-0.91)	0.46 (0.26-0.83)	0.74 (0.55-1.00)
Received omalizumab under Part D**	0.66 (0.41-1.05)	0.89 (0.51-1.53)	1.49 (0.79-2.82)	0.98 (0.66-1.44)
County-level characteristics				
Income, per capita, \$10,000s	1.04 (0.96-1.13)	1.15 (1.03-1.28)	1.07 (0.92-1.25)	1.03 (0.95-1.11)
Allergists/immunologists per 10,000 residents	1.00 (0.99-1.02)	0.98 (0.96-1.00)	1.01 (0.98-1.03)	1.00 (0.98-1.01)
Pulmonologists per 10,000 residents	1.00 (0.99-1.01)	1.01 (1.00-1.02)	1.00 (0.99-1.01)	1.00 (1.00-1.01)
Census region (reference Northeast)				
Midwest	0.87 (0.62-1.22)	1.34 (0.86-2.09)	0.72 (0.39-1.32)	1.01 (0.73-1.41)
South	1.07 (0.78-1.48)	1.30 (0.84-2.01)	0.89 (0.51-1.56)	1.32 (0.96-1.80)
West	0.96 (0.68-1.35)	1.29 (0.82-2.03)	0.84 (0.45-1.57)	1.41 (1.01-1.96)
Year of index date (reference 2012)				
2013	0.90 (0.68-1.18)	0.80 (0.56-1.14)	0.77 (0.48-1.25)	0.93 (0.72-1.20)
2014	0.80 (0.61-1.06)	0.70 (0.49-1.00)	0.66 (0.40-1.08)	0.72 (0.55-0.93)

(continued)

TABLE E2. (Continued)

Factor	OR (95% CI)			
	Augmentation*	Switch†	Restart‡	Other discontinuation§
Season of index date (reference summer)				
Fall	1.02 (0.78-1.33)	0.95 (0.67-1.33)	0.66 (0.40-1.08)	0.86 (0.66-1.11)
Winter	0.90 (0.68-1.20)	0.70 (0.48-1.02)	0.62 (0.37-1.04)	0.79 (0.60-1.04)
Spring	1.03 (0.79-1.36)	0.78 (0.54-1.12)	0.73 (0.45-1.19)	1.00 (0.77-1.29)

ORs were adjusted for the covariates listed. Reference indicates the reference group against which other factors within that group are compared.

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

*Patients received add-on of another asthma medication during continuous use of omalizumab.

†Patients started treatment with a new drug within 90 d of discontinuing the index biologic.

‡Patients used a new drug or resumed omalizumab therapy after a gap of ≥ 90 consecutive days; restart occurred within 1 y after the index date.

§Patients did not resume treatment before the end of the follow-up period.

||ORs indicate how odds of the outcome change if the mean value increases by 1.

¶Reference group contains those patients without the asthma-related comorbidity in the preindex period.

#Reference group contains those patients not using the specified drug in the preindex period.

**Reference group contains those patients who did not receive omalizumab under Part D.

TABLE E3. Factors associated with omalizumab discontinuation and adherence during the 12-mo follow-up by age group (<65 y or ≥65 y)

