



HHS Public Access

Author manuscript

J Allergy Clin Immunol Pract. Author manuscript; available in PMC 2022 November 01.

Published in final edited form as:

J Allergy Clin Immunol Pract. 2021 November ; 9(11): 3969–3976. doi:10.1016/j.jaip.2021.01.039.

Lower Use of Biologics for the Treatment of Asthma in Publicly Insured Individuals

Ayobami T. Akenroye, MD, MPH^{a,b,c}, James Heyward, MPH^{b,c}, Corinne Keet, MD, PhD^{a,b}, G. Caleb Alexander, MD, MS^{b,c,d}

^aDepartment of Pediatric Allergy and Immunology, Johns Hopkins University, Baltimore, Md

^bDepartment of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Md

^cCenter for Drug Safety and Effectiveness, Johns Hopkins Bloomberg School of Public Health, Baltimore, Md

^dDivision of General Internal Medicine, Johns Hopkins Medicine, Baltimore, Md

Abstract

BACKGROUND: Despite bearing a disproportionate burden of poorly controlled asthma, publicly insured individuals are less likely to receive biologics.

OBJECTIVE: To assess biologic use by payer among individuals with asthma.

METHODS: We used IQVIA's National Disease and Therapeutic Index, a nationally representative, all-payer audit of ambulatory care in the United States, to describe the patterns of use by payer.

RESULTS: Asthma treatment visits in which a biologic product was reported increased from approximately 0.1% of asthma-related visits in 2003 to 1% in 2015 and doubled to 2% by 2019. Omalizumab use initially increased from 2003 to 2006 and plateaued till 2015 when its use declined modestly, coinciding with the release of additional biologic products. In 2019, omalizumab accounted for 37% of biologic treatment visits, mepolizumab 21%, benralizumab 27%, dupilumab 15%, and reslizumab <1%. Biologic treatment visits were higher for privately insured individuals (28.3 per 1000 visits) compared with publicly insured individuals (16.3 per 1000 visits). This difference persisted after accounting for age, sex, and race using nationally representative estimates. Whites accounted for a disproportionate amount of biologic treatment visits among the publicly insured (80%) despite accounting for only 60% of publicly insured asthma treatment visits. No biologic treatment visits were observed for individuals who were

Corresponding author: Ayobami T. Akenroye, MD, MPH, Division of Pediatric Allergy and Immunology, Johns Hopkins University, 600 N. Wolfe St, CMSC 1102, Baltimore, MD 21287. aakenroye@jhmi.edu.

Conflicts of interest: A. T. Akenroye, J. Heyward, and C. Keet have no relevant conflicts of interest disclose. G. C. Alexander is past chair of Food and Drug Administration's Peripheral and Central Nervous System Advisory Committee; has served as a paid advisor to IQVIA; is a co-founding principal and equity holder in Monument Analytics, a health care consultancy whose clients include the life sciences industry as well as plaintiffs in opioid litigation; and is a member of OptumRx's National P&T Committee. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies. The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IQVIA or any of its affiliated or subsidiary entities.

uninsured. Half of dupilumab visits were for publicly insured patients, compared with 22% of mepolizumab/benralizumab and 27% of omalizumab visits.

CONCLUSION: Biologics were uncommonly used among patients with asthma, and the basis for disproportionately lower use of biologics among the publicly insured, where the burden of uncontrolled asthma is greatest, merits further investigation.

Keywords

Asthma; Monoclonal antibody; Omalizumab; Mepolizumab; Benralizumab; Reslizumab; Dupilumab; IQVIA's National Disease and Therapeutic Index; NDTI; Pharmacoepidemiology; Drug utilization; National Ambulatory Medical Care Survey; NAMCS

Asthma is a disease with substantial clinical and economic burden even for those with mild-to-moderate disease, but individuals with severe disease are especially impacted.¹⁻⁴ More than 80% of asthma-related deaths are in individuals with uncontrolled severe disease, and health care-related costs can be up to 5 times higher in these individuals when compared with those with mild asthma.^{5,6} These costs are a significant barrier to achieving asthma control in uninsured individuals, but insurance coverage in itself does not eliminate these cost barriers with publicly insured individuals accounting for a significant proportion of poorly controlled asthma.⁷⁻⁹

Five monoclonal antibodies, omalizumab, mepolizumab, reslizumab, benralizumab, and dupilumab, have now been approved for the treatment of severe asthma.¹⁰⁻¹² These biologics can cost up to \$48,000 per annum,¹³ although studies have shown that they are cost-effective especially when used in carefully selected patients and after incorporating considerable price discounts.¹⁴ Cost implications may, however, differ by biologic and demographic group. For instance, individuals with state or federal government-funded insurance plans are usually not eligible for the cost-saving programs for omalizumab, mepolizumab, and benralizumab, and racial and ethnic minorities are more likely to be publicly insured.^{4,9,15-17} Differences in eligibility criteria for biologics and administration protocols may also lead to differences in the populations using these biologics. Dupilumab is the only biologic that was approved for self-administration at initial approval. The schedules are also different, and an individual may prefer, for instance, the bimonthly benralizumab schedule to the biweekly or monthly omalizumab schedule. Other factors such as the presence of comorbidities could also influence choice of biologic. Nasal polyposis, which may lead to a preference for dupilumab, disproportionately affects African Americans and worsens asthma control.¹⁸

A recent study using predominantly commercial claims data to examine the use of biologics to treat asthma from 2003 and 2018 found that utilization was still low with a peak period prevalence of less than 0.3% in 2006 before introduction of the latter 4 biologics.¹⁹ They identified disparities in use of biologics with commercially insured individuals, those with higher income, and individuals with access to specialists more likely to receive biologics.¹⁹

This is a descriptive study using all-payer data to characterize the use of biologics among individuals with asthma by insurance status given that individuals with public insurance may be more likely to have uncontrolled disease.^{7,8,19}

