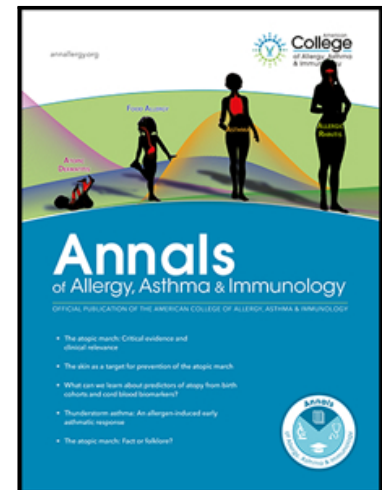


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Real-world effectiveness of mepolizumab in patients with severe asthma and associated comorbidities

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Abstract

Background: Patients with severe asthma frequently have associated comorbidities, which can compound existing symptoms, complicating asthma management.

Objective: To describe mepolizumab's real-world effectiveness in patients with severe asthma stratified by common overlapping comorbidities.

Methods: This was a retrospective analysis of patients with asthma from the MarketScan Commercial and Medicare Supplemental Database initiating

mepolizumab treatment (index date). Eligible patients had ≥ 1 claim (excluding claims for diagnostic tests) with a diagnosis code for ≥ 1 of seven comorbidities (atopic disease, nasal polyps, chronic sinusitis, obesity, respiratory infections, chronic obstructive pulmonary disease, and depression/anxiety) during the 12-month pre-index baseline period; these were used to stratify patients into seven nonmutually exclusive subgroups. Outcomes included asthma exacerbations and exacerbation-related healthcare resource utilization (HCRU) during the 12-month baseline and follow-up periods. Each patient acted as their own control.

Results: Of the 639 patients included, the most common comorbidities were atopic diseases (73.2%), respiratory infections (55.6%), and chronic sinusitis (45.1%). Across all seven comorbidity subgroups, there were significant ($P < 0.05$) reductions of 38–55% and 57–83% in exacerbations and exacerbations requiring hospitalization, respectively, during the follow-up versus baseline period, except for exacerbations requiring hospitalization in the nasal polyps subgroup, due to the small subgroup sample size. During the follow-up versus baseline periods, mean number of OCS claims was significantly ($P < 0.001$) reduced by 29–38%; 39–47% of patients achieved $\geq 50\%$ OCS dose reduction. Significant reductions in exacerbation-related HCRU were also observed.

Conclusion: Mepolizumab treatment provided real-world clinical benefits in patients.

Keywords

Asthma, Mepolizumab, Real World, Comorbidity, Allergic Rhinitis, Nasal Polyps, Copd, Anxiety, Depression, Obesity.

Abbreviations

COPD chronic obstructive pulmonary disease

CPT current procedural terminology

ED emergency department

HCRU healthcare resource utilization

HCPCS healthcare common procedure coding system

ICD International Classification of Disease

ICS inhaled corticosteroid

Ig immunoglobulin

IL interleukin

LABA long-acting β_2 -agonist

NDC national drug code

OCS oral corticosteroids

Introduction

Severe asthma is characterized by poor symptom control, airflow limitation, and frequent exacerbations despite the use of high dose inhaled corticosteroids (ICS) and a long-acting β_2 -agonist (LABA) or oral corticosteroids (OCS).¹ Patients with severe asthma frequently have associated atopic, respiratory, and other comorbidities. The most common atopic comorbidity is allergic rhinitis (49–68%),^{2–5} although other

conditions such as conjunctivitis (3–18%), atopic dermatitis (4–14%), eosinophilic esophagitis (2%), food allergies (0.5%), and an increased risk of anaphylaxis have been reported.⁵⁻⁸ Common respiratory-associated comorbid conditions include sinusitis (acute: 34%; chronic: 21–43%), nasal polyps (7–22%), chronic obstructive pulmonary disease (COPD; 15–32%), and respiratory infections (45%). Other asthma-associated comorbidities include obesity (21–48%), anxiety (81%), and depression (31%).²⁻⁴

Comorbidities can compound existing asthma symptoms and present unique challenges for asthma treatment, necessitating a holistic approach to management.^{9, 10} For example, allergic rhinitis, nasal polyps, and chronic rhinosinusitis are all associated with increased asthma symptom frequency and poorer quality of life.¹¹⁻¹⁴ Additionally, allergic rhinitis is an independent risk factor for long-term lung function decline, and chronic rhinosinusitis is a risk factor for asthma exacerbations.^{11, 15} Patients with asthma and comorbid COPD have demonstrated poorer lung function, and more frequent symptoms and exacerbations than patients without comorbid COPD.¹⁶ Similarly, respiratory infections, most commonly of viral etiology, can increase the risk of exacerbations.¹⁷ Comorbid obesity in patients with asthma is linked to other comorbid conditions such as metabolic syndrome, hypertension, and diabetes,^{18, 19} in addition to hypoventilation and deconditioning,^{20, 21} which contribute to increased breathing effort. OCS can also be ineffective for some patients with asthma and comorbid obesity, and these patients may also experience decreased responsiveness to the anti-immunoglobulin (Ig)-E biologic, omalizumab, complicating the management of asthma unresponsive to ICS/LABA therapy.²²⁻²⁴ Anxiety and depression can contribute to poor adherence to therapy and an increased

incidence of poor symptom control.^{25, 26} Finally, asthma comorbidities are associated with increased healthcare resource utilization (HCRU), and comorbid obesity, depression, and anxiety are associated with substantially higher costs.²⁷⁻³² Consequently, careful management of these comorbidities could provide clinical benefit for patients.

Mepolizumab is a targeted, humanized anti-interleukin (IL)-5 monoclonal antibody that prevents IL-5 from binding to its receptor on eosinophils, and selectively inhibits eosinophilic inflammation without complete eosinophil count depletion.³³ In clinical trials of patients with severe eosinophilic asthma, mepolizumab reduced clinically significant exacerbations, exacerbations requiring hospitalization, and maintenance OCS dose, and improved asthma control, health-related quality of life, and lung function.³⁴⁻³⁸ A meta-analysis of four Phase IIb/III randomized clinical trials indicated that mepolizumab treatment benefits in patients with severe eosinophilic asthma are consistent across a range of different comorbidities.³⁹ In real-world clinical practice, several studies have demonstrated the benefits of mepolizumab in a general population of patients with severe eosinophilic asthma.^{2, 40, 41} However, the real-world effectiveness of mepolizumab in patients with specific comorbidities has not yet been determined. These data would be valuable given the disease burden and complexities of managing patients with asthma and associated comorbidities in real-world clinical practice, where treatment responses and subsequent care are based primarily upon a comparison with an individual patient's history.