Factor	Age <65 y, OR (95% CI)		Age ≥65 y, OR (95% CI)	
	Discontinuation	Adherence	Discontinuation	Adherence
Age category (y)				
<45	1.66 (1.22-2.27)	0.77 (0.56-1.05)	—	—
45-54	1.24 (0.93-1.65)	0.95 (0.71-1.26)	—	—
55-64	Reference	Reference	—	—
65-69	—	—	0.67 (0.47-0.97)	1.39 (0.97-2.01)
70-74	—	—	0.61 (0.42-0.88)	1.50 (1.04-2.16)
75-79	—	—	0.84 (0.56-1.24)	0.99 (0.67-1.47)
≥80	—	—	Reference	Reference
Male sex (reference female)	0.70 (0.53-0.92)	1.53 (1.17-2.02)	1.23 (0.99-1.54)	1.03 (0.83-1.29)
Race (reference white)				
Black	0.96 (0.72-1.29)	1.25 (0.94-1.68)	0.99 (0.63-1.55)	0.91 (0.58-1.41)
Hispanic	1.50 (0.85-2.65)	0.87 (0.49-1.53)	1.95 (0.86-4.43)	0.64 (0.27-1.50)
Resource use in the 12 mo before the index date with primary asthma diagnosis				
No. of ED visits	0.98 (0.92-1.04)	1.04 (0.98-1.11)	0.83 (0.69-1.00)	1.19 (0.99-1.44)
No. of evaluation and management physician visits	0.95 (0.91-0.99)	1.02 (0.98-1.06)	0.96 (0.93-1.00)	1.04 (1.00-1.07)
No. of hospitalizations	1.09 (0.94-1.27)	0.82 (0.70-0.96)	1.07 (0.78-1.46)	0.98 (0.72-1.34)
RxHCC score*	1.08 (0.77-1.52)	1.02 (0.73-1.43)	0.83 (0.57-1.22)	1.20 (0.82-1.76)
Comorbid conditions†				
Anxiety or depression	1.25 (0.97-1.62)	0.75 (0.58-0.97)	1.07 (0.84-1.36)	0.94 (0.74-1.20)
Bronchitis	0.82 (0.35-1.91)	1.30 (0.56-3.02)	0.81 (0.44-1.49)	1.84 (0.99-3.45)
Chronic obstructive pulmonary disease or emphysema	1.17 (0.90-1.53)	1.03 (0.79-1.34)	0.88 (0.69-1.12)	1.07 (0.84-1.36)
LRTI excluding pneumonia	1.11 (0.48-2.57)	0.85 (0.37-1.95)	1.14 (0.62-2.12)	0.61 (0.33-1.15)
Pneumonia	1.02 (0.75-1.37)	0.94 (0.69-1.27)	1.19 (0.91-1.54)	0.88 (0.68-1.15)
Rhinitis	0.89 (0.68-1.16)	1.13 (0.87-1.48)	0.78 (0.62-0.98)	1.26 (1.00-1.59)
Sinusitis	0.92 (0.69-1.23)	0.90 (0.68-1.20)	1.01 (0.78-1.31)	1.14 (0.88-1.47)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	1.14 (0.80-1.62)	1.02 (0.72-1.46)	0.97 (0.71-1.32)	0.94 (0.69-1.28)
Use of asthma medication in the 12 mo before the index date‡				
ICS + LABA	0.93 (0.69-1.26)	1.17 (0.87-1.58)	0.90 (0.71-1.13)	1.34 (1.06-1.69)