METHODS

Data source

We used data from IQVIA's National Disease and Therapeutic Index (NDTI). IQVIA is a health care technology company that serves the life sciences industry and, among its many roles, provides data on medication use and prescribing practices across the United States. The NDTI is an ongoing survey of a nationally representative sample of approximately 3700 to 4100 office-based physicians across various specialties and geographic regions in the United States. The random sample of physicians is generated from the American Medical Association Masterfile, which contains information on physicians in the United States. Stratified cluster sampling is then used based on the 9 US census regions and almost 150 primary medical specialties/subspecialties that aggregate into 30 main specialty groups. Although all specialties are ultimately sampled, due to large sample sizes, primary care and specialties that are predominantly ambulatory, such as family medicine, are the most represented in the database.²⁰ As has been previously described,²¹ each quarter, selected physicians report patient contacts on 2 consecutive working days including patient's demographic information, diagnoses, comorbidities, medications with the indications, and provider's specialty. For any visit that is sampled, the provider reports medications that patients may be taking, whether or not those can be self-administered, such as an inhaled corticosteroid (ICS) or dupilumab, or administered at a doctor's office, such as omalizumab. The data collected are projected and sample weights applied to create estimates for the US population accounting for the stratified cluster sampling. Given the sampling methodology, it is possible that a patient is included in more than a single visit. The samples are weighted to reflect this and standard errors calculated to account for the potential that an individual could be counted more than once. The NDTI has previously been compared with the National Ambulatory Medical Care Survey (NAMCS), a nationally representative survey of nonfederal office-based physicians conducted by the National Center for Health Statistics, and yielded similar findings in analyses of drug utilization.^{21,22}

Our unit of analysis was a "treatment visit," defined as an ambulatory visit where the patient had an asthma diagnosis and was treated with 1 or more of the biologics of interest.

Study period and sample

We examined use of biologics to treat asthma between January 2003 and December 2019 and included each of the 5 biologics currently approved for the treatment of asthma. Our analytic sample included all persons 6 years or older with a diagnosis of asthma using International Classification of Diseases codes. We excluded those with the diagnosis of other chronic lung diseases including chronic obstructive pulmonary disease and cystic fibrosis, and instances in which these biologics were used for other indications including chronic idiopathic urticaria (omalizumab), atopic dermatitis (dupilumab), or eosinophilic vasculitis (mepolizumab).

Statistical analysis

For each year, we estimated the prevalent rate of use of biologics per 1000 asthma treatment visits. In the description of patient characteristics using each individual biologic, we limited our analyses to 2019 when all 5 biologics were on the market because the introduction of successive biologics may have shifted the patient population on a prior biologic. We used annual data from 2003 to 2019 so as to show the baseline trend of omalizumab before and after initiation of the other biologics.

Given our interest in whether biologic use among the publicly insured was proportional to their burden of disease, we also compared the population of biologic treatment visits with all asthma treatment visits in the United States as captured in the NDTI and in the NAMCS. Using a previously reported methodology, we generated category-specific rates of biologic treatment visits as a proportion of asthma treatment visits in the US population as per NDTI and the 2012–2015 NAMCS.²³ For instance, for individuals aged 6 to 14 years, we report biologic use per 1000 asthma-related physician visits of individuals aged 6 to 14 in NDTI (number of biologic treatment visits by those aged 6–14 in the NDTI divided by the total number of asthma-related visits by individuals aged 6–14 in NDTI multiplied by 1000). For the NAMCS estimate, this is the number of biologic treatment visits by those aged 6 to 14 in the NDTI divided by the total number of asthma-related visits estimated for individuals aged 6 to 14 in NAMCS multiplied by 1000. Furthermore, to account for differences in the age, sex, and race distribution of those publicly versus privately insured, we provide age-, sex-, and race-standardized NDTI rates using their distribution in NAMCS.

Analyses were stratified by payer type and by biologic. To smooth curves, we used Locally Weighted Scatterplot Smoothing (LOWESS) using moving averages. All statistical analyses were performed in STATA version 14.2 (STATCorp, College Station, Tex). Two-sided *P* values of less than .05 were considered significant.

RESULTS

Biologic treatment visits for asthma

Asthma treatment visits were relatively stable accounting for 14.2 million visits in 2003 and 15.0 million visits in 2019. Publicly insured patients accounted for 38% of these visits, of which 60.5% were for patients who were White, 17.9% Black, and 12.8% Hispanic, compared with 57.8% of visits having been for privately insured individuals, of which 67.7%, 14.1%, and 9.3% were for White, Black, and Hispanic, respectively. Of these visits, 9923 (0.1%) were biologic treatment visits in 2003 and increased to 107,568 (1%) in 2015, before a rapid increase to 337,039 (2%) biologic treatment visits in 2019. Table I shows various features of each biologic that may have influenced the utilization trends observed. Figure 1 depicts these trends, indicating the initial increase in biologic (omalizumab) use from 2003 to 2006, a relative plateauing of use of biologics between 2007 and 2015, and progressive increases in use between 2016 and 2019. In 2016 through 2019, use of mepolizumab, benralizumab, and dupilumab increased, whereas omalizumab use declined slightly. Overall biologic treatment visits increased regardless of payer (Figure 2). However, use remained consistently higher for privately insured visits.

Characteristics of biologic treatment visits

Table II describes patient visits across all 5 biologics. Of 337,039 treatment visits where a biologic was used in 2019, approximately one-third (36.6%) were accounted for by omalizumab, with the remainder attributable to benralizumab (26.7%), mepolizumab (21.4%), dupilumab (14.7%), and reslizumab (0.6%). Children 6 to 14 years of age accounted for more than 17% of all asthma treatment visits but less than 3% of biologic treatment visits. The majority (70.5%) of biologic treatment visits were for individuals aged 25 to 64 with an average of 26 to 33 biologic treatment visits per 1000 asthma-related visits for this age group compared with 4 per 1000 and 10 per 1000 for those aged 6 to 14 and 15 to 24 years, respectively. Females had a slightly higher prevalence of biologic treatment visits, 26 per 1000 asthma-related visits, versus 19 per 1000 in males. Privately insured visits accounted for 72.5% of biologic-treatment visits compared with 57.8% of all treatment visits. There was no biologic treatment visit in which the individual was uninsured compared with 4.2% of all treatment visits being uninsured. In the NDTI, biologic treatment visits were 16 per 1000 asthma-related visits in publicly insured individuals compared with 28 per 1000 among privately insured individuals. These were 28 and 39 per 1000 asthma treatment visits in the NAMCS, respectively.

