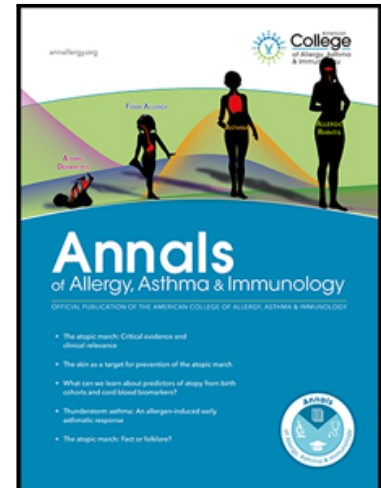


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**Mapping Geographic Variability of Severe Uncontrolled Asthma in the United States:
Management Implications**

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Short Title: Mapping of SUA in the US

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Background: United States population-level data on asthma morbidity and mortality are available primarily through state-level surveys. We hypothesize that significant county-level heterogeneity may be obscured by state-level data, thus impeding focused initiatives to improve asthma outcomes.

Objective: To assess heterogeneity in the prevalence of uncontrolled, severe, and severe uncontrolled asthma by examining state- and county-level morbidity reflected in large administrative claims datasets and identify relationships between pharmacotherapy-based morbidity and the Centers for Disease Control and Prevention's asthma mortality data.

Methods: Asthma prevalence and morbidity were identified using medical and pharmacy claims from the IQVIA Longitudinal Access and Adjudication Data database (7/2015-6/2018). Heatmaps ranked prevalence of severe uncontrolled asthma by deciles in all 50 states and the District of Columbia, plus 2935 counties. Mortality in states (2016) and 3147 counties (1999-2018) was similarly mapped and ranked and contrasted with claims-based morbidity.

Results: Among 4,506,527 individuals with asthma, 640,936 (14.2%) received agespecific therapy for severe asthma. Of those with severe asthma, 144,232 (22.5%) filled ≥ 2 annual courses of systemic steroids and were designated as having severe uncontrolled asthma. Most states with high mortality had relatively few patients with severe uncontrolled asthma. A significant correlation between mortality and morbidity and trends by urban/rural and metropolitan status were found at the county level. Conclusion: Intra-state heterogeneity in the morbidity and mortality of severe uncontrolled asthma at the county level is not evident in state-level analyses. Increased local awareness of systemic corticosteroid use as an indicator of uncontrolled asthma should prompt regional educational and public health efforts to improve outcomes.

Keywords: Heatmap, severity, uncontrolled asthma, mortality

Abbreviations: CDC, Centers for Disease Control and Prevention; ERS/ATS, European Respiratory Society/American Thoracic Society; GINA, Global Initiative for Asthma; HCP, health care provider; ICD, *International Classification of Diseases*; ICS, inhaled corticosteroid; LAAD, Longitudinal Access and Adjudication Data; LABA, long-acting β_2 -agonist; LM, leukotriene modifier; NAEPP, National Asthma Education and Prevention Program; PDC, proportion of days covered; SA, severe asthma; SABA, short-acting β_2 -agonist; SCS, systemic corticosteroid; SUA, severe uncontrolled asthma; UA, uncontrolled asthma; US, United States

INTRODUCTION

Asthma is characterized by variability in control and phenotype heterogeneity.¹ Severe asthma (SA) requires significant interventions, including the need for medium- to high-dosage inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA) therapy² and phenotypic assessments to determine additional treatments.³ Despite publication of the first National Asthma Education and Prevention Program Guidelines for the Diagnosis and Management of Asthma in 1991,⁴ asthma in the United States (US) has been associated with persistent morbidity.^{5, 6, 7}

Asthma control is independent of severity and reflects symptom-based impairment and exacerbation-based risk.^{2, 3} Asthma may be uncontrolled due to undertreatment or comorbidities; however, many patients with SA remain uncontrolled even with maximal therapy.^{3, 8} According to a probabilistic model, US adolescents and adults with uncontrolled asthma (UA) are estimated to lose 15 million quality-adjusted life years and produce \$963.5 billion in direct and indirect costs between 2019 and 2038.⁹

Epidemiologic data on the burden of asthma are inconsistent.¹⁰ Approximately 5% to 10% of patients with asthma have SA,^{8, 11-13} and 20% to 50% of those patients have severe uncontrolled asthma (SUA) due to exacerbations requiring hospitalizations, emergency department visits, and/or systemic corticosteroids (SCS).¹¹⁻¹³ The TENOR study revealed 83% of patients with severe or difficult-to-treat disease had UA.¹⁴ The CHOICE study found that only 14.3% of patients were well-controlled.¹⁵ A recent systematic review found the prevalence of SUA varied from 1.8% to 38.9% of patients with asthma.¹⁶ Despite these discrepancies, there is consensus that SUA accounts for a disproportionate amount of asthma-related disease burden, health care resource utilization, and costs.^{11, 16-18} Furthermore,

patients with SUA are at increased risk for long-term adverse health consequences and face adverse effects from SCS use.^{19, 20}

Asthma control and mortality may vary by city and state.²¹ According to the Centers for Disease Control and Prevention (CDC),²² approximately 50% of adults with asthma were uncontrolled between 2006 and 2010, with rates ranging from 34.9% in Washington, DC to 63.9% in Alabama.²³ Age-adjusted asthma-related mortality also varies geographically, from 5.5 deaths/million in Indiana to 20.8 deaths/million in Mississippi in 2016.²⁴ States with the highest prevalence of UA do not necessarily have the highest asthma-related mortality, and vice versa, suggesting different factors may underlie disease morbidity and mortality. Furthermore, state-level data are heterogeneous; higher-resolution analyses at the county level may help to reveal determinants of asthma morbidity and mortality.

To better quantify the heterogeneity of asthma severity and control across the US, we used retrospective medical and pharmacy claims data to identify patients with UA, SA, and SUA and then ranked and mapped these findings at the state and county levels. CDC data were similarly employed to compare state and county mortality rates. We hypothesized this analysis would reveal both state- and county-level heterogeneity and identify previously unrecognized determinants of disease burden that could inform clinically- and cost-effective interventions.

METHODS

Data Sources

We identified patients with asthma, UA, SA, and SUA using the IQVIA Longitudinal Access and Adjudication Data (LAAD) database (July 2015 to June 2018). LAAD is a medical and pharmacy open US claims database that contains 1.5 billion medical claims, covers 92% of retail and 72% of mail-order pharmacy claims, but does not capture hospital-setting prescriptions. This study of anonymized data did not require informed consent or IRB approval for the analyses performed. The waiver of informed consent complied with HIPAA and the Declaration of Helsinki.

We used the CDC's *Most Recent Asthma State or Territory Data*²⁵ and *Multiple Cause of Death Data*²⁴ to capture state and county age-adjusted asthma mortality rates. State-level data were reported as deaths per 100,000 in which the underlying cause of death is asthma and rates were age-adjusted to the 2000 standard population. County-level mortality was reported as age-adjusted mortality rate per 100,000 from 1999 to 2018. For counties with unreliable (i.e. <20 total deaths) or suppressed (i.e. <10 total deaths) values according to CDC guidelines,²⁶ we assigned a default death count of 5 per 100,000. We assessed correlations between state- and county-level mortality and morbidity for 39 states and 638 counties, where both asthma mortality and morbidity data were available and could be matched for analysis (Pearson Correlation Coefficient; additional details in the **eMethods**).

Patient Identification

Patients of all ages with both an *International Classification of Diseases* (ICD)-9/ICD-10-coded diagnosis of asthma in 2015 to 2018 and any medical/pharmacy claim in 2016 and ≥ 1 pharmacy claim for an ICS, leukotriene modifier (LM), fixed-dose combination ICS/LABA or ≥ 2 claims for a short-

acting β -agonist (SABA) were identified as “patients with asthma” (see **eMethods** for ICD-9/ICD-10 codes). The index date was defined as the date of first pharmacy claim for an asthma treatment in 2016. Patients with diagnostic codes for both asthma and chronic obstructive pulmonary disease were excluded.

Based upon consensus opinions, including the European Respiratory Society/American Thoracic Society (ERS/ATS), National Asthma Education and Prevention Program (NAEPP), and Global Initiative for Asthma (GINA),^{3, 8} we classified patients with ≥ 2 annual SCS pharmacy claims (oral or injectable) as having UA. Adherence, or treatment taken as agreed upon by the patient and health care provider (HCP), was measured according to proportion of days covered (PDC), i.e., the percentage of days in which the prescribed daily dose was available to the patient based on claims data.

SA was defined by age-specific pharmacologic treatment with $\geq 25\%$ of PDC as per NAEPP² and GINA²⁷ reports (**eTables 1 and 2**):

- 0–5 years: any ICS/LABA or medium-/high-dosage ICS with or without additional therapies
- 6–11 years: medium-/high-dosage ICS/LABA or medium-/high-dosage ICS with or without additional therapies
- ≥ 12 years: medium-/high-dosage ICS/LABA with or without additional therapies

Patients with criteria for SA and ≥ 2 annual pharmacy claims post-index for SCS were identified as having SUA.

Heat Map Generation

We used SAS[®] 9.4M5 to summarize the number and percentage of SUA patients in 50 states and

Washington, DC (97.6% of SUA population), number of SUA patients in 2935 counties (no minimum number of SA patients; 97.6% of SUA population), and percentage of patients with SA having SUA in 2112 counties (those with a minimum of 10 patients with SA per county in 2016; 97.1% of SUA population) using the *Patient Location* algorithm. The 85th to 100th percentile range represented the highest percentage or number of patients with SUA, and the 0 to 4th percentile had the lowest. Percentiles referred to relative ranking of states and counties on a scale from 0-100%, and corresponding analyses included the state/county count, average, minimum, and maximum values within a given percentile range.

Analysis of Counties by Urban-rural Classification Codes

To address the possible effects of population density and environmental factors on asthma mortality and morbidity, we further analyzed age-adjusted mortality rates and SUA prevalence using the 2013 National Center for Health Statistics *Urban-Rural Classification Scheme for Counties*, which is a classification scheme that designates counties by metropolitan statistical areas established by the United States Office of Management and Budget, and county populations per the 2010 United States Census. We stratified by overall county designations: urban (urban population ≥ 2500) versus rural (urban population < 2500 or classified as completely rural) and metropolitan/near metropolitan (in or adjacent to defined metropolitan statistical areas) versus non-metropolitan (not in or adjacent to metropolitan statistical areas). We averaged values for all counties within each designation, including for counties with suppressed or unreliable data, and performed two-sample t-tests within stratifications.

RESULTS

Analysis of data from 11,763,066 individuals in the IQVIA LAAD dataset between July 2015 and June 2018 identified 4,506,527 individuals with pharmacy claims for asthma therapies that meet the previously described case definition of a patient with asthma (**Figure 1**). Children aged 0-5 and 6-11 years, as well as adolescents and adults aged ≥ 12 years made up 12.1%, 17.7%, and 69.8% of the study population, respectively (**Table 1**). Females represented 56.2% of the cohort. The largest proportion of the population filled an ICS as their controller (33.3%), followed by an ICS/LABA (28.7%) and a LM (18.1%). Almost 20% of patients filled only SABA and no controller therapies. Of all patients, 34.5% had ≥ 1 claim for an SCS, 15.1% had ≥ 2 claims, and 7.3% ≥ 3 claims in the 12-month post-index period.

Age-specific controller therapy (**eTables 1 and 2**) and adherence definitions for SA were found for 640,936 patients (14.2% of the population; **Figure 1**). Among patients with SA, 42.6% had ≥ 1 claim for SCS during the 12-month post-index periods, 22.5% met the case definition of SUA with ≥ 2 claims, and 12.7% filled ≥ 3 SCS prescriptions (**Figure 2**). Overall, 144,232 patients or 3.2% of all asthma patients met the definition for SUA (**Figure 1**).

Of patients on age-specific controller therapy for SA, 67.0% showed $< 50\%$ adherence (PDC), with 45% adhering $< 25\%$ of the time; only 17.7% had $\geq 80\%$ adherence (**Figure 3**). As the PDC range progressively increased (25%–49%, 50%–64%, 65%–79%, and $\geq 80\%$), the percentage of patients with SA also having SUA was relatively stable at 20.9%, 22.4%, 23.1%, and 24.2%, respectively. For patients receiving age-specific SA regimens containing high-dose ICS with or without additional treatments and having $\geq 25\%$ PDC, the percentage of patients with UA was approximately 28% once $\geq 50\%$ PDC was achieved.

Geographic Mapping of Asthma-Related Mortality and Morbidity (SUA) at the State Level

CDC 2016 asthma mortality statistics (**Figure 4A**) showed IN having the lowest and MS the highest age-adjusted asthma-related mortality rates (5.5 and 20.8 deaths/million, respectively). Other states within the 85th to 100th percentile asthma mortality group (11.8–20.8 deaths/million) included AR, AZ, KS, MN, MS, NE, OR, and UT (**eTable 3**). The average percentage of patients with SA who had SUA was 22.5% (**Figure 4B, eTable 4**). AL, CT, GA, HI, LA, MS, TN, and WV fell within the 85th to 100th percentile range, accounting for 13% of all SUA patients.

Contrasting state-based mortality with morbidity revealed that these parameters did not generally align. Of the 8 states within the 85th to 100th percentile range of patients with SA also having SUA, only MS was among the group of states with the highest mortality rates. Although LA and HI were among the states with the highest percentage of patients with SA having SUA, they were among the group of states within the lowest 3 percentile ranges of mortality rates. Furthermore, although NE, OR, and UT fell within the lowest 2 percentile ranges for patients with SA also having SUA, they were among the group of states with the highest mortality rate. Overall, there was no correlation between state-level mortality and morbidity ($r=-0.03$, $p=0.85$).