The objective of this study is to describe the real-world effectiveness of mepolizumab and associated HCRU in the management of patients with severe asthma stratified by common overlapping comorbid conditions.

Methods

Data source and study design

This was a retrospective analysis of MarketScan Commercial and Medicare Supplemental Database patient data from November 1, 2014 to December 31, 2018 (GSK ID: HO-20-20025). The MarketScan Commercial Database included the linked medical and outpatient prescription claims of employees and their dependents, and the Medicare Supplemental Database includes the claims of retired employees. Patients were identified by their first healthcare common procedure coding system (HCPCS) code or a national drug code (NDC) claim for mepolizumab administration (defined as the index date; **eTable 1**) between November 1, 2015 and December 31, 2017. The index date and the prior 12 months was defined as the baseline period and the 12 months after the index date was considered the follow-up period. The study exclusively used de-identified patient records, and did not involve the collection, use, or transmittal of individually identifiable data; therefore, institutional review board approval was not required.

Population

Patients eligible for inclusion in this study were ≥ 12 years of age, had continuous enrollment with medical and pharmacy benefits during both the 12-month baseline and follow-up periods, had received ≥ 2 mepolizumab administrations during the 180 days since the index date, and had ≥ 1 asthma diagnosis code (ICD, International Classification of Disease [ICD]-9 493.xx, ICD-10 J45.xx) on a nondiagnostic medical claim (ie, a claim that is not for a diagnostic test) in any position during the baseline period and ≥ 1 nondiagnostic medical claim with a diagnosis code for ≥ 1 of seven

comorbidities commonly associated with asthma, during the baseline period . The seven comorbidities of interest identified from nondiagnostic medical claims were 1) atopic disease (allergic rhinitis, conjunctivitis, atopic dermatitis, food allergies, anaphylaxis, eosinophilic esophagitis), 2) nasal polyps, 3) chronic sinusitis, 4) obesity, 5) respiratory infections including pneumonia, 6) COPD, and 7) depression/anxiety. Patients with evidence of mepolizumab use during the baseline period, or omalizumab, reslizumab, benralizumab, or dupilumab use during the baseline or follow-up periods were excluded.

Patients were stratified into seven nonmutually exclusive subgroups based on nondiagnostic ICD-10 medical claims for the seven comorbidities listed above during the baseline period.

Variables and outcomes

Study variables included patient demographics at index and clinical characteristics during the baseline period. The primary outcomes were the change in the number of total exacerbations and exacerbations requiring hospitalization between the baseline and follow-up periods. The secondary and exploratory outcomes were the change in OCS use and exacerbation-related HCRU (inpatient admission, emergency department [ED] visits, outpatient visits, and pharmacy claims during an asthma exacerbation) between the baseline and follow-up periods, respectively. Therefore, each patient acted as their own control, reflecting real-world practice assessments of treatment benefit.

Exacerbations were defined as an outpatient/ED claim with a diagnosis of asthma in any position (ICD-9: 493.xx, ICD-10: J45.xx) and a claim for systemic corticosteroids

4 days pre- to 5 days post event OR an inpatient admission with an asthma diagnosis code in the primary position. Exacerbations requiring hospitalization were defined as an inpatient admission with an asthma diagnosis code in the primary position regardless of whether the inpatient admission was on the exacerbation start date. Exacerbation end dates were defined as 13 days after the discharge date, and exacerbations within 14 days of the initial event were considered a single event. Exacerbations on the index date were considered part of the baseline period. Claims for scheduled administrations of mepolizumab were excluded from the definition of an exacerbation. Claims were identified as mepolizumab administration-related if they met any of the following criteria: 1) the claim had a HCPCS code for mepolizumab, 2) the claim was for an outpatient encounter with an asthma-diagnosis on the same date as the medical claim with a HCPCS code for mepolizumab administration, or 3) the claim was the first outpatient claim with a current procedural terminology (CPT) code indicating subcutaneous/intramuscular drug administration in the 28 days following a pharmacy claim for mepolizumab.

OCS use was assessed as the percentage reduction in mean daily OCS use (any or $\geq 50\%$; $0 < 50\%$, $50 < 75\%$, $75 < 90\%$, $90-100\%$), the mean number of OCS claims, the proportion of patients with ≥ 1 OCS claim, the proportion of patients with OCS burst use, and the proportion of patients with chronic OCS use. OCS burst use was defined as a pharmacy claim with ≥ 20 mg/day prednisone equivalent for 3–28 days AND an outpatient/ED claim with an asthma diagnosis in any position 7 days pre- to 6 days post-pharmacy claim. Chronic OCS use was defined as ≥ 5 mg/day OCS over 12 months.

Statistical analysis

Demographic and clinical characteristics were analyzed descriptively. Changes in categorical outcomes between the baseline and follow-up periods were analyzed using McMemar's test, and continuous outcomes using paired *t*-tests. A post hoc analysis of the primary and secondary outcomes stratified by the number of mepolizumab claims (<5, 5–9, or ≥10) during the follow-up period was also performed using the same methodology as the primary analysis.

Results

Study population

In total, 639 patients met the study eligibility criteria and were included in the study (**Figure 1**). As patients were not mutually exclusively assigned to subgroups, there was a high degree of overlap between the subgroups (**Table 1**). Overall, the most common patient comorbidities were atopic diseases (n=468, 73.2%), followed by respiratory infections (n=355, 55.6%) and chronic sinusitis (n=288, 45.1%). In each individual subgroup, atopic disease was the most prevalent comorbidity except in the nasal polyps and COPD subgroups, in which chronic sinusitis and respiratory infections, respectively, were the most prevalent (**Table 1**). Respiratory infections were the leading comorbidity in the atopic asthma subgroup.

The mean age of patients in all comorbidity subgroups was approximately 50 years, with the exception of the COPD subgroup in which the mean age was 56 years (**Table 2**). The nasal polyps subgroup had the lowest proportion of female patients (50%) and the depression/anxiety subgroup had the highest (72%). The majority of patients in all

comorbidity subgroups were receiving short-acting β_2 -agonists (77.6–90.0%), leukotriene receptor antagonists (74.0–82.5%), and ICS/LABA (60.2–63.7%) during the baseline period (**Table 2**).