ICS	0.88 (0.68-1.14)	1.16 (0.90-1.50)	0.85 (0.68-1.02)	1.16 (0.93-1.46)
LAMA	0.99 (0.76-1.28)	1.10 (0.84-1.43)	1.01 (0.79-1.29)	0.95 (0.74-1.21)
LTRA	0.78 (0.59-1.03)	1.16 (0.88-1.54)	0.84 (0.67-1.05)	1.22 (0.98-1.52)
SABA + SAMA	0.93 (0.71-1.21)	1.12 (0.86-1.46)	1.11 (0.86-1.44)	1.01 (0.78-1.31)
SABA	0.82 (0.57-1.17)	1.20 (0.83-1.73)	0.98 (0.76-1.26)	0.86 (0.67-1.11)
SAMA	0.81 (0.53-1.24)	0.98 (0.64-1.49)	0.90 (0.61-1.34)	0.93 (0.63-1.38)
Oral systemic corticosteroid claims*	1.02 (0.99-1.05)	0.98 (0.96-1.01)	0.99 (0.96-1.02)	1.02 (0.99-1.06)
No. of 30-d supply equivalent prescriptions for nonasthma medications*	1.00 (0.97-1.02)	1.01 (0.98-1.04)	1.03 (1.00-1.06)	0.97 (0.95-1.00)
Part D drug benefit type (reference enhanced alternative)				
Defined standard	1.11 (0.60-2.03)	1.50 (0.81-2.77)	0.64 (0.24-1.69)	1.14 (0.43-3.00)
Actuarially equivalent standard	1.43 (1.01-2.02)	0.83 (0.59-1.17)	0.75 (0.56-1.00)	1.21 (0.91-1.62)
Basic alternative	1.44 (0.93-2.23)	0.96 (0.62-1.48)	0.72 (0.53-0.97)	1.15 (0.86-1.55)
Part D LIS status “none” (reference full-/partial-year LIS or plan switch)	1.20 (0.79-1.82)	1.25 (0.82-1.90)	0.52 (0.38-0.71)	1.54 (1.13-2.10)
Received omalizumab under Part D§	0.92 (0.60-1.41)	0.53 (0.34-0.81)	1.25 (0.78-2.01)	0.29 (0.18-0.48)
County-level characteristics*				
Income, per capita, \$10,000s	1.05 (0.94-1.16)	0.95 (0.86-1.06)	1.06 (0.98-1.15)	0.93 (0.85-1.01)
Allergists/immunologists per 10,000 residents	1.01 (0.99-1.03)	0.99 (0.97-1.01)	0.98 (0.97-1.00)	1.01 (0.99-1.03)
Pulmonologists per 10,000 residents	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.01 (1.00-1.01)	1.00 (0.99-1.00)
Census region (reference Northeast)				
Midwest	0.90 (0.62-1.30)	0.94 (0.65-1.36)	1.34 (0.91-1.97)	0.86 (0.59-1.25)
South	1.06 (0.74-1.53)	1.06 (0.74-1.53)	1.40 (0.98-2.01)	0.91 (0.64-1.29)
West	1.12 (0.75-1.68)	0.72 (0.48-1.08)	1.37 (0.94-1.98)	1.02 (0.71-1.47)
Year of index date (reference 2012)				
2013	0.85 (0.63-1.15)	1.23 (0.91-1.67)	0.93 (0.70-1.24)	0.98 (0.74-1.32)
2014	0.77 (0.57-1.06)	1.19 (0.87-1.63)	0.72 (0.53-0.96)	1.09 (0.82-1.47)