Characteristics of biologic treatment visits by payer and individual biologics

Privately insured individuals accounted for 3 times as many biologic treatment visits as the publicly insured. Whites accounted for 80% of biologic treatment visits among the publicly insured (Table III). Those 45 and older accounted for more than half of publicly insured biologic treatment visits, whereas those aged 15 to 44 years accounted for the majority of privately insured visits. The age-, sex-, and race-standardized rate of biologic treatment visits was 24.6 per 1000 visits for the privately insured and 20.7 per 1000 for the publicly insured. ICS in combination with a long-acting β -agonist (LABA) were listed as a concomitant medication in approximately 40% of both publicly and privately insured biologic treatment visits.

Comparing the proportion of biologic treatment visits by insurance status and individual biologic, the number of dupilumab treatment visits was approximately equal between publicly and privately insured individuals (Table IV). A total of 22% of mepolizumab/benralizumab and 27% of omalizumab visits were for publicly insured individuals. For publicly insured treatment visits for those aged 6 to 14 and 15 to 24, dupilumab was the most prevalent biologic and accounted for a third of biologic treatment visits in those 25 to 64 years. For publicly insured visits in those older than 65 years, mepolizumab or benralizumab treatment visits were the most prevalent. In privately insured individuals, dupilumab was the least prevalent with mepolizumab and benralizumab being the most prevalent except in visits for those aged 15 to 24 for whom omalizumab was the most prevalent. For publicly insured treatment visits by an Allergist/Immunologist, omalizumab was the associated biologic in 91% of the visits, but among privately insured individuals, omalizumab, mepolizumab/benralizumab, and dupilumab accounted for 36%, 43%, and 21%, respectively. Among visits by pulmonologists, mepolizumab had the highest prevalence.

DISCUSSION

Despite ample evidence of the benefits of targeted therapy with monoclonal antibodies for the treatment of severe asthma, relatively little is known about their utilization in the United States. We used a nationally representative, all-payer survey of ambulatory providers to characterize use of biologics between 2003 and 2019. We were especially interested in how such use varied based on whether an individual was privately or publicly insured. Use of biologics was uncommon but increasing, accounting for approximately 2% of asthma treatment visits in 2019. Individuals 24 years of age or younger accounted for fewer than 10% of biologic treatment visits despite accounting for 32% of asthma treatment visits. Biologic treatment visits were higher for the privately insured, and despite general increases in biologic use over time, biologic treatment visits remained lower for publicly insured visits.

Our work extends a prior analysis of biologic use using a predominantly commercial insurance claims database that found that individuals with public insurance were less likely to receive biologics for treatment of their asthma.¹⁹ Relatedly, we note that despite a higher prevalence of severe asthma among minority communities,^{9,24,25} 64% of asthma treatment visits were for individuals who were identified as White. Furthermore, despite accounting for only 60% of publicly insured asthma treatment visits in the NDTI, 80% of the biologic treatment visits among publicly insured individuals were in Whites. These findings underscore prior evidence suggesting the underutilization of outpatient services for asthma in minority populations.^{9,26–28} In addition, access and uptake of medical innovations could also differ by racial and ethnic groups even with similar insurance coverage.^{29,30} For instance, uptake of ICS metered dose inhalers for asthma in minority children was shown to lag behind the uptake in nonminority populations.³¹

Multilevel social determinants of health likely drive our findings. These include coverage and reimbursement policies that restrict the use of these products among the publicly insured, who are more likely to be racial and ethnic minorities.^{9,25,32} Other factors include individual-level factors, such as cultural beliefs, health literacy, and medication adherence, given that providers may be less inclined to prescribe these expensive medications for an individual with suboptimal adherence.^{24,25} Health care system-level barriers to diagnosis and treatment of severe asthma, such as provider-patient communication barriers, clinician competency, and underappreciation of disease severity in racial and ethnic minorities, are also possible contributors to these findings.^{9,33–35} Even in individuals with similar levels of asthma severity, there is ample evidence showing that long-term asthma control medications, specifically ICS, are commonly underprescribed in racial and ethnic minorities.^{28,36} All these factors may contribute to the differences by insurance type that also correlates with other sociodemographic variables such as race and ethnicity.

In addition, we found that among publicly insured biologic treatment visits, dupilumab was more likely than others to be used especially among Blacks and Hispanics. In a prior study on eligibility for monoclonal antibody therapy in a nationally representative population, individuals with severe asthma were most likely to be eligible for dupilumab.³⁷ However, it is unclear why there are these differences by race and payer. One reason for this may

be varying clinical indications of the biologics that we examined, given that some of these have been shown to be effective in the treatment of other comorbidities with asthma. The prevalence of these comorbidities may differ by race and ethnicity. For instance, atopic dermatitis and nasal polyposis, which are alternative indications for dupilumab, are more prevalent in blacks.^{18,38–41} Similarly, blacks with severe disease are more likely than whites to have allergic asthma.^{42–44} On the other hand, blacks may have very high total IgE levels prohibiting them from getting omalizumab.^{44–46} In addition, other factors could contribute to our findings of racial differences in biologic use. For example, there may be regional differences in the market penetration of different biologic products, which may in turn coincide with varying racial and ethnic composition of different geographic areas.^{33,34}

Furthermore, the differences in the distribution of private versus publicly insured visits between the biologic treatment visits suggest that there may be cost-related barriers to biologic use. Omalizumab, mepolizumab, and benralizumab have limited cost-sharing options for publicly insured individuals.^{15–17} Dupilumab's relatively higher use among publicly insured individuals is likely related to its being eligible for Medicare Part D prescription drug coverage given its approval for self-administration at initial approval versus other biologics that were mostly or completely facility administered in 2019, and would have been eligible for Medicare Part B not Part D coverage. Mepolizumab and benralizumab were approved for self-administration in June and October 2019, respectively. These differential utilization patterns of facility-administered versus home-administered monoclonal antibodies by payer type are not unique to asthma. A prior study of patients with rheumatoid arthritis (RA) showed that the majority of spending on biologics for RA was for facility-administered drugs covered under Medicare Part B.⁴⁷ However, low-income subsidy beneficiaries who had low out-of-pocket costs were more likely to receive self-administered biologics, such as adalimumab, covered under Part D.⁴⁷