Geographic Mapping of Absolute Numbers of Patients with SUA at the State Level

To better understand the discordance between state-level mortality and SUA, the latter parameter was mapped according to the absolute number of patients with SUA (**Figure 5A, eTable 5**). Rankings of the absolute number of patients with SUA weigh densely populated areas more heavily but also serves to identify the absolute magnitude of the morbidity of SUA. CA, FL, IL, NJ, NY, OH, PA, and TX were among the 8 states within the 85th to 100th percentile for number of patients with SUA (**Figure 5A**) and

accounted for 46.0% of all SUA, however none of these fell within the 85th to 100th percentile for mortality rates. Additionally, despite FL, PA, and TX being in the group of states with the highest numbers of patients with SUA, they were among the states within the lowest 3 percentile ranges in asthma mortality rates.

Geographic Mapping of Morbidity and Mortality at the County Level

Assessing morbidity (**Figure 5B, eTable 6, eFigure 1**) and mortality (**Figure 6, eTable 7**) at the more granular county level revealed large intrastate variability for numbers of patients with SUA and for death rates, which would be unappreciated if only state-level data were considered. In total, 440 of 2935 counties fell within the 85th to 100th percentile of absolute number of patients with SUA and accounted for 83.1% of all SUA. As states, AK, HI, ME, NE, NM, RI, UT, and VT did not rank highly in absolute numbers of patients with SUA, but each had counties ranking within the 85th to 100th percentile range for this parameter. A similar discordance between state and county mortality data was observed. Of the 414 counties in the 85th to 100th percentile for 1999-2018 mortality, only 13.8% were in the group of 8 states in the 85th to 100th percentile for 2016 mortality. However, 15.2% of counties with the highest death rates were in the 8 states with the highest proportion of patients with SA having SUA. Furthermore, a significant, albeit weak correlation was observed between county morbidity (as measured by the proportion of patients with SA having SUA) and county age-adjusted mortality ($r=0.14$, $p<0.001$).

Age-adjusted Mortality and SUA Prevalence by Urban-Rural Classifications

The average age-adjusted mortality rate in urban counties was 0.31 per 100,000 versus essentially 0.00 in rural counties ($p<0.001$), and 0.33 in metropolitan/near-metropolitan versus 0.06 in non-metropolitan

counties ($p < 0.001$). Average SUA prevalence as a percentage of patients with SA was slightly higher in metropolitan/near metropolitan counties versus in non-metropolitan counties (23.2% versus 21.2%, $p < 0.001$), but in urban and rural counties, SUA prevalence was comparable (22.8% and 22.9%, respectively; $p = 0.91$) (**Figure 7**).

DISCUSSION

Consensus on the prevalence of UA, SA, and SUA has been elusive and estimates using epidemiologic or other population approaches may not reflect real-world evidence from comprehensive insurance and pharmacy databases. To our knowledge, this is the first real-world report based on geographic mapping of asthma burden derived from claims data that includes children, adolescents, and adults; the major insurance types (Medicaid, Medicare, and commercial); and patients in primary and specialty care. This study combined publicly available information with representative administrative claims data to generate one of the largest analyses of asthma burden. Guidelines-based inclusion criteria and healthcare provider ZIP codes were used to map and rank the prevalence of SUA as a percentage of patients with SA and in absolute numbers. This study uniquely captured nuances of geographic heterogeneity down to the county level in identifying SUA, mortality, and trends therein.

This comprehensive methodology showed that 15.1% of patients with an asthma diagnosis filled ≥ 2 annual claims for SCS, fulfilling the pharmacologic-based definition of UA. 14.2% of patients had age-specific controller medication and dosage criteria for SA, of which 22.5% had SUA by SCS usage. Overall, 144,232 out of 4,506,527 patients were characterized as having SUA, accounting for 3.2% of all asthma.

Our findings may be more generalizable to patients with asthma in the US than other retrospective observational studies of medical claims databases that have used similar methodologies to define severity and control. A 2012 Commercial and Medicare Advantage, 2012 study of 552,895 patients¹¹ and a 2010–2011 ClinformaticsTM DataMart Multiplan IMPACT analysis of 222,817 patients¹⁷ examined only patients aged ≥ 12 years and did not include Medicaid or standard Medicare-insured populations. Disparate findings on asthma burden were observed between these studies, with 4.7% and 19.7% of patients, respectively, having SA, among whom 19.9% and 4.7% had SUA.

In the ClinformaticsTM DataMart Multiplan IMPACT study, only 12.5% and 2.5% of patients had ≥ 1 and ≥ 2 annual exacerbations,¹⁷ compared with 34.5% and 15.1%, respectively, in our study. These differences may be due to the IMPACT study employing less stringent inclusion criteria, absence of pediatric patients, and/or inclusion of only commercially insured populations that may have greater access to care and pharmacotherapy. SA characterization in the Commercial and Medicare Advantage study required adherence to therapies appropriate for severe asthma at ≥ 6 annual claims. This criterion could account for the SA prevalence being lower than in the current study, in which only 40% of patients on comparable therapy had similar claims-based adherence. Despite these adherence differences, the percentage of patients with SA having uncontrolled disease in the IMPACT analysis differed from our analysis by only 2.6% (19.9% vs. 22.5%, respectively).

The overall prevalence of SUA in the Commercial and Medicare Advantage study was comparable to our findings (2.3% vs. 3.2%, respectively). Additionally, for patients with similar adherence to age-specific therapies for severe asthma, 2.0% of our population was found to have SUA. The low treatment

adherence observed in our study may underlie the prevalence of uncontrolled disease, rather than failure of the medication used.

Despite this poor adherence to controllers by patients with SA in our study, increasing PDC $\geq 50\%$ did not reduce the percentage of patients experiencing ≥ 2 annual exacerbations for those receiving age-specific regimens for SA containing ICS at either medium/high or high dosages. The finding of steroid resistance is not new,²⁸ and it suggests that simply improving adherence may not reduce the burden of SUA for many patients, thus underscoring unmet need at the population level. Steroid resistance could result in decreased adherence to maintenance medications as patients discover these therapies do not mitigate symptoms or exacerbation burden.²⁸ Furthermore, findings from pragmatic and randomized controlled trials demonstrate that adherence to maintenance medications alone may not result in optimal exacerbation reduction and providing increased anti-inflammatory therapy at the time symptoms occur may be necessary across all asthma severities.²⁹⁻³²

Given low rates of adherence to controllers observed in this study, we believe that using more restrictive adherence standards for patient inclusion—such as in the HEDIS criteria³³—would have resulted in a narrower view of the burden of asthma in the US. Patient self-report may over- or underestimate the severity of asthma or the extent of symptom control¹⁶ and is confounded by patient and physician misperceptions.³⁶ The 2009 Asthma Insight and Management survey revealed that 71% of patients believed their asthma was completely or well-controlled, whereas the actual percentage dropped to 29% when using a definition of well-controlled asthma based on objective measures.³⁷ The INSPIRE study³⁴ used structured interviews to evaluate over 3000 patients from 11 countries—including the US—who were receiving maintenance therapy. Close to three-quarters of patients were uncontrolled based on

SABA use and/or Asthma Control Questionnaire scores. Although patients were aware of warning signs of worsening asthma, they most commonly turned to SABAs during the period of peak symptoms and used ICS-containing therapies to a lesser extent and later in the course of their deteriorations. Patients felt they could manage periods of symptom worsening without physician input and reported that when symptoms abated, they decreased SABA and anti-inflammatory therapy use. However, 51% reported that they had experienced an unplanned visit for an asthma exacerbation in the previous year.³⁴

SCS use is a marker of exacerbation-prone asthma and can identify uncontrolled disease, which is associated with both acute and chronic adverse health outcomes.^{20, 35} Cumulative lifetime doses as low as 0.5–1.0 g of SCS may increase corticosteroid side effects, including the risk of onset of type 2 diabetes; doses of 1.0–2.5 g can increase the risk of impaired glucose control (metabolic dysfunction), cardiovascular comorbidities, ophthalmologic abnormalities, and osteoporosis.^{19, 20} However, employing SCS use to define uncontrolled asthma, regardless of severity, may have excluded patients with UA and SUA having uncontrolled symptoms but without exacerbations. The most recent CDC report of uncontrolled asthma assessed symptom-based measures only and found the rates of uncontrolled disease were 38% for children and 50% for adults with asthma.²³ Consequently, the estimate of absolute numbers and percentages of patients with UA and SUA in our study may minimize the full burden of disease.

Additionally, using mortality data to evaluate uncontrolled disease may over- or underestimate the overall burden of asthma due to inaccuracies inherent in reporting of death and its relatively rare occurrence. Nevertheless, the observed disconnect between mortality and morbidity is underscored by findings from a 2014 database study of asthma deaths in the UK, which found that of 155 asthma deaths,

58% occurred in patients treated for mild or moderate asthma.³⁸ Patients with apparently mild asthma represent 30–37% of adults with acute asthma exacerbations and 16% of patients with near-fatal asthma.³⁹ Indeed, 15–20% of adults dying of asthma had symptoms less than weekly in the prior 3 months.³⁹

This claims-based study has limitations, as patients with asthma who are not receiving prescription medications are excluded, and prescription fill data indicate medication possession but not necessarily adherence or correct usage. The analyses were not adjusted for age, gender, or prior exacerbation history, and some patients may have incomplete information for medical and/or prescription history in the database. As the diagnosis of asthma is determined by coding from the HCP, it is unknown whether patients met all specified criteria for asthma or whether other possible diagnoses were excluded. These limitations may be particularly relevant to the characterization of infants and children, in whom the presence of comorbidities, history of respiratory infections, and degree of sensitization to aeroallergens were not able to be assessed. Uncontrolled asthma could potentially be overestimated if SCS were prescribed for a condition other than asthma or not used by patients. Alternatively, the proportions of patients with uncontrolled or severe asthma may be underestimated because the database does not include data from hospital settings in which SCS are often administered to manage exacerbations. However, inpatient hospital stays with asthma as the first-listed diagnosis only reflect 2% of the total annual incidence of asthma exacerbations in the US.^{7, 40} The impact of newer biologic therapies on the prevalence of SUA could not be ascertained due to the timing of this study, however, omalizumab and mepolizumab were available as therapeutic options. Using HCP location as a proxy for patient location does not consider that patients may travel between counties or states to receive care. The issues

described above, however, are mitigated by the large and representative real-world dataset employed and the emphasis on overall trends rather than direct comparisons of absolute numbers.

As demonstrated here, geographic mapping of SUA by state and county can help identify regional heterogeneity, unmasking local areas of high unmet need within states with an overall moderate-to-low disease burden. County-level heatmaps of SUA prevalence help elucidate the complex social, environmental, and pathophysiologic interactions between morbidity and mortality that may differ regionally throughout the US. Notably, county-level data in the present study indicate trends in age-adjusted asthma mortality and SUA prevalence by proximity to metropolitan areas and/or by urban/rural status; counties identified as urban also exhibited considerably greater age-adjusted asthma mortality. These findings are consistent with some aspects of the longstanding hygiene hypothesis, which proposes that environmental factors may play either a protective or provocative effect on the development of allergies and asthma.⁴¹⁻⁴³ At minimum, they suggest that more research into the urban and rural factors that contribute to these differences is needed.

Taken together, the present findings offer a focused assessment of local needs and could guide decisions on optimal allocation of future educational, clinical, and research resources. These data also highlight that for some patients, improved adherence to controller therapy alone may not reduce disease burden. Considerations as to why patients may be difficult to treat or refractory to ICS or SCS include lack of access to appropriate standard maintenance therapies, lack of recognition of the need for appropriate controller medication use, poor technique in delivery of inhaled therapies, unrecognized comorbidities, or the presence of steroid resistance. With the rapidly expanding use of advanced therapies, HCPs and patients now have options to improve both the acute burden of uncontrolled asthma and the long-term

consequences of SCS use over a lifetime, thus emphasizing the importance of accurately quantifying and characterizing the critical burden of SUA.

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Table 1. Demographic and Clinical Characteristics of Patients with Asthma^a

	Patients with asthma N=4,506,527	
	N	%
Age categories		
0–5 years	546,975	12.1
6–11 years	797,607	17.7
12+ years	3,112,387	69.1
Unknown	49,558	1.1
Sex		
Male	1,971,504	43.7
Female	2,534,549	56.2
Unknown	474	0.01
Medication class		
SABA only	895,717	19.9
LM	814,897	18.1
ICS	1,501,002	33.3
ICS/LABA	1,294,911	28.7
Annual exacerbations ^b		
0	2,950,919	65.5
≥1	1,555,608	34.5
≥2	681,257	15.1
≥3	327,098	7.3

ICS, inhaled corticosteroid; LABA long-acting β_2 agonist; LM, leukotriene modifier; SABA, short-acting β_2 agonist.

^aSee eMethods for additional notes/data sources.

^bAn exacerbation was defined by a pharmacy claim for systemic corticosteroids within 12 months of the first 2016 asthma pharmacy claim.

Figure legend

Figure 1. Identification of patients.^a

^aIndex date: date of first (2016) pharmacy claim for asthma medication.

