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Geographic variation in inhaled corticosteroid use

Geographic variation in inhaled corticosteroid use for children with persistent asthma in Medicaid

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ABSTRACT

Objective: Geographic variation in the rates of inhaled corticosteroid (ICS) use for children with persistent asthma in Medicaid has been reported, but the source of the variation is unknown. The objective of this study was to quantify the geographic variation in ICS use for children with persistent asthma in Medicaid that remains after adjusting for the characteristics of children in an area. *Methods:*

Data from the 2005--2007 Medicaid Analytic eXtract files were used. Frequent fills of short-acting beta₂-agonist (SABA) were used to identify children 5--18 years old with persistent asthma across the United States. A child was considered to have used an ICS if the child initially filled an ICS following frequent SABA use. Areas were determined using published methods, and the unadjusted ICS rate and the area treatment ratio for ICS, which adjusted for demographic and clinical characteristics, were calculated for each area. *Results:* Of 15,917 children, 13% used an ICS. The median unadjusted ICS rate for all areas was 10% but ranged from 0--64%. ICS use was less than expected for more than half of the areas based on the characteristics of the children in the area, but use was nearly five times what was expected in some areas. Areas with higher than expected ICS use were found contiguous to areas with lower than expected use.

Conclusions: Geographic variation in ICS not attributable to the demographic and clinical characteristics of the children in an area exists and could prove useful in the struggle to reduce asthma exacerbation rates.

KEYWORDS

Pediatrics; pharmacotherapy; treatment; management/control; rhinitis/sinusitis

Introduction

Inhaled corticosteroids (ICS) reduce the frequency of asthma symptoms and risk of severe asthma exacerbations [1, 2]. They are the preferred controller medication for mild persistent asthma due to their efficacy over other medications and are the backbone of all preferred regimens for moderate and severe persistent asthma according to national guidelines [3]. Yet ICS have drawbacks. Children and adults struggle to administer inhaled medications correctly [4-7]. Strong concerns about adverse effects related to ICS are reported by 21--43% of adults and parents [8-12], and these concerns have been linked to ICS adherence [9] and asthma control [13]. Concerns about ICS safety extend to clinicians and influence their prescribing decisions [14]. Subsequently, only a portion of children with persistent asthma are treated with ICS. Sixty-seven percent of children with persistent asthma in one state Medicaid program used an ICS during a one-year period [15]. To use an ICS, a child has to be prescribed an ICS, and that prescription has to be filled.

Children in Medicaid are more likely than privately insured children to suffer from severe asthma exacerbations [16]. Geographic variation in the rates of ICS use for children with persistent asthma in Medicaid has been reported [15]. Because the ICS rates were adjusted only for age, the variation may be attributable to the demographic and clinical characteristics of the children living in the areas. Variation in use that remains after adjusting for the children's characteristics reflects variation in area preference for using ICS. Unlike children's demographic and clinical characteristics, area preference for ICS can be changed. Changes to area preference for ICS could potentially result in lower asthma exacerbation rates for children in Medicaid,

which have been found to vary geographically [15, 17]. The objective of this study was to quantify the geographic variation in ICS use for children with persistent asthma in Medicaid that remains after adjusting for the characteristics of the children in an area.

Methods

Data and cohort

Data from the 2005--2007 Medicaid Analytic eXtract Personal Summary (PS), Other Therapy (OT), Inpatient (IP), and Prescription Drug files were used. We included children with persistent asthma because they are candidates for daily ICS according to national guidelines [3]. Children with persistent asthma were identified based on short-acting beta₂-agonist (SABA) use. Two SABA fills of 100 treatments (1 treatment = 2 puffs or 1 vial) or more in 30 days were required, which implied SABA use close to or in excess of one 200-puff inhaler or 100 vials per month if children were depleting one fill before initiating the next fill. A fill refers to a quantity of medication that is dispensed by a pharmacy to a child and reimbursed by Medicaid. Assuming a child is not using SABA to prevent exercise-induced bronchospasm or treat a temporary increase in symptoms resulting from exposure to a trigger, such frequent SABA usage indicates persistent asthma [3]. Each pair of consecutive SABA fills of ≥ 100 treatments each for a child was assessed to see if the fills occurred within 30 days of each other (Figure 1). The National Drug Code and the quantity dispensed on each prescription claim were used to determine the number of treatments that had been dispensed on a given fill. Each pair that met this inclusion criterion was then evaluated to see if it met the rest of the inclusion criteria (including the Medicaid enrollment criteria). The earliest pair for each child that met all the inclusion criteria was the