Of note, access to specialists may also contribute to our findings, given that more than 75% of biologic treatment visits were by an Allergist or Pulmonologist. Interestingly, only approximately 40% of individuals on biologics were on ICS/LABA concomitantly despite most insurance companies requiring the use of 2 or more preventer medications before authorization of biologic use. It is possible that some individuals may have discontinued ICS/LABA use because of improved symptoms while receiving the monoclonal antibodies. However, this may also be due to the well-described suboptimal adherence to preventer medications for the treatment of asthma.^{48,49} We also found lower rates of biologic use among children relative to their burden of asthma in this cohort. This likely reflects the general paucity of data regarding the efficacy and safety of these products in children and adolescents and in turn, the absence of Food and Drug Administration–approved indications for use of all but omalizumab among individuals less than 12 years of age for most of the year 2019. However, mepolizumab received approval for use in children 6 years in September 2019. The proportion of children with asthma who are eligible for these biologics is likely to increase if and when more of these biologics receive approval for use in younger children.

Finally, our results underscore some of the marketplace dynamics that are present with these products. For example, despite modest decreases since the market entry of other biologics

in 2015, which may indicate overlap in individuals with allergic and/or eosinophilic asthma eligible for biologic therapy, omalizumab still accounts for a greater market share than other products. This may be attributable to the prevalence of allergic asthma as well as the “first mover” advantage, reinforced by physician preference for an older agent with better postmarketing surveillance data.⁵⁰ By contrast, reslizumab, the only one of these biologics that is exclusively administered intravenously, is rarely used, accounting for fewer than 1% of biologic treatment visits. It is interesting to note that reslizumab has been reported to have the lowest annual average wholesale price of the anti-interleukin 5 agents, at approximately \$28,000 per annum.¹³ However, its relatively stricter eligibility criteria including higher age for eligibility,³⁷ and the intravenous route of administration may be related to its relatively low use.

Our results have limitations. First, this is a descriptive study and any of the patterns observed here could be due to sampling variation. Given that the NDTI is a cross-sectional design, we are unable to definitively explore factors underlying the patterns seen here. In addition, this data source is from a random survey of physicians and might not capture certain variations in biologics use. Although the estimates from the NDTI have been shown in prior studies to be similar to national estimates from the NAMCS,^{21,22} we found some differences in some of our estimates. For instance, although the NDTI showed that asthma treatment visits between 2003 and 2019 were relatively stable over the study period, data from the NAMCS have shown that asthma visits actually declined from 2001 to 2016.²³ The number of asthma treatment visits was also higher in the NDTI, and thus the estimates of biologic treatment visits per 1000 privately insured or publicly insured visits were lower in the NDTI. However, the overall patterns and conclusions remain unchanged. Secondly, we used aggregated data and are unable to ascertain disease severity on the patient level, or to evaluate which individuals who discontinued omalizumab indeed initiated therapy with the newer biologics. We are also unable to assess clinical outcomes from biologics use. Finally, we are unable to explore motivations for initiating biologics. The decision to initiate or not initiate biologic is a complex one that depends on patient-level, provider-level, and health care system factors.

In conclusion, this is a descriptive study that suggests that biologics may be less likely to be used in publicly insured individuals. It raises important questions that need to be further explored to ensure that those most in need of these biologics are receiving them, and that biologics do not contribute to the already well-recognized disparities in asthma outcomes.

Acknowledgment

The authors would like to thank Dr Jerome Shier for his helpful comments on an earlier draft of this manuscript.

A. T. Akenroye is supported by the Johns Hopkins University Provost’s Postdoctoral Fellowship Award and by the NIH/NIMHD K99/R00 MOSAIC (K99MD015767-01). C. Keet receives research support from the National Institute of Allergy and Infectious Diseases and the National Institute of Environmental Health Sciences.

Abbreviations used

ICS	Inhaled corticosteroid
LABA	Long-acting β -agonist

NAMCS	National Ambulatory Medical Care Survey
NDTI	National Disease and Therapeutic Index
RA	Rheumatoid arthritis