^bSee eMethods for age-specific therapies for SA.^{2, 26}

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; LM, leukotriene modifier; PDC, proportion of days covered; SA, severe asthma; SABA, short-acting β_2 -agonist; SCS, systemic corticosteroid; SUA, severe uncontrolled asthma.

Figure 2. Annual exacerbations^a among patients with severe asthma.^b

^aPharmacy claims for SCS were used as a proxy for asthma exacerbations.

^bSevere asthma defined by age-specific controller medication dosages (see Methods).

SCS, systemic corticosteroid, i.e., oral corticosteroid at any dose or injection of a systemic corticosteroid in a patient with an asthma diagnosis.

Figure 3. Medication adherence and exacerbations among patients filling age-specific therapies for severe asthma.^a

^aSee eMethods for additional notes/data sources.

^bSevere uncontrolled asthma defined as meeting SA criteria and with ≥ 2 annual SCS claims.

^cPatients filling high-dosage inhaled corticosteroid/long-acting β_2 -agonist therapies, with/without other therapies.

PDC, proportion of days covered; SA, severe asthma; SCS, systemic corticosteroid.

Figure 4. Comparison of state-level (A) population-adjusted asthma-related mortality rate^a and (B) percentage of patients with severe asthma having severe uncontrolled asthma.

^aMortality rates reported are per 100,000, 1999–2018. SA, severe asthma. See eMethods for additional notes/data sources.

Figure 5. Absolute number of patients with severe uncontrolled asthma (A) at the state level and (B) at the county level.

See eMethods for notes/data sources.

SUA, severe uncontrolled asthma.

Figure 6. Age-adjusted mortality rates^a at the county level.

^aMortality rates reported are per 100,000, 1999–2018. See eMethods for additional notes/data sources.

Figure 7. County-level stratifications of (A, B) age-adjusted mortality rates^a and (C, D) proportions of severe asthma patients with severe uncontrolled asthma by urban versus rural or metropolitan/near metropolitan versus non-metropolitan classifications.

Data labels (n's) indicate numbers of counties included. See eMethods for additional notes/data sources.

SUA, severe uncontrolled asthma.

Figure 1

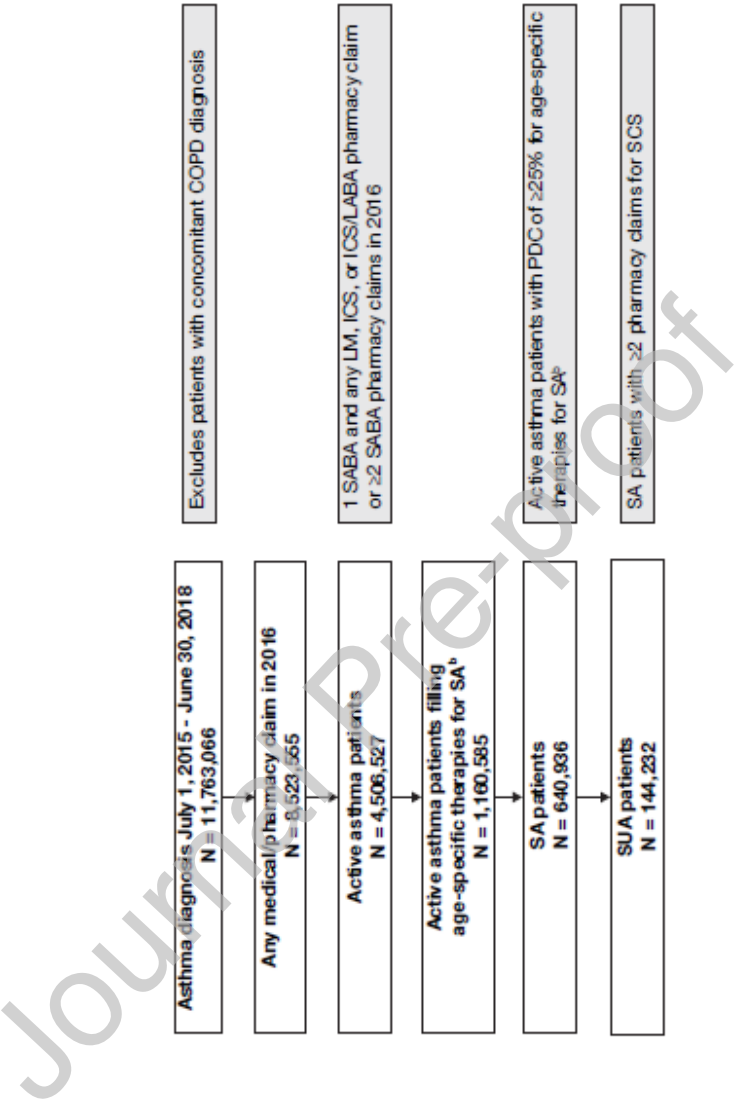


Figure 2

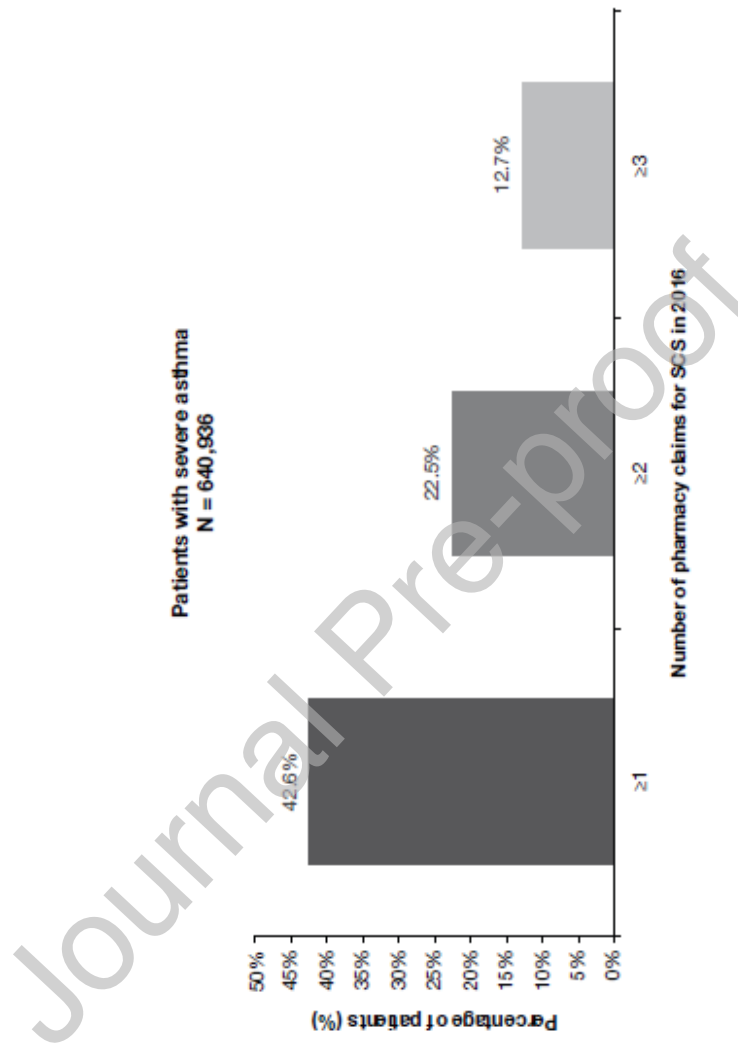


Figure 3

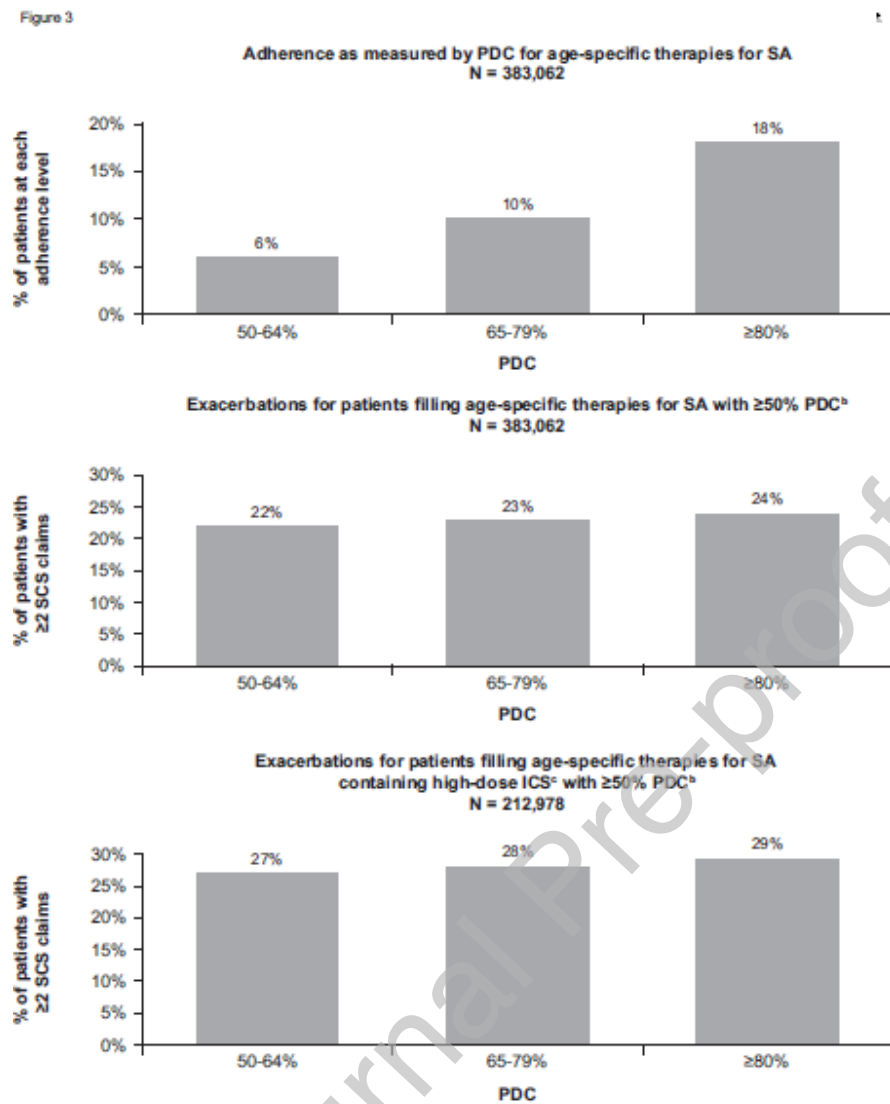


Figure 4A. [Click here to access/download/Figures/Fig4A.pdf](#)

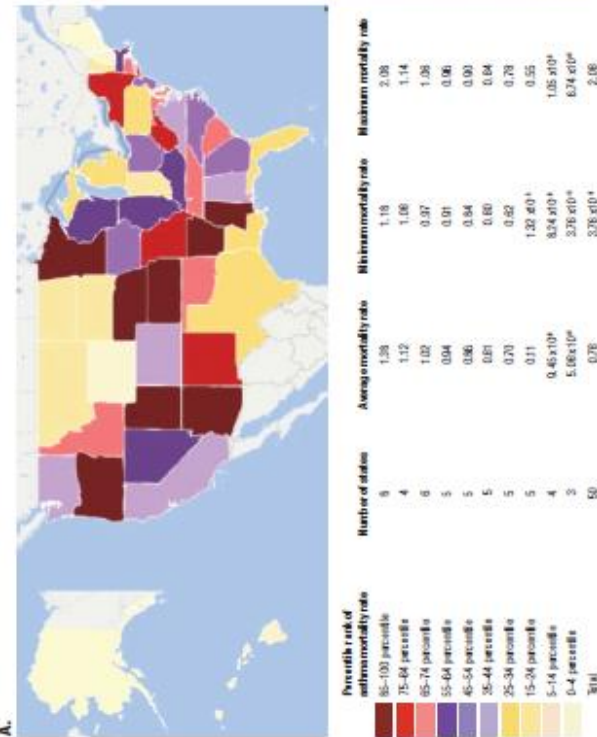


Figure 4B. [Click here to access/download/Figures/Fig4B.pdf](#)