(continued)

TABLE E3. (Continued)

Factor	Age <65 y, OR (95% CI)		Age ≥65 y, OR (95% CI)	
	Discontinuation	Adherence	Discontinuation	Adherence
Season of index date (reference summer)				
Fall	0.93 (0.68-1.28)	1.02 (0.75-1.40)	0.77 (0.58-1.02)	0.99 (0.75-1.31)
Winter	0.77 (0.55-1.07)	1.05 (0.75-1.46)	0.77 (0.57-1.03)	1.33 (0.98-1.79)
Spring	0.84 (0.61-1.14)	1.38 (1.01-1.89)	0.92 (0.69-1.22)	0.99 (0.75-1.32)

ORs were adjusted for the covariates listed. Reference indicates the reference group against which other factors within that group are compared.

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

*ORs indicate how odds of the outcome change if the mean value increases by 1.

†Reference group contains those patients without the asthma-related comorbidity in the preindex period.

‡Reference group contains those patients not using the specified drug in the preindex period.

§Reference group contains those patients who did not receive omalizumab under Part D.

TABLE E4. Factors associated with omalizumab discontinuation and adherence during the 12-mo follow-up, excluding patients with urticaria

Factor	OR (95% CI)	
	Discontinuation	Adherence
Age category (y) (reference age ≥ 80 y)		
<65	1.02 (0.69-1.50)	0.88 (0.60-1.29)
65-69	0.66 (0.46-0.95)	1.43 (0.99-2.08)
70-74	0.64 (0.44-0.93)	1.42 (0.97-2.07)
75-79	0.86 (0.57-1.29)	0.97 (0.64-1.46)
Male sex (reference female)	1.03 (0.86-1.22)	1.15 (0.97-1.38)
Race (reference white)		
Black	0.97 (0.75-1.24)	1.11 (0.87-1.43)
Hispanic	1.44 (0.88-2.36)	0.98 (0.60-1.61)
Other/unknown	0.93 (0.61-1.41)	1.38 (0.90-2.12)
Resource use in the 12 mo before the index date with primary asthma diagnosis		
No. of ED visits	0.99 (0.93-1.05)	1.01 (0.96-1.08)
No. of evaluation and management physician visits	0.98 (0.95-1.00)	1.01 (0.99-1.04)
No. of hospitalizations	1.03 (0.90-1.18)	0.92 (0.80-1.05)
RxHCC score*	1.00 (0.77-1.31)	1.01 (0.77-1.32)
Comorbid conditions†		
Anxiety or depression	1.17 (0.97-1.41)	0.83 (0.69-1.00)
Bronchitis	0.65 (0.39-1.10)	1.89 (1.12-3.21)
Chronic obstructive pulmonary disease or emphysema	1.00 (0.83-1.21)	1.05 (0.87-1.27)
LRTI excluding pneumonia	1.36 (0.81-2.28)	0.61 (0.36-1.03)
Pneumonia	1.10 (0.90-1.35)	0.94 (0.76-1.15)
Rhinitis	0.84 (0.69-1.00)	1.16 (0.97-1.40)
Sinusitis	1.01 (0.83-1.24)	0.99 (0.81-1.21)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	1.03 (0.81-1.32)	0.97 (0.76-1.25)
Use of asthma medication in the 12 mo before the index date‡		
ICS + LABA	0.94 (0.77-1.14)	1.21 (1.00-1.48)
ICS	0.84 (0.70-1.00)	1.16 (0.97-1.38)
LAMA	0.99 (0.83-1.19)	1.01 (0.84-1.22)
LTRA	0.78 (0.65-0.94)	1.25 (1.04-1.50)
SABA + SAMA	0.99 (0.82-1.20)	1.06 (0.88-1.28)
SABA	0.94 (0.75-1.17)	0.98 (0.78-1.22)
SAMA	0.78 (0.58-1.06)	0.96 (0.71-1.28)
Oral systemic corticosteroid claims*	1.00 (0.98-1.02)	1.01 (0.99-1.04)
No. of 30-d supply equivalent prescriptions for nonasthma medications*	1.01 (0.99-1.03)	1.00 (0.98-1.02)
Part D drug benefit type (reference enhanced alternative)		
Defined standard	0.68 (0.40-1.15)	1.84 (1.08-3.14)
Actuarially equivalent standard	0.97 (0.77-1.22)	1.02 (0.81-1.28)
Basic alternative	0.96 (0.75-1.25)	1.03 (0.80-1.33)
Part D LIS status "none" (reference full-/partial-year LIS or plan switch)	0.70 (0.54-0.91)	1.50 (1.16-1.93)

(continued)

TABLE E4. (Continued)

Factor	OR (95% CI)	
	Discontinuation	Adherence
Received omalizumab under Part D§	1.33 (0.95-1.86)	0.37 (0.26-0.52)
County-level characteristics*		
Income, per capita, \$10,000s	1.04 (0.97-1.11)	0.94 (0.88-1.01)
Allergists/immunologists per 10,000 residents	1.00 (0.99-1.01)	1.00 (0.98-1.01)
Pulmonologists per 10,000 residents	1.00 (1.00-1.01)	1.00 (0.99-1.01)
Census region (reference Northeast)		
Midwest	1.09 (0.83-1.45)	0.96 (0.73-1.27)
South	1.25 (0.96-1.63)	1.02 (0.78-1.32)
West	1.30 (0.97-1.73)	0.93 (0.70-1.24)
Year of index date (reference 2012)		
2013	0.93 (0.75-1.15)	1.08 (0.87-1.35)
2014	0.77 (0.62-0.96)	1.11 (0.89-1.39)
Season of index date (reference summer)		
Fall	0.88 (0.70-1.10)	0.97 (0.78-1.21)
Winter	0.80 (0.63-1.01)	1.18 (0.93-1.49)
Spring	0.92 (0.74-1.14)	1.08 (0.86-1.35)