Exacerbations in the baseline and follow-up periods

In all comorbidity subgroups, significant ($P<0.001$) reductions of 38–55% in the mean rate of exacerbations during the follow-up (1.0–1.5/year) versus baseline (2.2–2.6/year) periods were observed, with the greatest and lowest numerical improvements in the nasal polyps and depression/anxiety subgroups, respectively (**Figure 2A**). Similarly, there was a significant ($P<0.001$) reduction in the proportion of patients with ≥ 1 exacerbation from 82–89% during the baseline period to 52–67% during the follow-up period (**Table 3**).

The mean rate of exacerbations requiring hospitalization was reduced by 57–83% during the follow-up (0.01–0.07/year) versus baseline (0.06–0.22/year) periods in all comorbidity subgroups, with differences reaching statistical significance ($P<0.05$), except in the nasal polyps subgroup in which only 5 patients and 1 patient experienced these events in the baseline and follow-up period, respectively (**Figure 2B**). The proportion of patients with ≥ 1 exacerbation requiring hospitalization was 4–16% during the baseline period, reduced to 1–6% during the follow-up period (**Table 3**).

OCS use in the baseline and follow-up periods

In total, 67–79% of patients achieved a reduction in mean daily OCS dose during the follow-up versus baseline period and 39–47% achieved a $\geq 50\%$ reduction, with the obesity and respiratory infection subgroups generally demonstrating the lowest

proportion with a reduction and nasal polyps subgroup the highest proportion (**Figure 3A**). In all comorbidity subgroups, 13–25% of patients achieved a 50–74% OCS dose reduction during the follow-up versus baseline periods, 12–18% of patients a 75–89% dose reduction, and 23–30% of patients a 90–100% dose reduction (**Figure 3B**).

Patients with COPD had the numerically highest OCS use during the baseline period compared with other subgroups (**Table 3**). The mean number of OCS claims and proportion of patients with ≥ 1 OCS claim was significantly ($P < 0.05$) reduced by 29–38% and 9–17%, respectively, during the follow-up versus baseline periods in all comorbidity subgroups (**Table 3**). Similarly, the mean number of OCS bursts and proportion of patients requiring chronic OCS use was significantly ($P < 0.001$) reduced by 33–48% and 32–41%, respectively, in all subgroups, with the largest reductions observed in the obesity and nasal polyps subgroups, respectively (**Table 3**).

Exacerbation-related HCRU in the baseline and follow-up periods

The obesity, respiratory infection, COPD and depression/anxiety subgroups had the highest baseline period rates of inpatient admissions and ED visits (**Figure 4A and B**). The mean number of exacerbation-related inpatient admissions and ED visits was significantly ($P < 0.05$) reduced by at least 50% during the follow-up versus baseline periods in all comorbidity subgroups except the nasal polyps subgroup in which there was a nonsignificant reduction of 83% (**Figure 4A and B**). In all comorbidity subgroups, the mean number of exacerbation-related outpatient office visits was significantly ($P < 0.05$) reduced by 46–56%, and outpatient pharmacy claims by 36–51% in the follow-up versus baseline period (**Figure 4C and D**). The proportions of patients with any HCRU during the baseline and follow-up periods were generally consistent with mean HCRU data (**eTable 2**).

Post hoc stratification by number of mepolizumab claims during the follow-up period

In most subgroups, reductions in the follow-up versus baseline periods in the mean number of exacerbations and OCS use were numerically greater in patients with more mepolizumab administrations during the follow-up period (**eTable 3**).

Discussion

The results of this study suggest that patients with severe asthma achieve real-world clinical benefit with mepolizumab treatment regardless of the presence of a range of common comorbidities including upper and lower airway disease, obesity, and mood disorders. Irrespective of the comorbidities investigated, patients with severe asthma demonstrated a reduction in exacerbation rate, OCS use, and exacerbation-related HCRU with mepolizumab treatment. Treatment benefits were clearest in patients who had evidence of at least 10 mepolizumab administrations over the 12-month follow-up period.

To our knowledge, this is the first study to assess the real-world effectiveness of mepolizumab in patients with severe asthma and specific associated comorbid conditions. Previous insurance claims-based and observational cohort studies have demonstrated the treatment benefits of mepolizumab in general populations of patients with severe eosinophilic asthma.^{2, 40, 41} However, none of these real-world studies (which each involved fewer patients than the current analysis) examined the impact of mepolizumab in subgroups of patients with specific co-morbidities that can complicate disease management. A post-hoc meta-analysis of four randomized clinical trials evaluated the efficacy of mepolizumab in patients with and without a self-reported history of comorbid upper airways disease, defined as allergic rhinitis,

sinusitis, or nasal polyposis.³⁹ The current study, in contrast, examined outcomes with mepolizumab across seven different (although overlapping) comorbidity subgroups; these included a wider and more diverse range of respiratory-associated and atopic diseases, in addition to obesity and depression/anxiety.

Preventing exacerbations is a key goal of asthma management due to their association with accelerated lung function decline, future exacerbation risk and increased HCRU burden.⁴²⁻⁴⁴ In patients with severe asthma and associated comorbidities, exacerbations can worsen an already high disease burden,^{9, 10} underlining the importance of achieving reductions in exacerbation frequency, in addition to OCS use and HCRU. Of the patients included in this study, approximately 85% of patients across all comorbidity subgroups experienced exacerbations (mean rate: 2.2–2.6/year) during the baseline period. By contrast, the proportion of patients with exacerbations requiring hospitalization was variable (4–16%), with the highest proportions observed in patients with comorbid depression/anxiety (16%) and obesity (15%), both of which are known to contribute to increased exacerbation rates.^{45, 46} Importantly, significant reductions ranging from 38 to 55% in exacerbation rates with mepolizumab treatment during the follow-up period compared with the pretreatment baseline period were observed in all comorbidity subgroups. The greatest reduction was in the nasal polyps subgroup (55%) and the lowest in the depression/anxiety subgroup (38%), which may reflect the differential impact of specific comorbidities on asthma burden and/or the association of comorbidities such as anxiety and depression with decreased therapy adherence.^{25, 26} However, the study was not intended to directly compare the effectiveness of mepolizumab across comorbidities, and baseline characteristics were

not balanced between subgroups; consequently, any comparisons should be interpreted with caution.

Regardless of baseline rates, reductions in exacerbations requiring hospitalization were seen across all comorbidity subgroups and reached statistical significance in all subgroups except in patients with nasal polyps. This latter result was likely due to the small sample size of the group, with only 5 patients with nasal polyps requiring hospitalization in the year before mepolizumab treatment and only 1 patient during the year after the first mepolizumab administration.