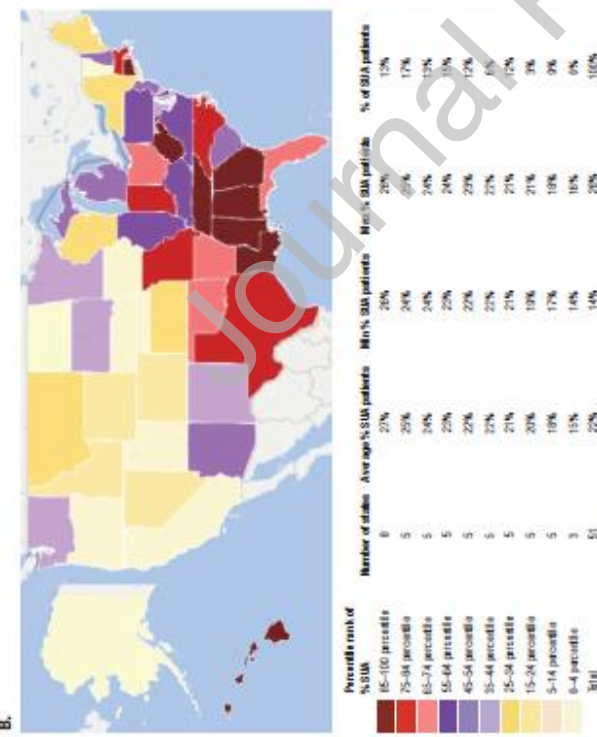


Figure 5A

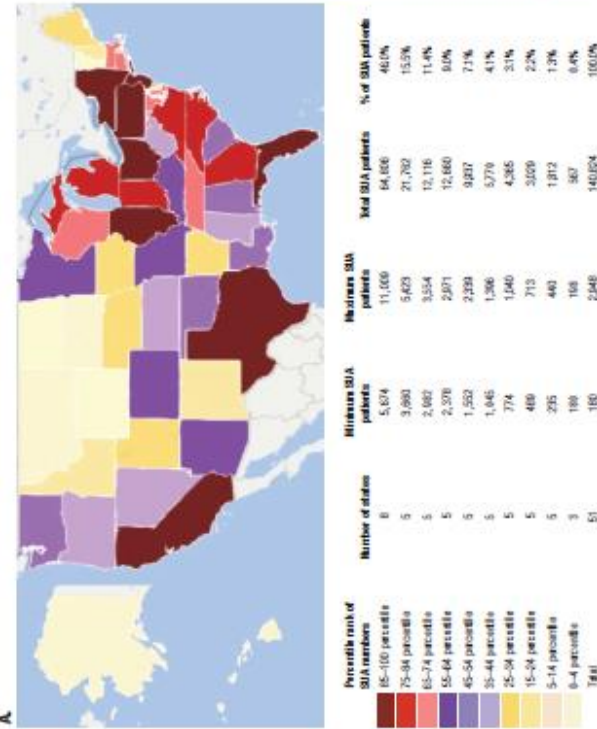


Figure 5B

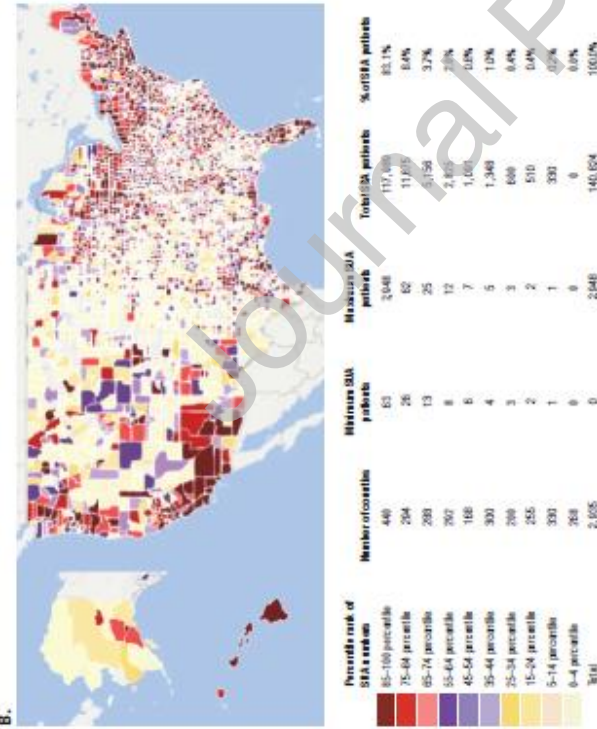


Figure 6 [Click here to access/download/Figure/Heatmap MS Fig6 page 1](#)

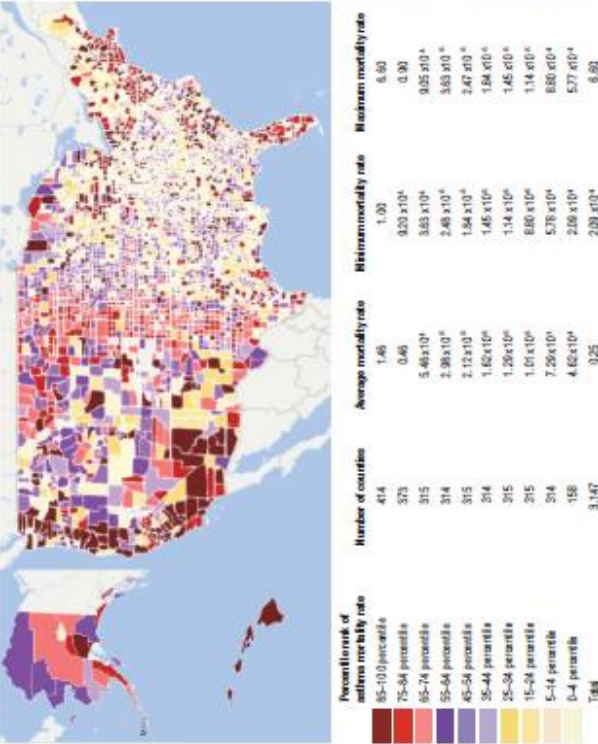
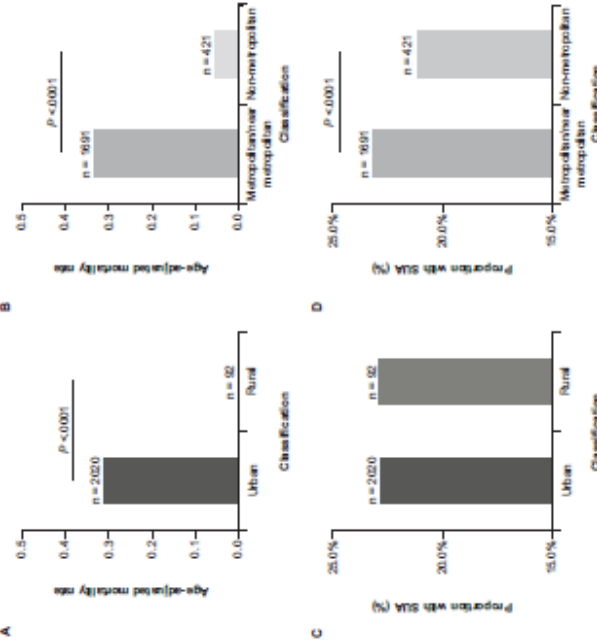


Figure 7 [Click here to access/download/Figure/Heatmap MS Fig7 age 1.](#)



eSupplement

eMethods

Data Sources

At the time of preparation of this article, mortality rates for AK, DC, DE, HI, ME, MO, ND, NH, RI, SD, VT, and WY were listed as “unreliable” or “suppressed,” and mortality data for Puerto Rico and Guam were unavailable. For locations with unreliable (i.e. <20 total deaths) or suppressed (i.e. <10 total deaths) values, death counts were assigned a default value of 5 per 100,000.

Data sources for specified Tables and Figures:

Figure 1: IQVIA patient-level medical and prescription claims data (September 2018 data transmission), 2016 data.

Figure 3: IQVIA patient-level medical and prescription claims data, 2016 data.

Figure 4A; eTable 3: Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death, 1999-2018 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at <http://wonder.cdc.gov/ucd-icd10.html> on Jun 19, 2020 10:45:28 AM.²⁴

Figure 6; Figure 7A,B; eTable 7: Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death, 1999-2018 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at <http://wonder.cdc.gov/ucd-icd10.html> on Jul 28, 2020 5:27:23 PM.²⁴

Table 1; Figure 4B; Figure 5; Figure 7C,D; eFigure 1: IQVIA LAAD database July 2015–June 2018 (September 2018 data transmission).

Notes on Tables and Figures:

Table 1: Patients with asthma were defined by any diagnosis of asthma 2015–2018, any medical or pharmacy claim in 2016, and ≥ 1 pharmacy claim for ICS/LABA, ICS, or LM or ≥ 2 pharmacy claims for SABA in 2016. Medication classes were defined hierarchically, without respect to additional controllers: patients on ICS/LABA were classified as “ICS/LABA”; patients on ICS (and not LABA) were classified as “ICS”; patients on LM (and not ICS or LABA) were classified as “LM”; patients with ≥ 2 pharmacy claims for a SABA in 12 months and not on LM, ICS, or ICS/LABA were classified as “SABA only.”

Figure 1, Figure 3: Age-specific therapies for SA defined as follows^{2, 26}: ICS/LABA or medium-/high-dosage ICS, with or without additional therapies, for patients 0–5 years of age; medium-/high-dosage ICS/LABA or medium-/high-dosage ICS, with or without additional therapies, for patients 6–11 years of age; and medium-/high-dosage ICS/LABA, with or without additional therapies, for patients ≥ 12 years of age.

ICS, inhaled corticosteroid; LABA, long-acting $\beta 2$ -agonist; SA, severe asthma.

Figure 4; eFigure 1: For each state, the percentage of patients with SA having SUA was calculated, and states were ranked into percentiles. For each county with ≥ 10 SA patients, the percentage of patients with SA with UA was calculated, and counties were ranked into percentiles.

SA, severe asthma; SUA, severe uncontrolled asthma; UA, uncontrolled asthma.

Figure 5: Data are unadjusted for population. Note: Washington DC and Puerto Rico are not included in the 50 state definitions but are included in county definitions. For each state, the absolute number of patients with SUA was calculated, and states were ranked into percentiles.

LAAD, Longitudinal Access and Adjudication Data; SA, severe asthma; UA, uncontrolled asthma.

Figure 7: Stratification performed by county designations: urban versus rural; metropolitan/near metropolitan versus non-metropolitan. **Figure 7A, 7B:** Mortality rates reported are per 100,000, 1999–2018. **Figure 7C, 7D:** For each county with ≥ 10 severe asthma patients, the percentage of patients with severe asthma with uncontrolled asthma was calculated.

LAAD, Longitudinal Access and Adjudication Data.

Adherence Determination

Medication adherence for determining SA was calculated based on the number of days' supply of age-appropriate maintenance therapy during the 12 months following the first maintenance prescription in 2016.

- Age 0–5 years: Sum of days' supply from first prescription filled of any dosage of ICS/LABA or medium-/high-dosage ICS in 2016 to last prescription filled within a period of 12 months/365 days
- Age 6–11 years: As above for medium-/high-dosage ICS/LABA or medium-/high-dosage ICS
- Age ≥ 12 years: As above for medium-/high-dosage ICS/LABA

68 **SUA Mapping and Ranking**

69 SUA was mapped and ranked in 2 ways: percentage of patients with SA who met criteria for SUA and
70 absolute number of patients with SUA. The first ranking is based on percentage of SA patients with
71 SUA and corrects for differences in population density across the country. The second analysis gives the
72 overall magnitude of SUA.

73

74 **Patient Location**

75 Patient location was identified using the IQVIA OneKey database containing ZIP codes of the primary
76 practice of the health care providers (HCPs) writing the highest number of prescriptions for asthma-
77 related respiratory medications in 2016. If this result yielded multiple locations (i.e., multiple HCPs), the
78 origin of the most recent prescription was used, which was resolved by random selection in the event of
79 a tie.

80

81 **Heat Map Generation**

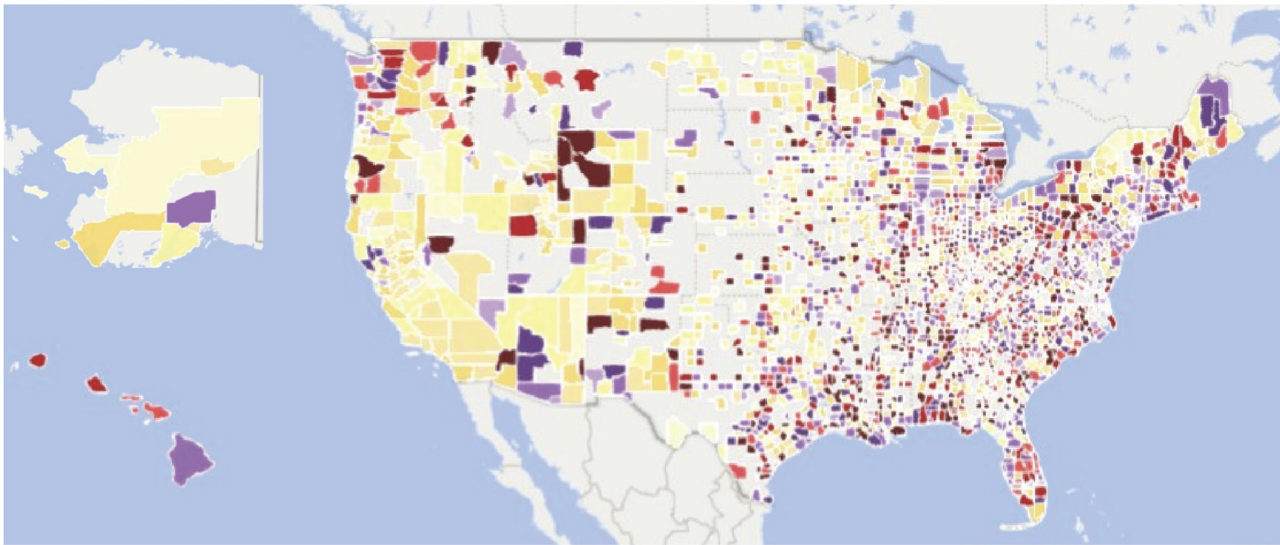
82 Relative ranking based on the percentage of patients with SA having SUA and the absolute number of
83 patients with SUA were calculated using the PERCENTRANK function in Microsoft® Excel® 2016 and
84 grouped into 10 percentile ranges, with the 85th to 100th percentile range having the highest and the 0 to
85 4th percentile having the lowest percentage or number of patients with SUA. These data were used to
86 generate heat maps with Excel® 2016. A state-level map of asthma mortality (CDC data) was also
87 created using Excel® 2016.