REFERENCES

1. 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. [PubMed: 24337046]
2. Antonicelli L, Bucca C, Neri M, De Benedetto F, Sabbatani P, Bonifazi F, et al. Asthma severity and medical resource utilisation. *Eur Respir J* 2004;23:723–9. [PubMed: 15176687]
3. Nurmagambetov T, Kuwahara R, Garbe P. The economic burden of asthma in the United States, 2008–2013. *Ann Am Thorac Soc* 2018;15:348–56. [PubMed: 29323930]
4. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010. *NCHS Data Brief* 2012; (94):1–8.
5. Van Ganse E, Antonicelli L, Zhang Q, Laforest L, Yin DD, Nocea G, et al. Asthma-related resource use and cost by GINA classification of severity in three European countries. *Respir Med* 2006;100:140–7. [PubMed: 16338597]
6. 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. [PubMed: 19454036]
7. Centers for Disease Control and Prevention (CDC). Insurance coverage and barriers to care for people with asthma; 2013. Available from: https://www.cdc.gov/asthma/asthma_stats/insurance_coverage.htm. Accessed July 4, 2020.
8. Hasegawa K, Stoll SJ, Ahn J, Kysia RF, Sullivan AF, Camargo CA Jr. Association of insurance status with severity and management in ED patients with asthma exacerbation. *West J Emerg Med* 2016;17:22–7. [PubMed: 26823926]
9. The Asthma and Allergy Foundation of America/The National Pharmaceutical Council: Ethnic Disparities in the Burden and Treatment of Asthma; 2005. Available from: <http://www.aafa.org/media/Ethnic-Disparities-Burden-Treatment-Asthma-Report.pdf>. Accessed December 17, 2019.
10. Global Initiative for Asthma (GINA). Pocket guide for asthma management and prevention (for adults and children older than 5 years). Based on the Global Asthma Strategy; 2019.
11. Expert Panel Report 3 (EPR-3): guidelines for the diagnosis and management of asthma—summary report 2007. *J Allergy Clin Immunol* 2007;120(Suppl):S94–138. [PubMed: 17983880]
12. Assaf SM, Hanania NA. Biological treatments for severe asthma. *Curr Opin Allergy Clin Immunol* 2019;19:379–86. [PubMed: 31169594]
13. Mauger D, Apter AJ. Indirect treatment comparisons and biologics. *J Allergy Clin Immunol* 2019;143:84–6. [PubMed: 30612667]
14. McQueen RB, Sheehan DN, Whittington MD, van Boven JFM, Campbell JD. Cost-effectiveness of biological asthma treatments: a systematic review and recommendations for future economic evaluations. *Pharmacoeconomics* 2018;36:957–71. [PubMed: 29736895]
15. GlaxoSmithKline. NUCALA Co-pay Program: GSK; 2020. Available from: <https://www.nucala.com/hes/savings-support/copay-program/>. Accessed June 20, 2020.
16. Genentech/Novartis. The XOLAIR Co-pay Program: Committed to helping you find assistance options for XOLAIR. Genentech/Novartis; 2020.
17. Zeneca Astra. Fasentra Affordability Programs: Astra Zeneca; 2020. Available from: <https://www.fasentrahcp.com/patient-support.html#StartStaySave>. Accessed June 20, 2020.
18. Mahdavinia M, Benhammuda M, Codispoti CD, Tobin MC, Losavio PS, Mehta A, et al. African American patients with chronic rhinosinusitis have a distinct phenotype of polyposis associated with increased asthma hospitalization. *J Allergy Clin Immunol Pract* 2016;4:65864.e1.

19. Inselman JW, Jeffery MM, Maddux JT, Shah ND, Rank MA. Trends and disparities in asthma biologic use in the United States. *J Allergy Clin Immunol Pract* 2020;8:549–554.e1. [PubMed: 31472294]
20. Suaya JA, Gessner BD, Fung S, Vuocolo S, Scaife J, Swerdlow DL, et al. Acute otitis media, antimicrobial prescriptions, and medical expenses among children in the United States during 2011–2016. *Vaccine* 2018;36:7479–86. [PubMed: 30385056]
21. Higashi A, Zhu S, Stafford RS, Alexander GC. National trends in ambulatory asthma treatment, 1997–2009. *J Gen Intern Med* 2011;26:1465–70. [PubMed: 21769507]
22. Stafford RS, Radley DC. The underutilization of cardiac medications of proven benefit, 1990 to 2002. *J Am Coll Cardiol* 2003;41:56–61. [PubMed: 12570945]
23. Akinbami LJ, Santo L, Williams S, Rechtsteiner EA, Strashny A. Characteristics of asthma visits to physician offices in the United States: 2012–2015 National Ambulatory Medical Care Survey. *Natl Health Stat Report* 2019; (128):1–20.
24. Canino G, Koinis-Mitchell D, Ortega AN, McQuaid EL, Fritz GK, Alegria M. Asthma disparities in the prevalence, morbidity, and treatment of Latino children. *Soc Sci Med* 2006;63:2926–37. [PubMed: 16956704]
25. Canino G, McQuaid EL, Rand CS. Addressing asthma health disparities: a multilevel challenge. *J Allergy Clin Immunol* 2009;123:1209–17. quiz 18–9. [PubMed: 19447484]
26. Cabana MD, Lara M, Shannon J. Racial and ethnic disparities in the quality of asthma care. *Chest* 2007;132(Suppl):810s–7s. [PubMed: 17998345]
27. Davidson E, Liu JJ, Sheikh A. The impact of ethnicity on asthma care. *Prim Care Respir J* 2010;19:202–8. [PubMed: 20422142]
28. Hahn BA. Children’s health: racial and ethnic differences in the use of prescription medications. *Pediatrics* 1995;95:727–32. [PubMed: 7724312]
29. Jung J, Feldman R. Racial-ethnic disparities in uptake of new hepatitis C drugs in medicare. *J Racial Ethn Health Disparities* 2017;4:1147–58. [PubMed: 27928769]
30. Okoli GN, Lam OLT, Racovitan F, Reddy VK, Righolt CH, Neilson C, et al. Seasonal influenza vaccination in older people: a systematic review and meta-analysis of the determining factors. *PLoS One* 2020;15:e0234702. [PubMed: 32555628]
31. Ferris TG, Kuhlthau K, Ausiello J, Perrin J, Kahn R. Are minority children the last to benefit from a new technology? Technology diffusion and inhaled corticosteroids for asthma. *Med Care* 2006;44:81–6. [PubMed: 16365616]
32. Shone LP, Dick AW, Klein JD, Zwanziger J, Szilagyi PG. Reduction in racial and ethnic disparities after enrollment in the State Children’s Health Insurance Program. *Pediatrics* 2005;115:e697–705. [PubMed: 15930198]
33. Wood SF, Podrasky J, McMonagle MA, Raveendran J, Bysshe T, Hogenmiller A, et al. Influence of pharmaceutical marketing on Medicare prescriptions in the District of Columbia. *PLoS One* 2017;12:e0186060. [PubMed: 29069085]
34. Corren J, Panettieri RA Jr. How important is adherence to inhaled medications before starting a biologic therapy for asthma? *J Allergy Clin Immunol Pract* 2018;6:1578–9. [PubMed: 30197071]
35. Halterman JS, Yoos HL, Kaczorowski JM, McConnochie K, Holzhauer RJ, Conn KM, et al. Providers underestimate symptom severity among urban children with asthma. *Arch Pediatr Adolesc Med* 2002;156:141–6. [PubMed: 11814375]
36. Kharat AA, Borrego ME, Raisch DW, Roberts MH, Blanchette CM, Petersen H. Assessing disparities in the receipt of inhaled corticosteroid prescriptions for asthma by Hispanic and non-Hispanic white patients. *Ann Am Thorac Soc* 2015;12:174–83. [PubMed: 25473731]
37. Akenroye A, McCormack M, Keet C. Severe asthma in the US population and eligibility for mAb therapy. *J Allergy Clin Immunol* 2020;145:1295–1297.e6. [PubMed: 31866437]
38. Corren J, Castro M, O’Riordan T, Hanania NA, Pavord ID, Quirce S, et al. Dupilumab efficacy in patients with uncontrolled, moderate-to-severe allergic asthma. *J Allergy Clin Immunol Pract* 2020;8:516–26. [PubMed: 31521831]
39. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP

- SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, doubleblind, placebo-controlled, parallel-group phase 3 trials. *Lancet* 2019;394:1638–50. [PubMed: 31543428]
40. Salo PM, Arbes SJ Jr, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005–2006. *J Allergy Clin Immunol* 2014;134:350–9. [PubMed: 24522093]
41. Fu T, Keiser E, Linos E, Rotatori RM, Sainani K, Lingala B, et al. Eczema and sensitization to common allergens in the United States: a multiethnic, population-based study. *Pediatr Dermatol* 2014;31:21–6. [PubMed: 24283549]
42. Zoratti EM, Krouse RZ, Babineau DC, Pongracic JA, O'Connor GT, Wood RA, et al. Asthma phenotypes in inner-city children. *J Allergy Clin Immunol* 2016;138:1016–29. [PubMed: 27720016]
43. Yang JJ, Burchard EG, Choudhry S, Johnson CC, Ownby DR, Favro D, et al. Differences in allergic sensitization by self-reported race and genetic ancestry. *J Allergy Clin Immunol* 2008;122:820–827.e9. [PubMed: 19014772]
44. Litonjua AA, Celedon JC, Hausmann J, Nikolov M, Sredl D, Ryan L, et al. Variation in total and specific IgE: effects of ethnicity and socioeconomic status. *J Allergy Clin Immunol* 2005;115:751–7. [PubMed: 15805994]
45. Vergara C, Murray T, Rafaels N, Lewis R, Campbell M, Foster C, et al. African ancestry is a risk factor for asthma and high total IgE levels in African admixed populations. *Genet Epidemiol* 2013;37:393–401. [PubMed: 23554133]
46. Joseph CL, Ownby DR, Peterson EL, Johnson CC. Racial differences in physiologic parameters related to asthma among middle-class children. *Chest* 2000;117:1336–44. [PubMed: 10807820]
47. Yazdany J, Tonner C, Schmajuk G. Use and spending for biologic disease-modifying antirheumatic drugs for rheumatoid arthritis among US Medicare beneficiaries. *Arthritis Care Res (Hoboken)* 2015;67:1210–8. [PubMed: 25776035]
48. Apter AJ, Boston RC, George M, Norfleet AL, Tenhave T, Coyne JC, et al. Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol* 2003;111:1219–26. [PubMed: 12789220]
49. Apter AJ. Understanding adherence requires pragmatic trials: lessons from pediatric asthma. *JAMA Pediatr* 2015;169:310–1. [PubMed: 25664425]
50. Andrade LF, Sermet C, Pichetti S. Entry time effects and follow-on drug competition. *Eur J Health Econ* 2016;17:45–60. [PubMed: 25501258]

What is already known about this topic?

Publicly insured individuals are disproportionately affected by asthma, and those with severe uncontrolled disease may benefit from monoclonal antibody therapy. However, these biologics are costly, and little is known about their utilization by payer status.

What does this add to our knowledge?

Biologic use is lower in publicly insured visits. Among publicly insured biologic treatment visits, blacks, in particular, are underrepresented relative to whites.

How does this study impact current management guidelines?

Providers should be aware of possible disparities in the use of biologics among those with severe asthma who are publicly insured and continue to advocate for these individuals.

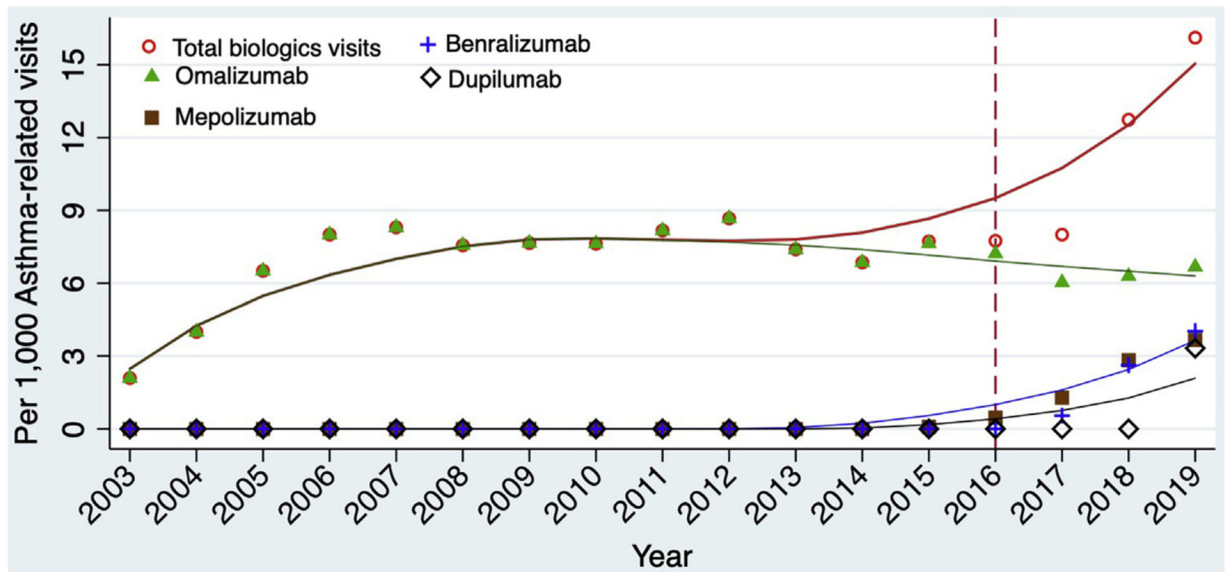


FIGURE 1.
Trends in ambulatory asthma visits treated with biologics in the United States, 2003–2019.