Patients with severe asthma can frequently require both burst and chronic OCS use for symptomatic control.^{1, 44} However, given the known complications associated with OCS,⁴⁷ reductions in their use would be advantageous and were a demonstrated clinical benefit in mepolizumab's clinical development program.³⁴ In the current study, OCS use during the baseline period was highest in patients with COPD, likely due to guideline recommendations for OCS use in managing COPD exacerbations.⁴⁸ Accordingly, these patients also had the highest mean number of exacerbations during the baseline period (2.6/year). Across all subgroups, OCS use including bursts and chronic (≥ 5 mg/day over 12 months) use were significantly reduced with mepolizumab. Additionally, at least two thirds of patients in all subgroups achieved a reduction from baseline in mean daily OCS dose with mepolizumab treatment during the follow-up period, with at least 40% achieving a 50% or greater dose reduction. The smallest proportion of patients achieving at least a 50% improvement in OCS dose were those with obesity (39%), a factor known to reduce corticosteroid sensitivity,²³ followed by patients with respiratory infections, which given the diverse nature of potential infection etiologies may be expected. By contrast, the nasal polyps

subgroup had the highest numerical proportion of patients with an OCS reduction, in addition to the largest exacerbation rate reduction. This is consistent with the results of a post hoc analysis of the MENSA and MUSCA trials, which suggested that patients with comorbid nasal polyps achieve greater reductions in clinically significant exacerbations compared with patients without this comorbidity.⁴⁹ This effect may be due to concurrent improvements in nasal polyp symptoms due to mepolizumab treatment, as demonstrated in the Phase III SYNPASE study,⁵⁰ which may in turn lead to improved overall asthma control.

Severe asthma is associated with increased HCRU,⁴³ with comorbidities further adding to that burden.²⁷⁻³² Furthermore, the COVID-19 pandemic has further highlighted the need to reduce medical visits, which may also translate into reduced exacerbation-related costs.² In the current study, exacerbation-related HCRU was significantly reduced from baseline in all comorbidity subgroups with mepolizumab, with reductions in medical visits of approximately 50% from the baseline period. Importantly, these reductions were also observed in the obesity, respiratory infections, COPD, and depression/anxiety subgroups, who had approximately double the baseline rates of inpatient admissions and ED visits versus patients with comorbid upper airway disease.

Improvements in disease outcomes with mepolizumab are in accordance with reports from clinical trials and prior observational studies and support the real-world efficacy of mepolizumab in treating patients with severe asthma.^{2, 34-38, 40, 41} They are also consistent with several previous post hoc meta-analyses of Phase IIb/III randomized clinical trials, which have indicated reductions of at least 50% with mepolizumab treatment in the rate of clinically significant exacerbations across a range of

comorbidities,³⁹ patient weights,⁵¹ and IgE concentrations.³⁶ Beyond this, improved asthma control is associated with decreased risk of anxiety and depression, which in turn can lead to further improvements in asthma control.^{52,53} Additionally, long-term improvements in general health-related quality of life have been observed in patients with controlled versus partially controlled and uncontrolled asthma.⁵⁴ It would be of interest to investigate whether improved asthma control decreases the use of treatments such as antianxiety medications, antidepressants, antimicrobial agents for respiratory infections, and therapies targeting upper airway disease. However, as the follow-up period of this study was only 12 months in duration, it may have been too short to assess whether mepolizumab treatment reduced medication usage. From the perspective of comorbidity management, there is a continued need for healthcare practitioners to use comorbidity-directed standard of care treatment to ensure holistic management of patients and provide potential secondary benefits to asthma control.⁹⁻

26, 55

There are several limitations of this study, which should be considered when interpreting the results. Firstly, as with all claims database studies, determination of comorbid conditions using ICD codes may not always be fully accurate. Secondly, medication use during inpatient admissions was not captured, which may have led to an underestimation of the proportion of patients receiving treatments, particularly systemic corticosteroids, nebulizers, antibiotics, and newly initiated inhaled therapies. However, given the low rate of hospitalization and high proportion of patients using OCS, the impact of this limitation was likely small. Furthermore, patients may be given an OCS prescription for optional use in a burst pattern if they experience symptoms, meaning that some OCS bursts may not have been recorded. Thirdly, as

this study also did not include a control group, each patient functioned as their own control, with comparisons being made between baseline and follow-up periods. Therefore, the study did not account for changes in patient clinical characteristics or background therapy during the baseline and follow-up periods, although as the study was limited to a duration of 2 years, any temporal changes are likely to be limited. Fourthly, the study also did not include patients who died in the 12 months after the first mepolizumab administration, and as these data were not captured in the claims databases used, it was not possible to determine how many patients were excluded for this reason. Fifthly, sample sizes in the subgroups were small, precluding the identification of mutually exclusive subgroups and inter-subgroup comparisons using propensity score matching. Sixthly, outpatient exacerbations were defined as an outpatient/ED claim with a diagnosis of asthma in any position and not in the primary position. Finally, results may not be generalizable beyond the private/Medicare insurance population used in the database and are limited by geographic bias and the predominance of females in the included study population.

In conclusion, this study further highlights the clinical benefits of mepolizumab beyond the randomized controlled trial setting, demonstrating its real-world clinical impact on reducing asthma exacerbations, OCS use, and exacerbation-related HCRU in patients with severe asthma with a diverse range of comorbid conditions, which can complicate holistic patient management.

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Conflicts of interests: TC has received consulting and speaking fees from GSK independent of this activity. NAM, JS, MB, and BH are employees of GSK and own stocks/shares. EP, DmM, and JW are employees of IBM Watson Health, which received funding from GSK for this study.

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Tables

Table 1. Overlap between comorbidity subgroups

Subgroups, n (%)	Atopic (n=468)	Nasal polyps (n=143)	Chronic sinusitis (n=288)	Obesity (n=171)	Respirat infectio (n=355)
Atopic		111 (78.0)	218 (76.0)	133 (78.0)	259 (73.0)
Nasal polyps	111 (24.0)		121 (42.0)	29 (17.0)	66 (19.0)
Chronic sinusitis	218 (47.0)	121 (85.0)		68 (40.0)	158 (45.0)
Obesity	133 (28.0)	29 (20.0)	68 (24.0)		105 (30.0)
Respiratory infection	259 (55.0)	66 (46.0)	158 (55.0)	105 (61.0)	
COPD	146 (31.0)	37 (26.0)	97 (34.0)	76 (44.0)	147 (41.0)
Depression/anxiety	121 (26.0)	27 (19.0)	81 (28.0)	55 (32.0)	104 (29.0)

COPD, chronic obstructive pulmonary disease.