88

89 **ICD-9/ICD-10 Codes for Asthma and COPD**

Description	ICD-9 Diagnosis code	ICD-10 Diagnosis code
Asthma	493.xx	J45xx
COPD	490.xx–492.xx, 496.xx	J40, J410, J411, J418, J42, J430–J432, J438, J439, J440, J441, J449
90 91	COPD, chronic obstructive pulmonary disease, ICD-9, International Classification of Diseases, 9 th revision; ICD-10, International Classification of Diseases, 10 th revision.	

eFigure 1. County Heat Map - Ranked by % of Patients with SA Having SUA.



Percentile rank of % SUA	Number of counties	Minimum % SUA patients	Maximum % SUA patients	Average % SUA patients	% of SUA patients
85–100 percentile	316	31%	73%	37%	5.1%
75–84 percentile	212	27%	31%	29%	9.6%
65–74 percentile	211	25%	27%	26%	17.1%
55–64 percentile	211	23%	25%	24%	16.2%
45–54 percentile	212	22%	23%	23%	18.1%
35–44 percentile	153	20%	22%	21%	12.3%
25–34 percentile	258	18%	20%	19%	11.8%
15–24 percentile	215	14%	18%	16%	7.5%
5–14 percentile	207	9%	14%	12%	1.7%
0–4 percentile	117	0%	9%	6%	0.1%
Total	2,112	0%	73%	23%	100.0%

See eMethods for additional notes/data sources.

LAAD, Longitudinal Access and Adjudication Data; SA, severe asthma; SUA, severe uncontrolled asthma.

eTable 1: Classification of ICS Products and Dosages Classified as Medium to High Dosage for the Purpose of Defining Severe Asthma

ICS product	ICS group	Daily dosage for medium/high ICS for age 0–11 years
Aerospan HFA (flunisolide) 80 µg/puff: ≥2 puffs bid (≥320 µg/day)	flunisolide	≥320 µg
Alvesco 80 (ciclesonide): >160 µg/day	ciclesonide	>160 µg
Alvesco 160 (ciclesonide): >160 µg/day	ciclesonide	>160 µg
Arnuity® Ellipta® 100, 200 (fluticasone F): >200 µg/day	fluticasone F	>200 µg
Asmanex® 110 twisthaler® (mometasone): ≥2 puffs qd (≥220 µg/day)	mometasone	≥220 µg
Asmanex® 220 twisthaler® (mometasone): ≥1 puffs qd (≥220 µg/day)	mometasone	≥220 µg
Asmanex® 200 HFA (mometasone): ≥1 puffs qd (≥200 µg/day)	mometasone HFA	≥200 µg
Flovent Diskus 50, 100, 250 (fluticasone P): >400 µg/day	fluticasone P	>400 µg
Flovent HFA 44, 110 and 220 (fluticasone P): >400 µg/day	fluticasone P	>400 µg
Pulmicort Flexhaler 90 µg (budesonide): >360 µg/day	budesonide	>360 µg
Pulmicort Flexhaler 180 µg (budesonide): >360 µg/day	budesonide	>360 µg
Pulmicort Respules 0.25, 0.50 mg vials (budesonide): >1.0 mg/day	budesonide	>1 mg
QVAR® HFA (40 and 80 µg), Beclovent HFA (40 and 80 µg), Vanceril and Vanceril DS (42 and 84 µg) HFA (beclomethasone): >160 µg/day	beclomethasone	>160 µg
QVAR® RediHaler™ 40 (beclomethasone): >160 µg/day	beclomethasone	>160 µg
QVAR® RediHaler™ 80 (beclomethasone): >160 µg/day	beclomethasone	>160 µg

Bid, twice daily; F, Furoate; HFA, hydrofluoroalkane; ICS, inhaled corticosteroid; P, propionate; qd, once daily.

eTable 2. Classification of ICS/LABA Products and Dosages Classified as Medium/High Dosage by Age Group for the Purpose of Defining Severe Asthma

ICS/LABA	Dosage (µg)	Age 0–5 years	Age 6–11 years	Age ≥12 years
Advair Diskus	250/50	Y	Y	Y
Advair Diskus	500/50	Y	Y	Y
Advair Diskus	100/50	Y	N	N
Advair HFA	115/21	Y	Y	Y
Advair HFA	230/21	Y	Y	Y
Advair HFA	45/21	Y	N	N
Symbicort [®]	80/4.5	Y	Y	Y
Symbicort [®]	160/4.5	Y	Y	Y
Breo	100/25	Y	Y	Y
Breo	200/25	Y	Y	Y
Dulera [®]	100/5	Y	Y	Y
Dulera [®]	200/5	Y	Y	Y
AirDuo RespiClick [®]	113/14	Y	Y	Y
AirDuo RespiClick [®]	232/14	Y	Y	Y
AirDuo RespiClick [®]	55/14	Y	N	N

HFA, hydrofluoroalkane; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist.

eTable 3: Ranking of States From Highest to Lowest Asthma Mortality Rate^a

State name	Population	Number of deaths	Crude death rate per 100,000	Age-adjusted death rate per 100,000
Mississippi	2988726	64	2.141	2.08
Oregon	4093465	68	1.661	1.45
Arkansas	2988248	44	1.472	1.40
Utah	3051217	33	1.082	1.33
Arizona	6931071	98	1.414	1.27
Nebraska	1907116	26	1.363	1.19
Kansas	2907289	39	1.341	1.19
Minnesota	5519952	72	1.304	1.18
New York	19745289	250	1.266	1.14
West Virginia	1831102	23	1.256	1.13
Missouri	6093000	69	1.132	1.12
New Mexico	2081015	23	1.105	1.08
Idaho	1683140	20	1.188	1.06
Tennessee	6651194	73	1.098	1.06
Maryland	6016447	66	1.097	1.03
Connecticut	3576452	41	1.146	1.03
Oklahoma	3923561	40	1.019	0.98
South Carolina	4961119	53	1.068	0.97
Massachusetts	6811779	80	1.174	0.96
Kentucky	4436974	45	1.014	0.96
Illinois	12801539	135	1.055	0.94
Wisconsin	5778708	62	1.073	0.93
Nevada	2940058	27	0.918	0.91
Ohio	11614373	120	1.033	0.90
North Carolina	10146788	93	0.917	0.87
New Jersey	8944469	86	0.961	0.85
Georgia	10310371	86	0.834	0.84
Iowa	3134693	32	1.021	0.84
California	39250017	356	0.907	0.84
Washington	7288000	68	0.933	0.83
Virginia	8411808	72	0.856	0.80
Colorado	5540545	44	0.794	0.80
Alabama	4863300	42	0.864	0.80
Michigan	9928300	83	0.836	0.78
Pennsylvania	12784227	116	0.907	0.74
Louisiana	4681666	36	0.769	0.73
Florida	20612439	164	0.796	0.64
Texas	27862596	171	0.614	0.62
Indiana	6633053	41	0.618	0.55
Alaska	741894	Suppressed	Suppressed	Suppressed
Delaware	952065	10	Unreliable	Unreliable

District of Columbia	681170	Suppressed	Suppressed	Suppressed
Hawaii	1428557	15	Unreliable	Unreliable
Maine	1331479	Suppressed	Suppressed	Suppressed
Montana	1042520	15	Unreliable	Unreliable
New Hampshire	1334795	11	Unreliable	Unreliable
North Dakota	757952	10	Unreliable	Unreliable
Rhode Island	1056426	Suppressed	Suppressed	Suppressed
South Dakota	865454	16	Unreliable	Unreliable
Vermont	624594	12	Unreliable	Unreliable
Wyoming	585501	Suppressed	Suppressed	Suppressed

^aThe age-adjusted mortality rate is per 100,000 in 2016. See eMethods for additional notes/data sources.

eTable 4: Ranking of States From Highest to Lowest Based on Percentage of Patients With SA Having SUA

State	SA	SUA2+	% SUA 2+	Percent rank
West Virginia	3745	1045	28%	1.00
Mississippi	3916	1091	28%	0.98
Louisiana	6927	1903	27%	0.96
Alabama	8538	2339	27%	0.94
Hawaii	1636	440	27%	0.92
Georgia	17,621	4683	27%	0.90
Connecticut	11,575	2982	26%	0.88
Tennessee	12,499	3202	26%	0.86
Indiana	14,613	3660	25%	0.84
Missouri	9803	2440	25%	0.82
Texas	41,911	10,208	24%	0.80
Massachusetts	14,699	3554	24%	0.78
North Carolina	17,037	4116	24%	0.76
Oklahoma	6498	1552	24%	0.74
Rhode Island	2825	673	24%	0.72
Arkansas	3255	774	24%	0.70
Ohio	30,626	7279	24%	0.68
Florida	31,630	7506	24%	0.66
Delaware	2473	583	24%	0.64
Virginia	16,499	3880	24%	0.62
Pennsylvania	32,840	7706	23%	0.60
Illinois	28,639	6712	23%	0.58
Kentucky	10,437	2431	23%	0.56
South Carolina	8960	2066	23%	0.54
Arizona	12,931	2971	23%	0.52
New Hampshire	2541	571	22%	0.50
Michigan	24,650	5423	22%	0.48
New Jersey	25,945	5674	22%	0.46
Minnesota	11,177	2440	22%	0.44
South Dakota	1619	353	22%	0.42
Maryland	15,234	3314	22%	0.40
Washington	9552	2077	22%	0.38
New Mexico	3291	713	22%	0.36
Kansas	5330	1144	21%	0.34
Wisconsin	14,568	3064	21%	0.32
New York	52,474	11,009	21%	0.30
Maine	4216	870	21%	0.28
Montana	2018	415	21%	0.26
Nevada	5322	1094	21%	0.24
Wyoming	918	180	20%	0.22

Colorado	12,209	2378	19%	0.20
District of Columbia	1911	369	19%	0.18
Idaho	2559	489	19%	0.16
Oregon	7610	1396	18%	0.14
Nebraska	4305	787	18%	0.12
Iowa	5845	1040	18%	0.10
Utah	5235	894	17%	0.08
California	51,080	8712	17%	0.06
Alaska	1450	235	16%	0.04
Vermont	1282	189	15%	0.02
North Dakota	1452	198	14%	0.00

Total asthma population: 4,506,527 with diagnosis of asthma between July 2015 and June 2018; ≥ 1 pharmacy claim for asthma controller medication or ≥ 2 pharmacy claims for SABA in 2016.

SA, severe asthma defined by age-specific controller medication dosages (see Methods).

SUA, severe asthma patients with ≥ 2 pharmacy claims for systemic corticosteroids in the 12 months post-index date.

eTable 5: Ranking of States From Highest to Lowest Based on Absolute Number of Patients With SUA

State	SA	SUA2+	Percent rank
New York	52,474	11,009	1.00
Texas	41,911	10,208	0.98
California	51,080	8712	0.96
Pennsylvania	32,840	7706	0.94
Florida	31,630	7506	0.92
Ohio	30,626	7279	0.90
Illinois	28,639	6712	0.88
New Jersey	25,945	5674	0.86
Michigan	24,650	5423	0.84
Georgia	17,621	4683	0.82
North Carolina	17,037	4116	0.80
Virginia	16,499	3880	0.78
Indiana	14,613	3660	0.76
Massachusetts	14,699	3554	0.74
Maryland	15,234	3314	0.72
Tennessee	12,499	3202	0.70
Wisconsin	14,568	3064	0.68
Connecticut	11,575	2982	0.66
Arizona	12,931	2971	0.64
Missouri	9803	2440	0.60
Minnesota	11,177	2440	0.60
Kentucky	10,437	2431	0.58
Colorado	12,209	2378	0.56
Alabama	8538	2339	0.54
Washington	9552	2077	0.52
South Carolina	8960	2066	0.50
Louisiana	6927	1903	0.48
Oklahoma	6498	1552	0.46
Oregon	7610	1396	0.44
Kansas	5330	1144	0.42
Nevada	5322	1094	0.40
Mississippi	3916	1091	0.38
West Virginia	3745	1045	0.36
Iowa	5845	1040	0.34
Utah	5235	894	0.32
Maine	4216	870	0.30
Nebraska	4305	787	0.28
Arkansas	3255	774	0.26
New Mexico	3291	713	0.24
Rhode Island	2825	673	0.22

Delaware	2473	583	0.20
New Hampshire	2541	571	0.18
Idaho	2559	489	0.16
Hawaii	1636	440	0.14
Montana	2018	415	0.12
District of Columbia	1911	369	0.10
South Dakota	1619	353	0.08
Alaska	1450	235	0.06
North Dakota	1452	198	0.04
Vermont	1282	189	0.02
Wyoming	918	180	0.00

Total asthma population: 4,506,527 with diagnosis of asthma between July 2015 and June 2018; ≥ 1 pharmacy claim for asthma controller medication or ≥ 2 pharmacy claims for SABA in 2016.

SA, severe asthma defined by age-specific controller medication dosages (see Methods).