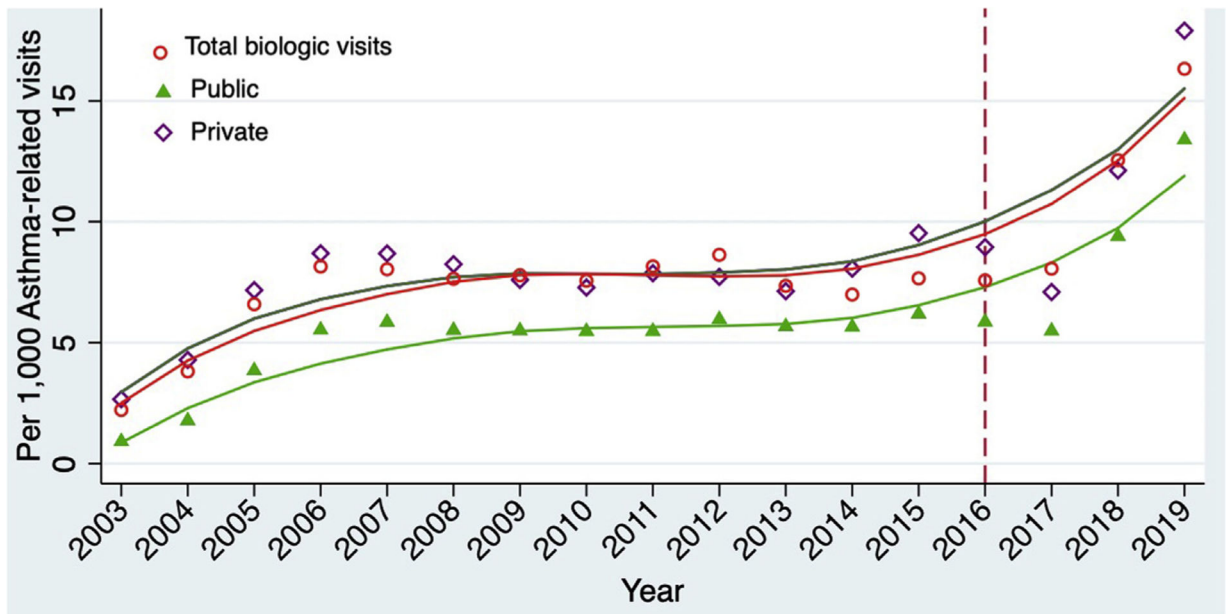


FIGURE 2.
Trends in biologic treatment visits per 1000 asthma-related visits for each payer.

Summary of biologics approved by US Food and Drug Administration for treatment of asthma

TABLE I.

Name	Approval	Biologic class	Age criteria (y)	Route	Timing of administration	Place of administration
Omalizumab	June 2003	Anti-IgE	6	SQ	Biweekly/monthly	Doctor's office
Mepolizumab	November 2015	Anti-IL5	6	SQ/IV	Monthly	At home/doctor's office
Reslizumab	March 2016	Anti-IL5	18	IV	Monthly	Infusion suite
Benralizumab	November 2017	Anti-IL5R	12	SQ	Bimonthly*	At home/doctor's office
Dupilumab	October 2018	Anti-IL4R α	12	SQ	Biweekly	At home/doctor's office

IV, Intravenous; IL, interleukin; SQ, subcutaneous.

* Benralizumab dosed monthly for first 3 doses.

TABLE II.

Characteristics of asthma treatment visits, 2019

	NDTI visits		Standardized category-specific rates	
	Biologics (337,039 treatment visits)	All visits (14,954,593 treatment visits)	Biologic use per 1000 asthma-related physician visits	
			NDTI	NAMCS
N			14,954,593 visits	10,161,000 visits
Biologics, n (%)				
Omalizumab	123,330 (36.6)	-	-	-
Mepolizumab	72,010 (21.4)	-	-	-
Reslizumab	1984 (0.6)	-	-	-
Benralizumab	90,025 (26.7)	-	-	-
Dupilumab	49,690 (14.7)	-	-	-
Age category, n (%)				
6-14	9475 (2.8)	2,603,550 (17.4)	3.6 (2.6-4.0)	4.1
15-24	20,889 (6.3)	2,130,852 (14.2)	9.8 (8.5-13.7)	23.2
25-44	100,605 (29.8)	3,852,187 (25.8)	26.1 (21.2-30.8)	54.4
45-64	137,199 (40.7)	4,131,186 (27.6)	33.2 (29.0-42.1)	53.4
65	68,871 (20.4)	2,236,819 (15.0)	30.8 (27.9-45.0)	44.2
Sex, n (%)				
Male	136,501 (40.5)	7,252,978 (48.5)	18.8 (16.9-23.0)	29.1
Female	200,538 (59.5)	7,701,615 (51.5)	26.0 (21.9-29.3)	36.7
Race and ethnicity, n (%)				
White	222,783 (66.1)	9,585,894 (64.1)	23.3 (19.6-25.7)	34.6
Black	54,263 (16.1)	2,542,281 (17.0)	21.5 (15.0-22.7)	34.0
Hispanic	37,748 (11.2)	1,555,278 (10.4)	24.3 (15.3-24.7)	22.6
Asian/other race	22,919 (6.8)	1,271,140 (8.5)	18.0 (17.6-32.7)	51.6
ICS-LABA use, n (%)	131,782 (39.1)	5,368,699 (35.9)	24.5 (22.5-31.8)	39.6
Insurance type, n (%)				
Public	92,759 (27.5)	5,682,745 (38.0)	16.3 (13.3-18.4)	28.3
Private	244,280 (72.5)	8,643,755 (57.8)	28.3 (23.8-31.5)	39.2
No insurance/unknown	1 (0.0)	628,093 (4.2)	0.0	0