Table 2. Patient demographics and clinical characteristics

Characteristics	Atopic (n=468)	Nasal polyps (n=143)	Chronic sinusitis (n=288)	Obesity (n=171)	Respiratory infection (n=355)
Age , mean (SD)	51.0 (13.6)	50.2 (12.3)	51.4 (12.3)	52.4 (11.6)	51.3 (13.5)
Female , n (%)	275 (59.0)	71 (50.0)	179 (62.0)	120 (70.0)	229 (65.0)
Geographic region , n (%)					
Northeast	108 (23.0)	38 (27.0)	60 (21.0)	40 (23.0)	85 (24.0)
North Central	102 (22.0)	34 (24.0)	75 (26.0)	38 (22.0)	81 (23.0)
South	193 (41.0)	46 (32.0)	104 (36.0)	76 (44.0)	146 (41.0)
West	63 (13.0)	24 (17.0)	48 (17.0)	17 (10.0)	41 (12.0)
Unknown	2 (0.0)	1 (1.0)	1 (0.0)	0 (0.0)	2 (1.0)
Payer type , n (%)					
Commercial	423 (90.0)	133 (93.0)	263 (91.0)	153 (89.0)	319 (90.0)
Medicare	45 (10.0)	10 (7.0)	25 (9.0)	18 (11.0)	36 (10.0)
CCI score , mean (SD)	1.5 (1.1)	1.4 (1.2)	1.5 (1.2)	1.9 (1.4)	1.6 (1.2)
≥1 medication claim during the baseline period , n (%)					
ICS	202 (43.2)	83 (58.0)	158 (54.9)	63 (36.8)	166 (46.8)
ICS/LABA	295 (63.0)	87 (60.8)	176 (61.1)	103 (60.2)	226 (63.7)
LABA/LAMA	11 (2.4)	4 (2.8)	8 (2.8)	2 (1.2)	10 (2.8)
ICS/LABA/LAMA	99 (21.2)	22 (15.4)	65 (22.6)	43 (25.1)	68 (19.2)
SABA	391 (83.5)	111 (77.6)	247 (85.8)	150 (87.7)	308 (86.8)
LAMA	157 (33.5)	32 (22.4)	93 (32.3)	72 (42.1)	120 (33.8)
LTRA	370 (79.1)	113 (79.0)	230 (79.9)	141 (82.5)	279 (78.6)

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; LABA, long-acting β_2 -agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, short-acting β_2 -agonist; SD, standard deviation.

Table 3. Summary of exacerbation and oral corticosteroid outcomes

Characteristics	Atopic (n=468)	Nasal polyps (n=143)	Chronic sinusitis (n=288)	Obesity (n=171)	Respirato infection (n=355)
Patients with ≥ 1 exacerbation					
Baseline period, n (%)	399 (85.3)	121 (84.6)	250 (86.8)	148 (86.5)	316 (89.0)
Follow-up period, n (%)	286 (61.1)	75 (52.4)	172 (59.7)	106 (62.0)	239 (67.3)
Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$
Patients with ≥ 1 exacerbation requiring hospitalization					
Baseline period, n (%)	36 (7.7)	5 (3.5)	20 (6.9)	25 (14.6)	36 (10.1)
Follow-up period, n (%)	15 (3.2)	1 (0.7)	9 (3.1)	10 (5.8)	19 (5.4)
Difference between periods	$P<0.001$	$P=0.046$	$P=0.012$	$P=0.004$	$P=0.008$
Patients with ≥ 1 OCS claim					
Baseline period, n (%)	436 (93.2)	134 (93.7)	277 (96.2)	156 (91.2)	340 (95.8)
Follow-up period, n (%)	367 (78.4)	110 (76.9)	232 (80.6)	132 (77.2)	301 (84.8)
Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$
OCS claims					
Baseline period, mean (SD)	5.5 (4.1)	6.2 (4.2)	6.3 (4.4)	6.1 (4.5)	6.3 (4.3)
Follow-up period, mean (SD)	3.7 (4.0)	4.0 (4.7)	4.3 (4.8)	3.8 (4.2)	4.5 (4.7)
Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$
OCS burst use*					
Baseline period, mean (SD)	2.0 (2.1)	1.8 (1.7)	1.9 (1.9)	2.3 (2.3)	2.2 (2.2)
Follow-up period, mean (SD)	1.2 (1.6)	1.2 (1.6)	1.2 (1.6)	1.2 (1.7)	1.4 (1.7)
Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$
Patients with chronic OCS use†					
Baseline period, n (%)	188 (40.2)	66 (46.2)	133 (46.2)	80 (46.8)	179 (50.4)
Follow-up period, n (%)	124 (26.5)	39 (27.3)	85 (29.5)	49 (28.7)	117 (33.0)

Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$
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*OCS burst use was defined as a pharmacy claim with ≥ 20 mg/day prednisone equivalent for 3–28 days AND an outpatient/emergency department claim with an asthma diagnosis in any position 7 days pre- to 6 days post pharmacy claim; †chronic OCS use was defined as ≥ 5 mg/day OCS over 12 months.

COPD, chronic obstructive pulmonary disease; OCS, oral corticosteroid; SD, standard deviation.

eTable 1. Mepolizumab administration procedure codes

Code Type	Codes
HCPCS	Q0081, Q0083, Q0084, Q0085, S9329, S9330, S9331
CPT	96365, 96366, 96367, 96368, 96369, 96370, 96371, 96372, 96373, 96374, 96375, 96376, 96379, S9325, S9326, S9327, S9328, 96401, 96402, 96405, 96406, 96420, 96422, 96423, 96425, 96440, 96446, 96450, 96521, 96522, 96523, 96542, 96545, 96549, 99601, 99602, 96409, 96411, 96413, 96415, 96416, 96417

CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System.

eTable 2. Healthcare resource utilization during the baseline and follow-up periods