SUA, severe asthma patients with ≥ 2 pharmacy claims for systemic corticosteroids in the 12 months post-index date.

eTable 6: List/Ranking of the 440 Counties in the 85th to 100th Percentile of Patients with SA Having SUA

County, State	SUA Patients	Percentage SUA
Cook, IL	2948	23%
Los Angeles, CA	2276	17%
Maricopa, AZ	2268	24%
Harris, TX	1490	24%
Nassau, NY	1337	23%
Dallas, TX	1293	24%
New York, NY	1259	19%
Tarrant, TX	1109	26%
Philadelphia, PA	1102	20%
Oakland, MI	1081	26%
Orange, CA	1070	20%
Hennepin, MN	1019	24%
Cuyahoga, OH	997	21%
Hartford, CT	997	27%
Franklin, OH	954	26%
New Haven, CT	938	28%
Bexar, TX	927	27%
Suffolk, NY	912	24%
Bronx, NY	895	23%
St. Louis, MO	883	28%
Hamilton, OH	880	27%
Miami-Dade, FL	867	20%
Clark, NV	828	21%
Fulton, GA	811	26%
Kings, NY	782	17%
Montgomery, PA	777	21%
Allegheny, PA	776	28%
King, WA	763	24%
Wayne, MI	748	22%
Jefferson, KY	741	21%
Milwaukee, WI	710	21%
Orange, FL	691	25%
Bergen, NJ	679	23%
DuPage, IL	657	26%
Queens, NY	656	17%
Broward, FL	654	24%
Middlesex, MA	646	22%
Mecklenburg, NC	641	26%
Oklahoma, OK	641	26%

Fairfield, CT	624	23%
San Diego, CA	622	18%
Marion, IN	620	27%
Palm Beach, FL	620	28%
Erie, NY	608	27%
Travis, TX	599	24%
Westchester, NY	592	21%
Jefferson, AL	588	27%
Macomb, MI	586	27%
Hillsborough, FL	584	23%
Collin, TX	576	25%
Wake, NC	574	22%
Baltimore, MD	572	21%
Shelby, TN	565	32%
Summit, OH	536	25%
Essex, NJ	525	21%
Delaware, PA	518	22%
Montgomery, MD	513	21%
Fairfax, VA	488	21%
Middlesex, NJ	488	21%
Duval, FL	478	24%
Lake, IL	473	22%
Gwinnett, GA	467	29%
Davidson, TN	466	26%
Salt Lake, UT	460	17%
Albany, NY	459	21%
Pima, AZ	453	22%
Lucas, OH	452	23%
Montgomery, OH	449	23%
Suffolk, MA	449	26%
Monmouth, NJ	448	20%
Denver, CO	442	21%
Worcester, MA	439	24%
Washtenaw, MI	438	23%
Camden, NJ	436	23%
Monroe, NY	435	29%
Fresno, CA	434	14%
Kent, MI	432	17%
Jackson, MO	431	22%
Johnson, KS	418	19%
New Castle, DE	416	23%
Bucks, PA	407	24%
Pinellas, FL	405	23%
Essex, MA	403	27%

Tulsa, OK	403	26%
Hamilton, TN	391	20%
Cobb, GA	386	28%
Lake, IN	382	28%
Providence, RI	381	23%
Knox, TN	378	24%
Hampden, MA	376	24%
Baltimore City, MD	369	21%
District of Columbia, DC	369	19%
Bernalillo, NM	368	24%
Burlington, NJ	364	23%
Allen, IN	361	21%
Santa Clara, CA	361	19%
Greenville, SC	344	21%
Bristol, MA	340	28%
Alameda, CA	335	21%
Lancaster, PA	333	20%
Prince Georges, MD	331	22%
Berks, PA	326	21%
Cumberland, ME	324	19%
Sacramento, CA	321	14%
Richmond, NY	316	23%
Union, NJ	315	23%
Anne Arundel, MD	309	23%
Chester, PA	307	23%
Contra Costa, CA	305	18%
Genesee, MI	304	23%
Passaic, NJ	304	22%
Hinds, MS	300	28%
Seminole, FL	299	26%
El Paso, CO	298	20%
Ventura, CA	297	17%
Guilford, NC	293	23%
Douglas, NE	291	21%
Onondaga, NY	290	19%
Butler, OH	288	26%
Lee, FL	286	26%
Charleston, SC	282	22%
East Baton Rouge, LA	282	27%
Forsyth, NC	282	23%
Orange, NY	279	22%
Honolulu, HI	275	28%

Jefferson, CO	275	19%
Madison, AL	275	31%
Norfolk, MA	272	22%
San Bernardino, CA	271	16%
St. Joseph, IN	271	25%
Multnomah, OR	270	18%
Hudson, NJ	268	19%
Mercer, NJ	268	22%
Morris, NJ	268	21%
Riverside, CA	264	17%
Fayette, KY	263	23%
Henrico, VA	263	24%
Ocean, NJ	261	23%
Jefferson, LA	258	29%
Lubbock, TX	257	28%
DeKalb, GA	256	23%
Ramsey, MN	256	23%
Sedgwick, KS	256	26%
Washington, OR	255	20%
Denton, TX	253	23%
Kane, IL	247	26%
Arapahoe, CO	246	19%
Dutchess, NY	245	22%
Pierce, WA	245	24%
Montgomery, TX	244	30%
Rockland, NY	244	25%
Lehigh, PA	242	24%
Waukesha, WI	242	18%
Will, IL	242	22%
Mobile, AL	237	24%
Gloucester, NJ	235	24%
Lancaster, NE	233	17%
Polk, IA	231	19%
York, PA	231	26%
Pulaski, AR	230	25%
Spokane, WA	229	20%
Kanawha, WV	227	28%
Nueces, TX	223	25%
Peoria, IL	222	22%
Brown, WI	221	22%
Atlantic, NJ	220	27%
Northampton, PA	214	25%
Ingham, MI	212	18%
Mahoning, OH	212	31%

Buncombe, NC	211	19%
Richmond City, VA	211	28%
Somerset, NJ	211	20%
El Paso, TX	209	22%
Minnehaha, SD	208	23%
San Francisco, CA	208	16%
Hillsborough, NH	204	29%
Plymouth, MA	204	26%
Ada, ID	201	18%
Polk, FL	200	27%
St. Louis City, MO	200	27%
Virginia Beach City, VA	199	22%
Winnebago, IL	198	25%
Richland, SC	197	22%
Frederick, MD	194	25%
Stark, OH	194	22%
Volusia, FL	194	27%
Montgomery, AL	192	29%
Larimer, CO	190	18%
Washoe, NV	190	19%
Barnstable, MA	185	27%
St. Tammany, LA	183	23%
Fort Bend, TX	182	24%
Kent, RI	182	26%
Leon, FL	181	21%
Outagamie, WI	181	20%
Richmond, GA	179	27%
Snohomish, WA	179	29%
Chatham, GA	178	24%
Howard, MD	176	21%
Lorain, OH	176	19%
San Joaquin, CA	176	15%
Washington, MD	175	26%
Sangamon, IL	174	21%
Lafayette, LA	171	29%
Chesterfield, VA	168	27%
Lackawanna, PA	168	32%
Orleans, LA	168	29%
Adams, CO	166	20%
Dane, WI	166	27%
Hidalgo, TX	164	23%
Dakota, MN	162	25%
Marion, OR	162	22%

Hall, GA	159	24%
Osceola, FL	159	26%
Sarasota, FL	158	23%
Cabell, WV	157	33%
Luzerne, PA	155	27%
Champaign, IL	153	26%
Williamson, TX	153	21%
Williamson, TN	152	24%
Boulder, CO	150	17%
St. Charles, MO	150	26%
Monterey, CA	149	19%
Placer, CA	149	20%
San Mateo, CA	149	15%
Saratoga, NY	149	21%
Smith, TX	148	22%
Escambia, FL	147	22%
Kern, CA	145	16%
Winnebago, WI	145	20%
Norfolk City, VA	144	23%
Fredericksburg City, VA	143	26%
Racine, WI	143	24%
Rutherford, TN	143	27%
New London, CT	139	23%
Alachua, FL	138	22%
Warren, NY	138	32%
Pasco, FL	136	22%
Clarke, GA	135	28%
Durham, NC	135	21%
Hamilton, IN	135	26%
Cumberland, PA	133	26%
Hampshire, MA	133	20%
Kalamazoo, MI	132	21%
Lexington, SC	132	26%
Potter, TX	132	20%
Tippecanoe, IN	132	27%
Bibb, GA	130	28%
Lake, OH	130	20%
York, ME	130	24%
Lake, FL	129	30%
Penobscot, ME	129	24%
Cherokee, GA	127	27%
Loudoun, VA	127	18%
Lane, OR	126	12%

Warren, KY	126	19%
Westmoreland, PA	126	25%
Brevard, FL	125	27%
McHenry, IL	125	19%
Anchorage, AK	124	16%
Centre, PA	124	33%
Scott, IA	124	19%
Spartanburg, SC	124	23%
Prince William, VA	123	27%
Vanderburgh, IN	123	32%
Dauphin, PA	122	22%
Florence, SC	121	33%
Carroll, MD	120	26%
Douglas, CO	120	20%
Henry, GA	120	33%
Houston, AL	120	29%
Harford, MD	118	22%
Schenectady, NY	118	17%
Kenosha, WI	117	22%
St. Clair, IL	117	26%
Tuscaloosa, AL	117	26%
Marathon, WI	116	23%
Cleveland, OK	114	24%
Pueblo, CO	114	25%
Rockingham, NH	114	14%
Clark, WA	113	20%
Collier, FL	113	28%
Anoka, MN	112	21%
Davis, UT	112	17%
Ottawa, MI	112	16%
Santa Cruz, CA	112	20%
Horry, SC	111	26%
Johnson, IN	110	28%
Broome, NY	109	24%
Cumberland, NC	109	20%
Muscogee, GA	109	20%
Santa Barbara, CA	109	17%
Sumner, TN	109	30%
Tulare, CA	109	17%
Catawba, NC	108	24%
Clay, MO	108	24%
Galveston, TX	107	23%
Bartholomew, IN	106	32%
Jackson, OR	106	26%

Monroe, PA	106	24%
Sullivan, TN	106	24%
Winchester City, VA	105	26%
Kenton, KY	104	24%
York, SC	104	30%
Hunterdon, NJ	103	19%
Bell, TX	102	28%
Erie, PA	102	22%
Marion, FL	102	22%
Warren, OH	102	25%
Cabarrus, NC	101	31%
Stanislaus, CA	101	16%
Saginaw, MI	100	25%
Sonoma, CA	100	25%
St. Clair, MI	99	29%
Baldwin, AL	98	28%
Hanover, VA	98	29%
La Crosse, WI	98	27%
Trumbull, OH	98	28%
Oneida, NY	97	19%
Washington, TN	97	26%
Weld, CO	97	25%
Caddo, LA	96	25%
Niagara, NY	96	22%
Rensselaer, NY	96	21%
Deschutes, OR	95	19%
Greene, MO	95	23%
Lee, MS	95	32%
Madison, IL	95	21%
Fairfield, OH	94	32%
Linn, IA	94	23%
Manatee, FL	94	23%
New Hanover, NC	94	24%
Washington, PA	94	28%
Blair, PA	93	22%
Forsyth, GA	93	27%
Madison, IN	93	33%
Floyd, GA	92	30%
Beaver, PA	91	29%
Chesapeake City, VA	91	21%
Washington, MN	91	26%
Clackamas, OR	90	19%
Olmsted, MN	90	21%
Delaware, OH	89	30%

Elkhart, IN	89	19%
Fayette, GA	89	23%
Jefferson, TX	89	26%
Thurston, WA	89	21%
Monroe, IN	88	18%
St. Louis, MN	88	17%
Sussex, DE	88	23%
Macon, IL	87	22%
McLean, IL	87	29%
Ouachita, LA	87	28%
Cumberland, NJ	86	23%
Gregg, TX	86	22%
Johnson, IA	86	22%
Yellowstone, MT	86	21%
Rapides, LA	85	29%
Utah, UT	85	19%
Clermont, OH	84	29%
Dougherty, GA	84	32%
Gaston, NC	84	27%
Lynchburg City, VA	84	22%
Tolland, CT	84	25%
Chittenden, VT	83	13%
Merrimack, NH	83	28%
Mesa, CO	83	15%
Benton, AR	82	24%
Monongalia, WV	82	24%
Clark, OH	81	28%
Kootenai, ID	81	25%
Pitt, NC	81	31%
Chautauqua, NY	80	23%
San Luis Obispo, CA	80	12%
Weber, UT	80	13%
Anderson, SC	79	24%
Boone, KY	79	27%
Calcasieu, LA	79	31%
Dona Ana, NM	79	22%
Greene, OH	79	23%
Kent, DE	79	27%
Muskegon, MI	79	22%
Benton, WA	78	15%
Dorchester, SC	78	19%
Orange, NC	77	28%
Rock Island, IL	77	21%
Androscoggin, ME	76	23%

Hampton City, VA	76	25%
Hardin, KY	76	21%
Fairfax City, VA	75	20%
Boyd, KY	74	35%
Hawaii, HI	74	23%
McLennan, TX	74	20%
Middlesex, CT	74	22%
Santa Fe, NM	74	20%
Shelby, AL	74	24%
Berkshire, MA	73	20%
Cambria, PA	73	27%
Carroll, GA	73	25%
Clayton, GA	73	28%
Daviess, KY	73	37%
Forrest, MS	73	35%
Montour, PA	73	37%
Brazoria, TX	72	23%
DeSoto, MS	72	30%
Indian River, FL	72	27%
Nash, NC	72	30%
Newport News City, VA	72	24%
Union, NC	72	34%
Yavapai, AZ	72	24%
Medina, OH	71	16%
Litchfield, CT	70	23%
Sussex, NJ	70	19%
Floyd, IN	69	18%
Porter, IN	69	23%
Reno, KS	69	24%
Allegany, MD	68	22%
Cameron, TX	68	24%
Eau Claire, WI	68	22%
Hendricks, IN	68	28%
Rockdale, GA	68	32%
Taylor, TX	68	23%
Wyandotte, KS	68	24%
Blue Earth, MN	67	20%
Charlotte, FL	67	29%
Lee, AL	67	22%
Sheboygan, WI	67	16%
Wicomico, MD	67	24%
Cascade, MT	66	27%
Kennebec, ME	66	19%

Washington, AR	66	21%
Washington, WI	66	21%
Bay, MI	65	26%
McCracken, KY	64	29%
Vigo, IN	64	25%
Ellis, TX	63	32%
Iredell, NC	63	26%
Kankakee, IL	63	21%
Maui, HI	63	27%
Moore, NC	63	28%

Total asthma population: 4,506,527 with diagnosis of asthma between July 2015 and June 2018; ≥ 1 pharmacy claim for asthma controller medication or ≥ 2 pharmacy claims for SABA in 2016.