ORs were adjusted for the covariates listed. Reference indicates the reference group against which other factors within that group are compared.

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

*ORs indicate how odds of the outcome change if the mean value increases by 1.

†Reference group contains those patients without the asthma-related comorbidity in the preindex period.

‡Reference group contains those patients not using the specified drug in the preindex period.

§Reference group contains those patients who did not receive omalizumab under Part D.

TABLE E5. Sensitivity analysis based on the use of alternative PDC cutoff points to define adherence

Factor	OR (95% CI)	
	Adherence (PDC ≥ 0.70)	Adherence (PDC ≥ 0.90)
Age category (y) (reference age ≥ 80 y)		
<65	0.95 (0.65-1.39)	0.96 (0.67-1.39)
65-69	1.37 (0.95-1.98)	1.25 (0.88-1.77)
70-74	1.46 (1.00-2.12)	1.41 (0.99-2.00)
75-79	1.03 (0.69-1.54)	0.83 (0.57-1.22)
Male sex (reference female)	1.13 (0.95-1.34)	1.31 (1.11-1.55)
Race (reference white)		
Black	1.03 (0.81-1.31)	1.02 (0.81-1.29)
Hispanic	0.72 (0.46-1.15)	0.54 (0.33-0.88)
Other/unknown	1.30 (0.87-1.95)	1.17 (0.80-1.71)
Resource use in the 12 mo before the index date with primary asthma diagnosis		
No. of ED visits	1.04 (0.98-1.10)	1.00 (0.95-1.05)
No. of evaluation and management physician visits	1.04 (1.01-1.07)	1.02 (1.00-1.05)
No. of hospitalizations	0.88 (0.77-1.01)	0.93 (0.82-1.05)
RxHCC score*	1.14 (0.88-1.47)	1.11 (0.87-1.41)
Comorbid conditions†		
Anxiety or depression	0.80 (0.67-0.95)	0.90 (0.76-1.07)
Bronchitis	1.20 (0.73-1.99)	1.54 (0.95-2.50)
Chronic obstructive pulmonary disease or emphysema	1.05 (0.88-1.26)	1.05 (0.89-1.25)
LRTI excluding pneumonia	0.89 (0.54-1.48)	0.73 (0.45-1.18)
Pneumonia	0.93 (0.76-1.14)	0.99 (0.82-1.20)
Rhinitis	1.26 (1.06-1.51)	1.17 (0.99-1.39)
Sinusitis	0.97 (0.79-1.18)	0.99 (0.82-1.19)
Upper respiratory tract infection, laryngitis, or nasopharyngitis	1.05 (0.83-1.33)	0.94 (0.75-1.17)
Use of asthma medication in the 12 mo before the index date‡		
ICS + LABA	1.16 (0.96-1.40)	1.33 (1.12-1.59)
ICS	1.21 (1.02-1.44)	1.15 (0.98-1.35)
LAMA	0.96 (0.80-1.15)	0.89 (0.75-1.06)
LTRA	1.16 (0.97-1.39)	1.19 (1.01-1.41)
SABA + SAMA	1.07 (0.89-1.29)	1.08 (0.90-1.28)
SABA	1.10 (0.89-1.36)	1.24 (1.02-1.51)
SAMA	1.05 (0.78-1.40)	0.86 (0.65-1.13)
Oral systemic corticosteroid claims*	1.00 (0.98-1.02)	1.01 (0.99-1.03)
No. of 30-d supply equivalent prescriptions for nonasthma medications*	0.99 (0.98-1.01)	0.99 (0.98-1.01)
Part D drug benefit type (reference enhanced alternative)		
Defined standard	1.56 (0.95-2.58)	1.41 (0.88-2.27)
Actuarially equivalent standard	1.01 (0.82-1.26)	1.07 (0.87-1.31)
Basic alternative	1.07 (0.84-1.37)	1.06 (0.84-1.34)
Part D LIS status “none” (reference full-/partial-year LIS or plan switch)	1.57 (1.23-2.01)	1.43 (1.41-1.81)