Characteristics	Atopic (n=468)	Nasal polyps (n=143)	Chronic sinusitis (n=288)	Obesity (n=171)	Respiratory infection (n=355)	COPD (n=221)	Depression/ anxiety (n=173)
Inpatient admissions							
Baseline period, n (%)	34 (7.3)	5 (3.5)	20 (6.9)	24 (14)	34 (9.6)	22 (10.0)	27 (15.6)
Follow-up period, n (%)	17 (3.6)	1 (0.7)	9 (3.1)	11 (6.4)	21 (5.9)	15 (6.8)	11 (6.4)
Difference between periods	<i>P</i> =0.005	<i>P</i> =0.046	<i>P</i> =0.012	<i>P</i> =0.012	<i>P</i> =0.042	<i>P</i> =0.162	<i>P</i> =0.002
ED visits							
Baseline period, n (%)	104 (22.2)	25 (17.5)	58 (20.1)	58 (33.9)	99 (27.9)	69 (31.2)	48 (27.7)
Follow-up period, n (%)	58 (12.4)	12 (8.4)	34 (11.8)	26 (15.2)	53 (14.9)	41 (18.6)	33 (19.1)
Difference between periods	<i>P</i> <0.001	<i>P</i> =0.005	<i>P</i> =0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> =0.029
Outpatient office visits							
Baseline period, n (%)	386 (82.5)	118 (82.5)	243 (84.4)	143 (83.6)	309 (87.0)	188 (85.1)	138 (79.8)
Follow-up period, n (%)	262 (56.0)	67 (46.9)	153 (53.1)	95 (55.6)	220 (62.0)	130 (58.8)	105 (60.7)
Difference between periods	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001	<i>P</i> <0.001
Outpatient pharmacy claims							
Baseline period, n (%)	390 (83.3)	118 (82.5)	246 (85.4)	142 (83.0)	306 (86.2)	192 (86.9)	137 (79.2)
Follow-up period, n (%)	290 (62.0)	76 (53.1)	172 (59.7)	109 (63.7)	241 (67.9)	148 (67.0)	114 (65.9)

Difference between periods	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P=0.001$
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COPD, chronic obstructive pulmonary disease; ED, emergency department.

eTable 3. Exacerbations and oral corticosteroid claims during the baseline and follow-up periods stratified by number of mepolizumab administrations during the follow-up period

Characteristics	Atopic			Nasal polyps		Chronic sinusitis			Obesity		Respiratory infection			COPD		Depression/ anxiety	
	Number of mepolizumab claims during the follow-up period																
	<5 (n=48)	5-9 (n=123)	≥10 (n=297)	5-9 (n=34)	≥10 (n=102)	<5 (n=32)	5-9 (n=69)	≥10 (n=187)	5-9 (n=40)	≥10 (n=116)	<5 (n=40)	5-9 (n=85)	≥10 (n=230)	5-9 (n=49)	≥10 (n=146)	5-9 (n=47)	≥10 (n=109)
Exacerbations																	
Baseline period, mean (SD)	22(1.4)	22(1.6)	23(1.7)	22(1.7)	21(1.5)	24(1.2)	22(1.7)	24(1.7)	25(1.7)	26(1.8)	24(1.4)	22(1.6)	27(1.7)	26(1.7)	27(1.8)	22(1.7)	26(1.9)
Follow-up period, mean (SD)	15(1.4)	15(1.5)	11(1.3)	16(1.5)	08(1.2)	16(1.5)	16(1.6)	12(1.4)	16(1.6)	11(1.2)	15(1.6)	17(1.6)	13(1.3)	19(1.8)	12(1.4)	17(1.8)	13(1.3)
Difference between periods	P=0.002	P<0.001	P<0.001	P=0.027	P<0.001	P=0.003	P<0.001	P<0.001	P=0.004	P<0.001	P=0.002	P=0.011	P<0.001	P=0.013	P<0.001	P=0.066	P<0.001
Patients with ≥1 OCS claim																	
Baseline period, n (%)	46 (95.8)	116 (94.3)	274 (92.3)	32 (94.1)	95 (93.1)	32 (100)	66 (95.7)	179 (95.7)	37 (92.5)	105 (90.5)	36 (90.0)	81 (95.3)	223 (97.0)	49 (100.0)	138 (94.5)	45 (95.7)	99 (90.8)
Follow-up period, n (%)	38 (79.2)	105 (85.4)	224 (75.4)	28 (82.4)	77 (75.5)	25 (78.1)	57 (82.6)	150 (80.2)	38 (95.0)	84 (72.4)	34 (85.0)	76 (89.4)	191 (83.0)	46 (93.9)	113 (77.4)	42 (89.4)	88 (80.7)
Difference between periods	P=0.005	P=0.016	P<0.001	P=0.102	P<0.001	P=0.008	P=0.007	P<0.001	P=0.564	P<0.001	P=0.414	P=0.059	P<0.001	P=0.083	P<0.001	P=0.180	P=0.022

Groups with fewer than 30 patients are not shown.

COPD, chronic obstructive pulmonary disease; OCS, oral corticosteroid; SD, standard deviation.

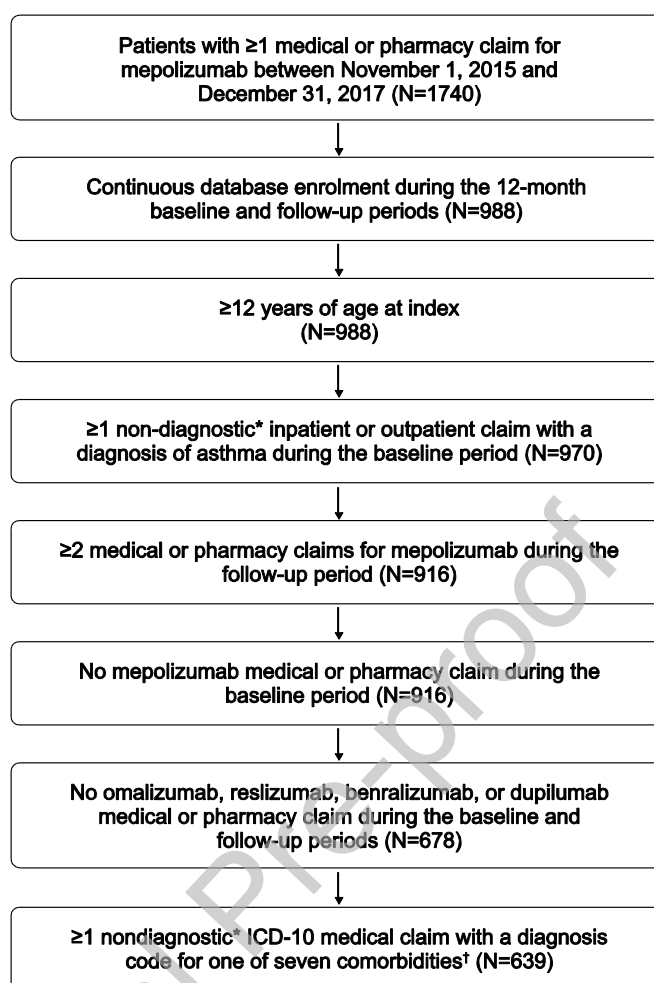


Figure 1. Study population disposition

*A claim that is not for a diagnostic test; †atopic disease (allergic rhinitis, conjunctivitis, atopic dermatitis, food allergies, anaphylaxis, eosinophilic esophagitis), nasal polyps, chronic sinusitis, obesity, respiratory infections including pneumonia, COPD, and depression/anxiety.