SA, severe asthma defined by age-specific controller medication dosages (see Methods).

UA, uncontrolled asthma defined by ≥ 2 pharmacy claims for systemic corticosteroids in the 12 months post-index date.

eTable 7: List/Ranking of the 414 Counties in the 85th to 100th Percentile of Age-adjusted Mortality Rate^a

County, State	Deaths	Population	Crude rate	Age-adjusted mortality rate per 100,000
Holmes County, MS	26	390,145	6.7	6.6
Phillips County, AR	21	446,597	4.7	4.4
Washington County, MS	43	1,066,007	4.0	4
Bronx County, NY	1006	27,727,811	3.6	3.8
Sunflower County, MS	21	605,000	3.5	3.7
Miller County, AR	34	852,357	4.0	3.6
Crittenden County, AR	34	1,002,157	3.4	3.5
Buena Vista County, IA	20	404,282	4.9	3.5
Bolivar County, MS	24	711,573	3.4	3.4
Orangeburg County, SC	65	1,820,251	3.6	3.2
Adams County, MS	24	651,600	3.7	3.2
Iosco County, MI	23	524,192	4.4	3.2
Leflore County, MS	21	662,796	3.2	3.2
Baltimore city, MD	384	12,497,715	3.1	3.1
St. Louis city, MO	194	647,5681	3.0	3.0
Richmond city, VA	124	413,9720	3.0	3.0
Colquitt County, GA	25	887,686	2.8	2.9
Beaufort County, NC	30	932,810	3.2	2.8
Petersburg city, VA	20	649,396	3.1	2.8
Umatilla County, OR	39	1,491,562	2.6	2.5
Monroe County, MS	21	739,321	2.8	2.5
Merced County, CA	96	4,961,784	1.9	2.4
Faulkner County, AR	41	2,147,839	1.9	2.4
Lamar County, TX	27	986,609	2.7	2.4
Montgomery County, AL	105	4,522,497	2.3	2.3
Coos County, OR	35	1,261,746	2.8	2.3
Klamath County, OR	34	1,313,692	2.6	2.3
Pike County, MS	21	792,085	2.7	2.3
Essex County, NJ	350	15,810,730	2.2	2.2
Wilson County, NC	36	1,575,454	2.3	2.2
Muskogee County, OK	33	1,396,976	2.4	2.2
Siskiyou County, CA	23	884,162	2.6	2.2
Brown County, TX	20	758,793	2.6	2.2
Robeson County, NC	51	2,604,825	2.0	2.1
Jefferson County, OH	36	1,398,399	2.6	2.1
Sampson County, NC	28	1,248,823	2.2	2.1
Halifax County, NC	25	1,093,567	2.3	2.1
Dallas County, AL	20	867,923	2.3	2.1
Cook County, IL	2064	1.05E+08	2.0	2.0

Kings County, NY	967	50,388,367	1.9	2.0
Montgomery County, TN	53	3,323,910	1.6	2.0
Houston County, AL	41	1,960,022	2.1	2.0
Sutter County, CA	37	1,814,101	2.0	2.0
Forrest County, MS	28	1,483,791	1.9	2.0
Chaves County, NM	26	1,275,210	2.0	2.0
Blue Earth County, MN	24	1,244,105	1.9	2.0
St. Mary Parish, LA	23	1,065,518	2.2	2.0
Warren County, MS	20	969,221	2.1	2.0
New York County, NY	641	31,870,648	2.0	1.9
Hinds County, MS	90	4,917,533	1.8	1.9
Racine County, WI	77	3,868,818	2.0	1.9
Bibb County, GA	60	3,085,317	1.9	1.9
Ector County, TX	45	2,747,740	1.6	1.9
Craven County, NC	44	1,979,963	2.2	1.9
Portsmouth city, VA	39	1,940,288	2.0	1.9
Fremont County, CO	24	937,098	2.6	1.9
Kershaw County, SC	24	1,187,374	2.0	1.9
Lenoir County, NC	23	1,176,476	2.0	1.9
Gibson County, TN	21	976,168	2.2	1.9
Ravalli County, MT	20	793,392	2.5	1.9
Wayne County, MI	705	37,659,231	1.9	1.8
Philadelphia County, PA	560	30,539,412	1.8	1.8
Orleans Parish, LA	149	7,958,348	1.9	1.8
Norfolk city, VA	77	4,839,512	1.6	1.8
Maui County, HI	59	2,996,896	2.0	1.8
Florence County, SC	49	2,676,618	1.8	1.8
Rockingham County, NC	39	1,847,613	2.1	1.8
Marquette County, MI	28	1,325,400	2.1	1.8
Salem County, NJ	28	1,296,346	2.2	1.8
Rutherford County, NC	28	1,316,579	2.1	1.8
Stephenson County, IL	23	948,148	2.4	1.8
Hall County, NE	23	1,150,149	2.0	1.8
Lake County, IN	178	9,787,591	1.8	1.7
Douglas County, NE	166	10,207,508	1.6	1.7
Utah County, UT	94	9,772,963	1.0	1.7
Cumberland County, NC	91	6,310,332	1.4	1.7
Hampton city, VA	48	2,782,126	1.7	1.7
Pitt County, NC	47	3,187,691	1.5	1.7
Linn County, OR	46	2,277,319	2.0	1.7
Cowlitz County, WA	42	1,999,416	2.1	1.7
Sumter County, SC	38	2,129,454	1.8	1.7
Walworth County, WI	37	2,003,574	1.8	1.7
Twin Falls County, ID	30	1,492,312	2.0	1.7

Wayne County, IN	30	1,378,195	2.2	1.7
Grays Harbor County, WA	29	1,415,739	2.0	1.7
Jefferson County, AR	27	1,546,328	1.7	1.7
Matanuska-Susitna Borough, AK	26	1,674,179	1.6	1.7
Chippewa County, WI	25	1,212,564	2.1	1.7
Darlington County, SC	24	1,359,348	1.8	1.7
Jones County, MS	23	1,337,744	1.7	1.7
Bastrop County, TX	23	1,439,193	1.6	1.7
Washington County, VT	23	1,178,426	2.0	1.7
Jackson County, AL	20	1,062,839	1.9	1.7
San Bernardino County, CA	533	39,604,783	1.3	1.6
Shelby County, TN	290	18,434,466	1.6	1.6
Fresno County, CA	261	18,104,122	1.4	1.6
Salt Lake County, UT	249	20,223,070	1.2	1.6
Lane County, OR	127	6,940,892	1.8	1.6
Marion County, OR	107	6,232,007	1.7	1.6
St. Clair County, IL	89	5,262,114	1.7	1.6
Caddo Parish, LA	82	5,025,816	1.6	1.6
St. Louis County, MN	80	3,999,998	2.0	1.6
Jackson County, OR	79	4,006,678	2.0	1.6
Saginaw County, MI	74	4,033,132	1.8	1.6
Clayton County, GA	67	5,212,959	1.3	1.6
Weld County, CO	63	4,878,563	1.3	1.6
Wyandotte County, KS	50	3,171,392	1.6	1.6
Douglas County, OR	47	2,115,352	2.2	1.6
Madera County, CA	41	2,883,583	1.4	1.6
Skagit County, WA	40	2,292,697	1.7	1.6
Brazos County, TX	37	3,738,652	1.0	1.6
Dorchester County, SC	35	2,563,596	1.4	1.6
Lowndes County, GA	31	2,095,139	1.5	1.6
Dougherty County, GA	30	1,877,173	1.6	1.6
Suffolk city, VA	26	1,602,096	1.6	1.6
Grant County, IN	25	1,401,995	1.8	1.6
Christian County, KY	20	1,455,635	1.4	1.6
Hamilton County, OH	263	16,292,587	1.6	1.5
Duval County, FL	251	17,135,803	1.5	1.5
Suffolk County, MA	194	14,542,088	1.3	1.5
Spokane County, WA	152	9,219,209	1.6	1.5
Tulare County, CA	108	8,490,142	1.3	1.5
Lancaster County, NE	81	5,633,563	1.4	1.5
Shasta County, CA	61	3,504,265	1.7	1.5
Davis County, UT	57	5,884,609	1.0	1.5
Muscogee County, GA	55	3,816,102	1.4	1.5
Washington County, MD	51	2,878,845	1.8	1.5

Rock County, WI	50	3,168,146	1.6	1.5
Minnehaha County, SD	49	3,355,710	1.5	1.5
Berkeley County, SC	45	3,496,497	1.3	1.5
Humboldt County, CA	44	2,650,955	1.7	1.5
Clark County, OH	43	2,785,955	1.5	1.5
Taylor County, TX	38	2,613,223	1.5	1.5
Wichita County, TX	38	2,627,275	1.4	1.5
Ellis County, TX	36	2,855,727	1.3	1.5
Delaware County, IN	35	2,353,530	1.5	1.5
Dubuque County, IA	35	1,859,727	1.9	1.5
Terrebonne Parish, LA	31	2,196,652	1.4	1.5
Madison County, MS	28	1,826,035	1.5	1.5
Lewis County, WA	28	1,474,478	1.9	1.5
Reno County, KS	27	1,279,009	2.1	1.5
Harrison County, WV	25	1,368,005	1.8	1.5
Kauai County, HI	24	1,312,891	1.8	1.5
Spalding County, GA	21	1,249,735	1.7	1.5
Lawrence County, OH	21	1,239,033	1.7	1.5
Creek County, OK	21	1,386,125	1.5	1.5
Cache County, UT	21	2,161,614	1.0	1.5
Colbert County, AL	20	1,090,125	1.8	1.5
Washington County, VA	20	1,071,103	1.9	1.5
Alameda County, CA	437	30,420,360	1.4	1.4
Sacramento County, CA	392	27,926,092	1.4	1.4
Pima County, AZ	299	19,005,257	1.6	1.4
Contra Costa County, CA	297	20,846,589	1.4	1.4
Milwaukee County, WI	270	18,885,325	1.4	1.4
Marion County, IN	241	17,993,246	1.3	1.4
Fulton County, GA	232	18,162,309	1.3	1.4
Jefferson County, AL	201	13,173,132	1.5	1.4
Jackson County, MO	186	13,429,975	1.4	1.4
District of Columbia, DC	173	12,218,084	1.4	1.4
Lucas County, OH	129	8,871,144	1.5	1.4
Anchorage Borough, AK	64	5,672,535	1.1	1.4
Sangamon County, IL	63	3,894,593	1.6	1.4
Richmond County, GA	55	3,991,323	1.4	1.4
Weber County, UT	55	4,479,251	1.2	1.4
Berrien County, MI	53	3,151,510	1.7	1.4
Pueblo County, CO	48	3,106,838	1.5	1.4
Lycoming County, PA	39	2,338,873	1.7	1.4
Gregg County, TX	33	2,375,835	1.4	1.4
Potter County, TX	32	2,380,615	1.3	1.4
Garland County, AR	31	1,884,888	1.6	1.4
Muskingum County, OH	27	1,713,327	1.6	1.4

Berkeley County, WV	27	1,968,068	1.4	1.4
St. Mary's County, MD	26	2,028,826	1.3	1.4
Talladega County, AL	25	1,624,530	1.5	1.4
Lauderdale County, MS	23	1,571,860	1.5	1.4
Valencia County, NM	22	1,457,395	1.5	1.4
Belknap County, NH	20	1,192,975	1.7	1.4
Hamblen County, TN	20	1,227,704	1.6	1.4
Rutland County, VT	20	1,233,023	1.6	1.4
Honolulu County, HI	279	18,806,377	1.5	1.3
Multnomah County, OR	191	14,508,544	1.3	1.3
San Joaquin County, CA	159	13,385,258	1.2	1.3
Hudson County, NJ	158	12,742,266	1.2	1.3
Denver County, CO	142	12,127,773	1.2	1.3
Ramsey County, MN	133	10,334,405	1.3	1.3
Stanislaus County, CA	120	10,129,730	1.2	1.3
Pulaski County, AR	97	7,565,325	1.3	1.3
Adams County, CO	89	8,628,924	1.0	1.3
Richland County, SC	89	7,416,749	1.2	1.3
Henrico County, VA	82	5,974,291	1.4	1.3
Yavapai County, AZ	74	4,058,545	1.8	1.3
Lackawanna County, PA	72	4,256,715	1.7	1.3
Kitsap County, WA	67	4,970,468	1.3	1.3
Boulder County, CO	66	5,988,242	1.1	1.3
Thurston County, WA	65	4,882,388	1.3	1.3
Lubbock County, TX	63	5,462,714	1.2	1.3
Kanawha County, WV	61	3,849,151	1.6	1.3
York County, SC	51	4,289,212	1.2	1.3
Peoria County, IL	49	3,690,743	1.3	1.3
Monroe County, PA	45	3,223,019	1.4	1.3
Kootenai County, ID	40	2,676,454	1.5	1.3
Madison County, IN	40	2,623,529	1.5	1.3
Johnson County, TX	38	2,948,083	1.3	1.3
Columbiana County, OH	33	2,161,077	1.5	1.3
Alexandria city, VA	33	2,789,101	1.2	1.3
Sandoval County, NM	31	2,410,777	1.3	1.3
Lee County, AL	30	2,743,639	1.1	1.3
Kings County, CA	30	2,916,248	1.0	1.3
Allen County, OH	30	2,123,467	1.4	1.3
Josephine County, OR	30	1,632,247	1.8	1.3
San Juan County, NM	28	2,461,378	1.1	1.3
Eau Claire County, WI	28	1,961,892	1.4	1.3
Roanoke city, VA	27	1,930,912	1.4	1.3
Missoula County, MT	26	2,138,598	1.2	1.3
Warren County, KY	24	2,201,643	1.1	1.3