(continued)

TABLE E5. (Continued)

Factor	OR (95% CI)	
	Adherence (PDC ≥ 0.70)	Adherence (PDC ≥ 0.90)
Received omalizumab under Part D§	0.53 (0.39-0.73)	0.29 (0.20-0.41)
County-level characteristics*		
Income, per capita, \$10,000s	0.94 (0.88-1.00)	0.92 (0.87-0.98)
Allergists/immunologists per 10,000 residents	1.01 (1.00-1.02)	1.00 (0.99-1.02)
Pulmonologists per 10,000 residents	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Census region (reference Northeast)		
Midwest	0.90 (0.69-1.18)	0.92 (0.71-1.18)
South	0.95 (0.74-1.23)	1.02 (0.80-1.30)
West	0.81 (0.62-1.06)	0.85 (0.66-1.10)
Year of index date (reference 2012)		
2013	1.05 (0.85-1.30)	1.07 (0.87-1.30)
2014	1.11 (0.90-1.38)	1.09 (0.89-1.34)
Season of index date (reference summer)		
Fall	1.03 (0.83-1.27)	0.98 (0.80-1.21)
Winter	1.23 (0.98-1.55)	1.17 (0.95-1.45)
Spring	1.18 (0.95-1.46)	1.08 (0.88-1.33)

ORs were adjusted for the covariates listed. Reference indicates the reference group against which other factors within that group are compared.

ED, Emergency department; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; LRTI, lower respiratory tract infection; LTRA, leukotriene receptor antagonist; RxHCC, prescription drug hierarchical condition category; SABA, short-acting β_2 agonist; SAMA, short-acting muscarinic antagonist.

*ORs indicate how odds of the outcome change if the mean value increases by 1.

†Reference group contains those patients without the asthma-related comorbidity in the preindex period.

‡Reference group contains those patients not using the specified drug in the preindex period.

§Reference group contains those patients who did not receive omalizumab under Part D.

REFERENCES

- E1. Peterson AM, Nau DP, Cramer JA, Benner J, Gwadry-Sridhar F, Nichol M. A checklist for medication compliance and persistence studies using retrospective databases. *Value Health* 2007;10:3-12.
- E2. Lafeuille MH, Gravel J, Zhang J, Gorsh B, Figliomeni M, Lefebvre P. Association between consistent omalizumab treatment and asthma control. *J Allergy Clin Immunol Pract* 2013;1:51-7.
- E3. Lauffenburger JC, Franklin JM, Krumme AA, Shrank WH, Matlin OS, Spettell CM, et al. Predicting adherence to chronic disease medications in patients with long-term initial medication fills using indicators of clinical events and health behaviors. *J Manag Care Spec Pharm* 2018;24:469-77.
- E4. Center for Medicare & Medicaid Services. Medicare 2019 Part C & D star ratings technical notes; 2019. Available from: <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/Downloads/2019-Technical-Notes-preview-2.pdf>. Accessed July 12, 2019.
- E5. Pharmacy Quality Alliance. PQA measure overview; 2019. Available from: https://www.pqaalliance.org/assets/Measures/2019_PQA_Measure_Overview.pdf. Accessed July 10, 2019.