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Provider specialty, n (%)	Standardized category-specific rates		
	NDTI visits		NAMCS
	Biologics (337,039 treatment visits)	All visits (14,954,593 treatment visits)	Biologic use per 1000 asthma-related physician visits
Allergy/immunology	159,048 (47.2)	1,988,961 (13.3)	80.0 (64.4–104.0)
Pulmonology	120,666 (35.8)	2,362,826 (15.8)	51.1 (48.8–78.9)
Internal medicine	24,880 (7.4)	3,304,965 (22.1)	7.5 (6.9–10.4)
Family medicine	25,412 (7.5)	3,319,920 (22.2)	7.6 (7.0–10.6)
Pediatrics	1 (0.0)	1,839,415 (12.3)	0.0
Other	7078 (2.1)	2,138,507 (14.3)	3.3 (2.9–4.6)

ICS, Inhaled corticosteroid; LABA, long-acting β -agonist; NAMCS, National Ambulatory Medical Care Survey; NDTI, National Drug Therapeutic Index.

TABLE III.

Characteristics of biologic treatment visits by payer, 2019

Age category	Public insurance (92,759 treatment visits)	Private insurance (244,280 treatment visits)
6–14	11.4 (6.3–32.2)	1.9 (1.1–2.8)
15–24	15.6 (8.7–44)	37.1 (20.7–55.6)
25–44	17.1 (9.5–48.2)	48.9 (27.3–73.3)
45–64	30.0 (16.7–84.6)	10.0 (5.6–15.0)
65	25.8 (14.3–72.8)	2.1 (1.2–3.1)
Sex		
Male	43.5 (27.2–68.6)	32.5 (29.8–62.3)
Female	56.5 (31.4–72.8)	67.5 (37.7–70.2)
Race and ethnicity		
White	80.2 (44.5–100.0)	60.6 (33.9–90.8)
Black	11.6 (6.4–32.7)	17.7 (9.9–26.5)
Hispanic	7.1 (5.1–20.0)	12.7 (7.1–19.0)
Asian/other race	0.8 (0.4–2.3)	8.9 (5.0–13.3)
Concomitant medications*		
ICS	1.1 (0.6–3.1)	3.0 (1.7–4.5)
ICS/LABA	43.6 (24.2–100.0)	35.6 (19.9–53.4)
LAMA	7.8 (4.3–22.0)	4.7 (2.6–7.0)
LTRA	17.5 (9.7–49.4)	15.3 (8.6–23.0)
Oral steroids	1.9 (1.1–5.4)	3.3 (1.8–4.9)
Physician specialty		
Allergy/immunology	33.5 (18.6–94.5)	52.4 (29.3–78.6)
Pulmonology	50.9 (28.3–100.0)	30.1 (16.8–45.1)
Family practice/general internal medicine	15.6 (8.7–44.0)	17.5 (9.8–26.2)
Biologic use per 1000 asthma-related physician visits		
Crude	16.3 (13.3–18.4)	28.3 (23.8–31.5)
Age-standardized	22.2 (18.2–24.3)	21.0 (16.4–24.5)
Sex-standardized	22.7 (18.5–25.6)	24.0 (20.2–27.2)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Percentage (95% CI)	Public insurance (92,759 treatment visits)	Private insurance (244,280 treatment visits)
Race-standardized	17.0 (13.8–19.2)	29.2 (24.7–32.4)
Age-, sex-, race-standardized	20.7 (16.8–23.0)	24.6 (22.5–28.0)

CI, Confidence interval; *ICS*, inhaled corticosteroid; *LABA*, long-acting β -agonist; *LAMA*, long-acting muscarinic agent; *LTRA*, leukotriene receptor antagonist.

* These do not add up to 100% because some patients were not receiving any of these medications.

TABLE IV.

Characteristics of asthma treatment visits by individual biologic and payer, 2019

Category-specific rates*: rates per 100 biologic-treatment visits in that category	Public insurance (N = 92,759) (27.5%)			Private insurance (N = 244,280) (72.5%)		
	OMA	MEP/BENRA	DUP	OMA	MEP/BENRA	DUP
N, treatment visits	33,546	34,835	23,386	89,784	127,200	26,304
Age category (%)						
6–14	29.9	0.3	69.8	19.5	79.9	0.6
15–24	29.4	12.3	58.3	61.6	38.2	0.2
25–44	0.1	63.1	36.8	37.3	55.9	6.7
45–64	60.8	4.8	34.5	35.8	47.3	16.9
65	38.1	54.0	7.9	23.8	76.1	0.1
Sex (%)						
Male	21.6	46.9	31.5	40.0	52.3	7.7
Female	47.2	31.6	21.2	34.5	52.3	13.2
Race and ethnicity (%)						
White	41.4	35.1	23.6	29.5	58.6	11.9
Black	0.1	59.8	40.1	37.3	42.5	20.2
Hispanic	0.8	59.4	39.9	30.0	69.9	0.0
Asian/other race	4.8	0.1	0.1	95.9	4.1	0.0
Concomitant medications [†] (%)						
ICS/ICS-LABA use	52.4	28.5	19.1	41.3	52.2	6.5
LTRA	21.2	47.2	31.7	72.3	27.6	0.1
Physician specialty (%)						
Allergy/immunology	90.8	9.2	0.0	35.9	43.1	21.0
Pulmonology	13.2	49.5	37.3	29.4	70.6	0.0
Family practice/internal medicine	0.0	59.8	40.2	58.1	25.5	16.4

Actual total number is 335,055 visits (337,039 excluding the 1,984 for reslizumab).

BENRA, Benralizumab; *DUP*, dupilumab; *ICS*, inhaled corticosteroid; *LABA*, long-acting β-agonist; *LTRA*, leukotriene receptor antagonist; *MEP*, mepolizumab; *OMA*, omalizumab.

* Category-specific rates indicate the rate per 100 visits (%) for that category. For instance, among children aged 6–14 with public insurance, omalizumab accounted for 30% of the “biologic treatment visits.”

[†] These categories are not mutually exclusive and do not add up to 100% because some patients were not receiving any of these medications.