COPD, chronic obstructive pulmonary disease; ICD-10, International Classification of Disease 10th edition.

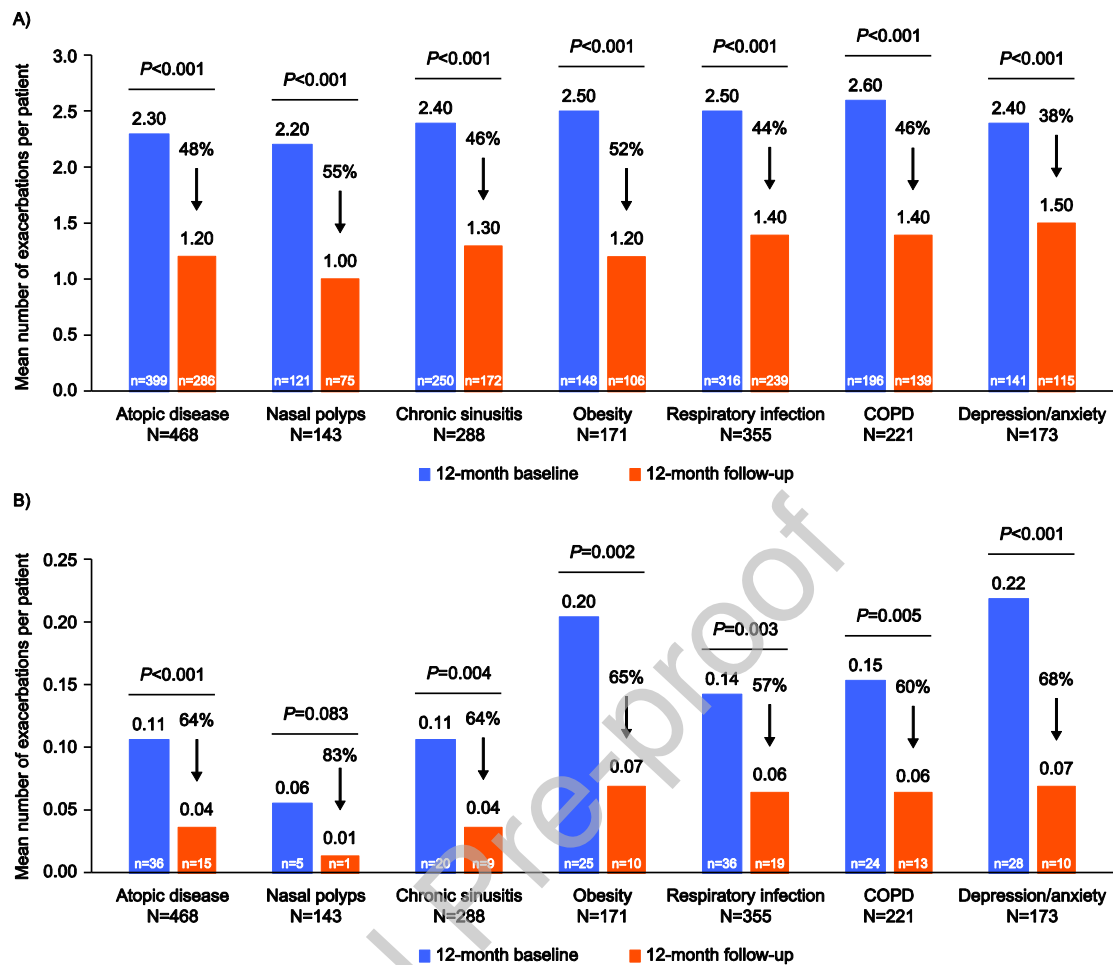


Figure 2. Mean number of A) exacerbations and B) exacerbations requiring hospitalization during the baseline and follow-up periods. Numbers on baseline and follow-up bars represent the number of patients with ≥ 1 event. COPD, chronic obstructive pulmonary disease.