Chelan County, WA	24	1,425,463	1.7	1.3
Clinton County, NY	23	1,628,961	1.4	1.3
Lynchburg city, VA	23	1,465,565	1.6	1.3
Putnam County, FL	21	1,458,999	1.4	1.3
Los Angeles County, CA	2153	1.97E+08	1.1	1.2
Cuyahoga County, OH	359	26,112,068	1.4	1.2
Hennepin County, MN	279	23,236,512	1.2	1.2
St. Louis County, MO	255	20,081,963	1.3	1.2
Prince George's County, MD	204	17,237,976	1.2	1.2
Oklahoma County, OK	168	14,342,755	1.2	1.2
Davidson County, TN	147	12,456,321	1.2	1.2
Tulsa County, OK	142	11,963,070	1.2	1.2
Passaic County, NJ	130	9,982,084	1.3	1.2
Hampden County, MA	126	9,265,346	1.4	1.2
Sedgwick County, KS	117	9,715,792	1.2	1.2
Greenville County, SC	111	8,807,763	1.3	1.2
Genesee County, MI	109	8,544,561	1.3	1.2
Mobile County, AL	100	8,149,298	1.2	1.2
Clackamas County, OR	99	7,470,894	1.3	1.2
Solano County, CA	97	8,331,290	1.2	1.2
Monterey County, CA	91	8,324,693	1.1	1.2
Escambia County, FL	80	6,039,694	1.3	1.2
Atlantic County, NJ	71	5,366,386	1.3	1.2
Galveston County, TX	69	5,795,628	1.2	1.2
Santa Cruz County, CA	66	5,231,698	1.3	1.2
Broome County, NY	63	3,979,730	1.6	1.2
Lexington County, SC	60	5,069,691	1.2	1.2
McLennan County, TX	58	4,628,105	1.3	1.2
Yakima County, WA	58	4,741,735	1.2	1.2
Leon County, FL	54	5,362,190	1.0	1.2
Mohave County, AZ	51	3,808,477	1.3	1.2
Anderson County, SC	49	3,659,913	1.3	1.2
Dona Ana County, NM	48	3,983,539	1.2	1.2
Chesapeake city, VA	47	4,404,851	1.1	1.2
Rensselaer County, NY	42	3,148,065	1.3	1.2
Merrimack County, NH	41	2,899,708	1.4	1.2
Cumberland County, NJ	40	3,056,561	1.3	1.2
Newport News city, VA	40	3,634,228	1.1	1.2
Licking County, OH	39	3,236,135	1.2	1.2
Washington County, UT	39	2,614,844	1.5	1.2
Benton County, WA	38	3,398,543	1.1	1.2
Kent County, DE	37	3,093,478	1.2	1.2
Black Hawk County, IA	37	2,596,990	1.4	1.2
Santa Fe County, NM	36	2,822,912	1.3	1.2

Ouachita Parish, LA	34	3,044,040	1.1	1.2
Charles County, MD	31	2,859,426	1.1	1.2
Windham County, CT	30	2,306,345	1.3	1.2
Kankakee County, IL	29	2,188,582	1.3	1.2
Onslow County, NC	29	3,416,121	0.8	1.2
Saline County, AR	27	2,051,428	1.3	1.2
Woodbury County, IA	27	2,043,527	1.3	1.2
Parker County, TX	26	2,229,008	1.2	1.2
Burke County, NC	25	1,795,985	1.4	1.2
Dodge County, WI	25	1,759,122	1.4	1.2
Wood County, WV	24	1,733,942	1.4	1.2
Carroll County, GA	23	2,119,193	1.1	1.2
Cecil County, MD	23	1,951,768	1.2	1.2
Cascade County, MT	23	1,618,965	1.4	1.2
Flagler County, FL	22	1,712,522	1.3	1.2
Clarke County, GA	22	2,294,020	1.0	1.2
Bonneville County, ID	22	1,984,207	1.1	1.2
Polk County, OR	22	1,457,731	1.5	1.2
Glynn County, GA	21	1,539,056	1.4	1.2
Vermilion County, IL	21	1,628,458	1.3	1.2
Crow Wing County, MN	21	1,216,623	1.7	1.2
Orange County, TX	21	1,668,077	1.3	1.2
Victoria County, TX	21	1,746,851	1.2	1.2
Franklin County, MA	20	1,427,384	1.4	1.2
Jefferson County, WI	20	1,630,113	1.2	1.2
Queens County, NY	521	44,933,313	1.2	1.1
Dallas County, TX	437	47,506,558	0.9	1.1
Tarrant County, TX	325	35,062,294	0.9	1.1
Franklin County, OH	231	23,241,798	1.0	1.1
Hartford County, CT	218	17,670,065	1.2	1.1
San Mateo County, CA	191	14,451,528	1.3	1.1
Baltimore County, MD	187	15,983,709	1.2	1.1
Ventura County, CA	179	16,221,018	1.1	1.1
Pierce County, WA	162	15,717,859	1.0	1.1
Kern County, CA	151	15,978,315	0.9	1.1
DeKalb County, GA	146	13,919,861	1.0	1.1
Montgomery County, OH	133	10,838,803	1.2	1.1
Camden County, NJ	123	10,220,710	1.2	1.1
Berks County, PA	109	8,033,742	1.4	1.1
Arapahoe County, CO	107	11,268,784	0.9	1.1
Richmond County, NY	103	9,263,049	1.1	1.1
Marion County, FL	90	6,309,923	1.4	1.1
Clark County, WA	84	8,283,643	1.0	1.1
Orange County, NY	81	7,337,403	1.1	1.1

Hamilton County, TN	81	6,651,326	1.2	1.1
Charleston County, SC	79	7,011,247	1.1	1.1
Pinal County, AZ	74	6,303,557	1.2	1.1
Nueces County, TX	70	6,738,595	1.0	1.1
Mahoning County, OH	65	4,845,029	1.3	1.1
St. Joseph County, IN	62	5,334,008	1.2	1.1
Oneida County, NY	62	4,673,979	1.3	1.1
Anoka County, MN	60	6,537,053	0.9	1.1
Dauphin County, PA	60	5,283,940	1.1	1.1
Frederick County, MD	49	4,558,477	1.1	1.1
Linn County, IA	46	4,160,790	1.1	1.1
Clay County, MO	46	4,290,938	1.1	1.1
Washington County, MN	44	4,629,216	1.0	1.1
St. Clair County, MI	43	3,272,906	1.3	1.1
Sullivan County, TN	43	3,106,826	1.4	1.1
Shawnee County, KS	42	3,499,207	1.2	1.1
Outagamie County, WI	40	3,486,163	1.1	1.1
Rock Island County, IL	39	2,943,281	1.3	1.1
Clermont County, OH	39	3,868,565	1.0	1.1
Hampshire County, MA	38	3,146,073	1.2	1.1
Davidson County, NC	38	3,174,940	1.2	1.1
Scott County, IA	37	3,286,820	1.1	1.1
Porter County, IN	36	3,200,608	1.1	1.1
Aiken County, SC	36	3,124,699	1.2	1.1
Kenosha County, WI	36	3,244,646	1.1	1.1
Mesa County, CO	35	2,761,871	1.3	1.1
Yellowstone County, MT	35	2,893,974	1.2	1.1
Monroe County, MI	34	3,005,553	1.1	1.1
Stearns County, MN	32	2,932,108	1.1	1.1
Nevada County, CA	30	1,943,051	1.5	1.1
LaSalle County, IL	30	2,243,288	1.3	1.1
Moore County, NC	28	1,720,635	1.6	1.1
Rankin County, MS	27	2,730,467	1.0	1.1
Sarpy County, NE	27	3,058,737	0.9	1.1
Bay County, MI	26	2,154,797	1.2	1.1
Comal County, TX	26	2,116,351	1.2	1.1
Lenawee County, MI	25	1,995,972	1.3	1.1
Mendocino County, CA	24	1,748,676	1.4	1.1
Clark County, IN	24	2,141,832	1.1	1.1
Comanche County, OK	24	2,389,490	1.0	1.1
Coweta County, GA	23	2,383,956	1.0	1.1
Ashtabula County, OH	23	2,020,790	1.1	1.1
Wright County, MN	22	2,340,818	0.9	1.1
Coconino County, AZ	21	2,613,508	0.8	1.1

Hunt County, TX	20	1,701,610	1.2	1.1
Laramie County, WY	20	1,801,278	1.1	1.1
Maricopa County, AZ	764	74,588,439	1.0	1.0
King County, WA	366	38,492,591	1.0	1.0
Santa Clara County, CA	329	35,521,209	0.9	1.0
Hillsborough County, FL	238	24,116,664	1.0	1.0
New Haven County, CT	197	17,007,803	1.2	1.0
San Francisco County, CA	192	16,173,141	1.2	1.0
Worcester County, MA	173	15,842,584	1.1	1.0
Snohomish County, WA	134	13,998,414	1.0	1.0
Summit County, OH	129	10,855,076	1.2	1.0
Volusia County, FL	127	9,834,174	1.3	1.0
Bristol County, MA	126	10,964,014	1.1	1.0
Bernalillo County, NM	126	12,688,915	1.0	1.0
Union County, NJ	117	10,741,992	1.1	1.0
New Castle County, DE	113	10,660,051	1.1	1.0
Washington County, OR	103	10,386,556	1.0	1.0
El Paso County, CO	99	12,147,608	0.8	1.0
Guilford County, NC	96	9,515,165	1.0	1.0
Stark County, OH	85	7,515,924	1.1	1.0
Mercer County, NJ	77	7,277,164	1.1	1.0
Forsyth County, NC	71	6,846,276	1.0	1.0
Albany County, NY	66	6,069,444	1.1	1.0
Northampton County, PA	66	5,800,269	1.1	1.0
Lorain County, OH	64	5,955,927	1.1	1.0
Washtenaw County, MI	59	6,911,922	0.9	1.0
Winnebago County, IL	58	5,747,166	1.0	1.0
St. Lucie County, FL	57	5,201,940	1.1	1.0
Madison County, IL	56	5,302,222	1.1	1.0
Spartanburg County, SC	56	5,577,204	1.0	1.0
Butte County, CA	55	4,353,129	1.3	1.0
Ingham County, MI	53	5,665,347	0.9	1.0
Jefferson County, TX	53	5,032,413	1.1	1.0
Trumbull County, OH	49	4,253,174	1.2	1.0
Gaston County, NC	43	4,061,711	1.1	1.0
Whatcom County, WA	42	3,901,791	1.1	1.0
Hawaii County, HI	38	3,550,108	1.1	1.0
Vanderburgh County, IN	37	3,556,642	1.0	1.0
Elkhart County, IN	36	3,904,521	0.9	1.0
Fayette County, PA	34	2,781,415	1.2	1.0
Calhoun County, MI	32	2,733,522	1.2	1.0
Alamance County, NC	32	2,940,202	1.1	1.0
Iredell County, NC	30	3,035,162	1.0	1.0
Richland County, OH	30	2,503,363	1.2	1.0

Kennebec County, ME	29	2,411,374	1.2	1.0
Johnston County, NC	29	3,205,354	0.9	1.0
Cass County, ND	29	2,961,451	1.0	1.0
Imperial County, CA	28	3,305,085	0.8	1.0
Boone County, MO	28	3,162,806	0.9	1.0
Sussex County, NJ	28	2,935,531	1.0	1.0
Etowah County, AL	26	2,070,034	1.3	1.0
Sebastian County, AR	26	2,456,422	1.1	1.0
Wayne County, NC	26	2,395,742	1.1	1.0
Grayson County, TX	26	2,393,781	1.1	1.0
Androscoggin County, ME	24	2,136,298	1.1	1.0
Adams County, PA	23	1,979,503	1.2	1.0
Tom Green County, TX	23	2,198,836	1.0	1.0
Clallam County, WA	23	1,403,815	1.6	1.0
Daviess County, KY	22	1,913,642	1.1	1.0
Pottawattamie County, IA	21	1,825,937	1.2	1.0
Cleveland County, NC	21	1,943,774	1.1	1.0
Pennington County, SD	21	1,984,337	1.1	1.0
Cabell County, WV	21	1,917,613	1.1	1.0
Johnson County, IA	20	2,581,869	0.8	1.0
Wicomico County, MD	20	1,909,836	1.0	1.0
Grafton County, NH	20	1,740,885	1.1	1.0
Manitowoc County, WI	20	1,625,032	1.2	1.0

^aSee eMethods for notes/data sources.