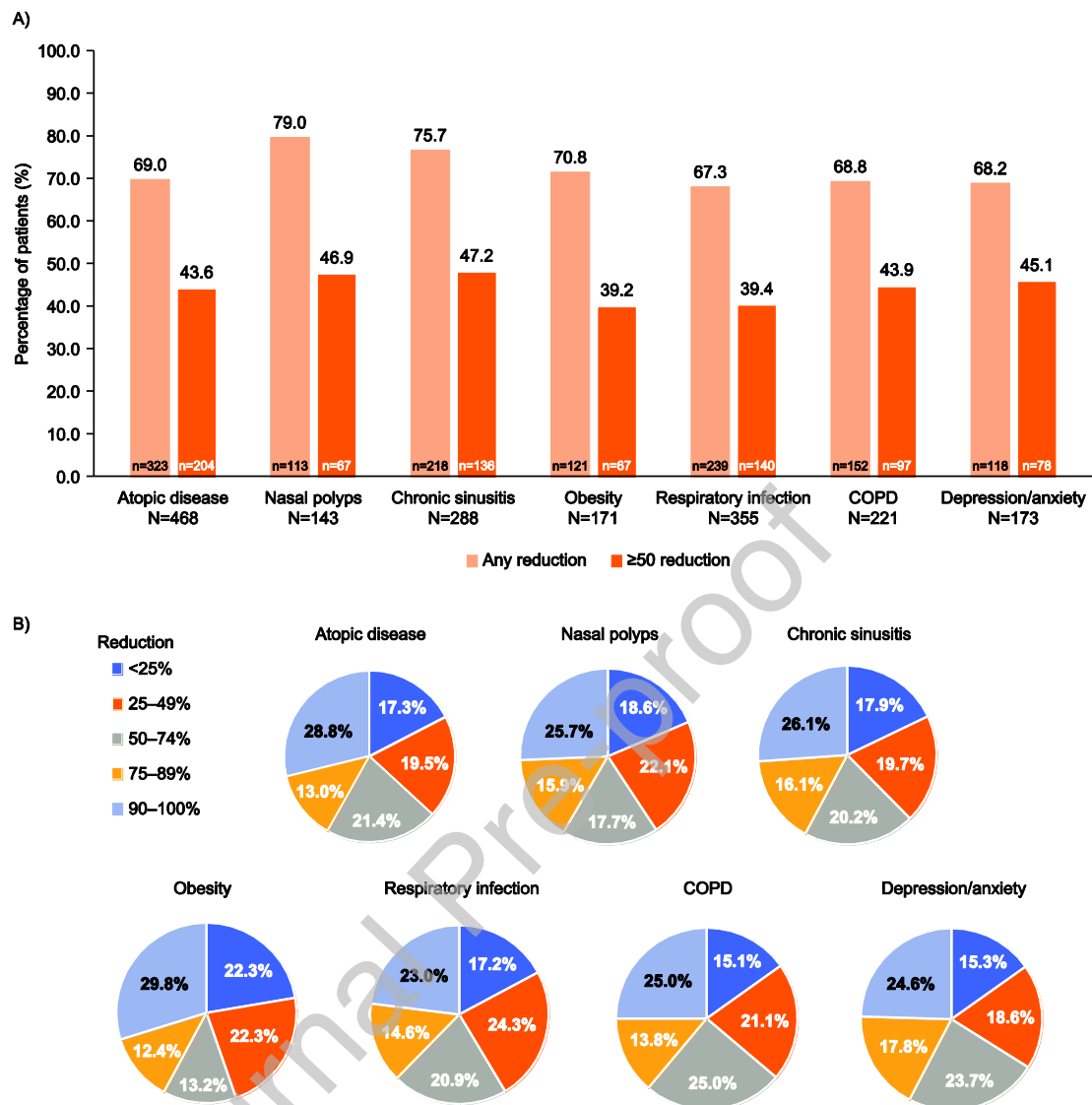


Figure 3. A) Proportion of patients with a reduction in mean daily OCS dose and B) the proportion of patients with percentage reductions in OCS dose during the follow-up versus baseline period

COPD, chronic obstructive pulmonary disease; OCS, oral corticosteroid.

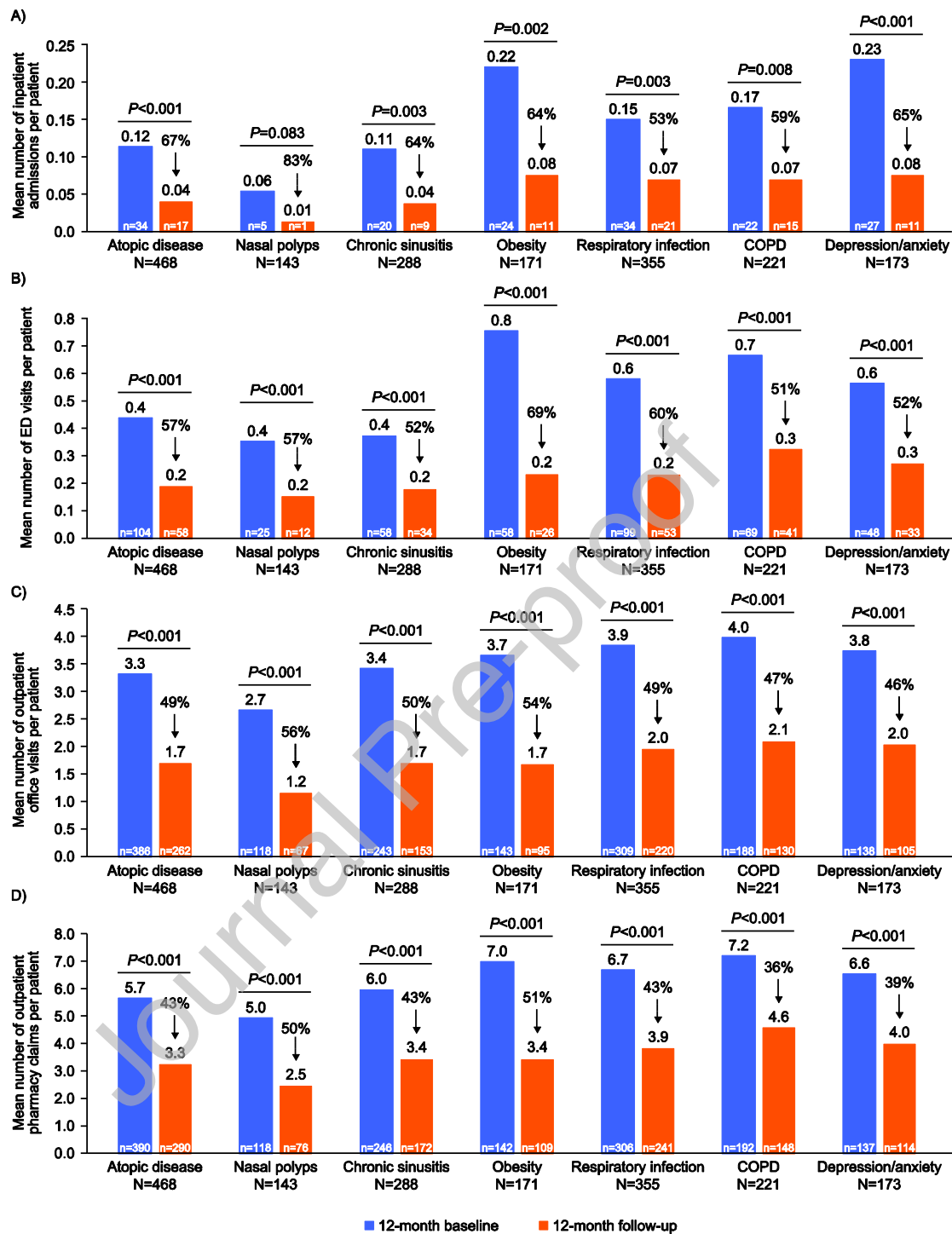


Figure 4. Asthma exacerbation-related healthcare utilization A) inpatient admissions, B) ED visits, C) outpatient office visits, and D) outpatient pharmacy claims during the baseline and follow-up periods

Numbers on baseline and follow-up bars represent the number of patients with ≥ 1

event; COPD, chronic obstructive pulmonary disease; ED, emergency department; OCS, oral corticosteroid.

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