index pair. The fill date of the earlier SABA fill of the index pair was the index date. The index date began the index 30-day window. The remaining inclusion criteria will now be described. Children were required to be 5--18 years old on the index date. Any consecutive pair of SABA fills of ≥ 100 treatments each occurring in the 90 days prior to the index date had to occur more than 30 days apart. To ensure the frequent SABA use was not occurring despite controller treatment, a fill for a controller medication in the 90 days prior to the index date or during the index 30-day window was prohibited. An OT or IP claim in the year prior to the index date with a primary *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9)* diagnostic code for asthma (493.xx) was required to ensure the child was actively receiving medical care for asthma, making the earliest index date 1/1/06. Children with an OT or IP claim with a primary *ICD-9* diagnostic code for cystic fibrosis (277.0), bronchopulmonary dysplasia (770.7), or tracheomalacia (748.3) in the year prior to the index date were excluded from the study [18].

Children had to be enrolled in a state Medicaid program according to the eligibility rules of their state to be included in the study. They also had to be eligible for full Medicaid benefits and could not be covered by Medicare or private insurance during the 12 months prior to the index month, the index month, or the three months following the index month. States are required to submit fee-for-service (FFS) claims and managed care encounter data to the Centers for Medicare and Medicaid Services (CMS) [19]. CMS has not enforced the requirement for states to submit encounter data [20], so utilization of managed care-covered services by children enrolled in managed care plans is not observable in the data for all states. Subsequently, children enrolled in a comprehensive managed care organization, prepaid ambulatory health plan, or

prepaid inpatient health plan covering outpatient and/or inpatient medical services in the 12 months prior to the index month or the index month were excluded. Children were included if they were enrolled in one of these plans during the three months following the index month, so long as prescription drugs were carved out of the plan's contract and reimbursed by the state on a FFS basis, because only prescription drug utilization needed to be observable during this period. Children were included if they were enrolled in a dental plan, transportation plan, behavioral health organization, or primary care case management throughout the study because their outpatient and inpatient medical services and prescription drugs would be reimbursed by the state on a FFS basis, so claims for these services would appear in the data.

Children from Maine were excluded because the OT and IP files for Maine do not exist for the study period. Children from Arizona were excluded because Arizona had difficulty with prescription drug claims processing during the study period [21], affecting their prescription drug claims counts and raising concern not all their FFS prescription drug claims would appear in the data. Children from Alaska and Hawaii were excluded due to the method we used to examine geographic variation, described later in this section.

Measures

Use of an ICS as initial controller medication was assessed in the 60-day window following the index 30-day window (Figure 1). The first fill date for a controller medication in the 60-day window was observed. All controller medications filled on that date were determined. If the child received an ICS on that date, which included ICS in fixed combination with a long-acting beta₂-agonist, the child was considered to have used an ICS.

Birthdate, sex, race/ethnicity, and ZIP code were selected from the PS file of the index year. Age was measured as age in years on the index date. The number of SABA treatments dispensed in the index 30-day window was measured, along with the season and year of the index date. The frequency of visits for asthma was defined as a count of the number of visits to a physician, outpatient hospital, clinic, or nurse practitioner with a primary *ICD-9* diagnostic code for asthma, in the 30 days prior to the index date. A second measure of frequency of visits was created using a window of 90 days prior to the index date. An asthma exacerbation in the 30 days prior to the index date was determined by a 3--10 day oral corticosteroid fill or emergency department visit or hospitalization with a primary *ICD-9* diagnostic code for asthma. A second measure of asthma exacerbation was created using a window of 90 days prior to the index date. Recent medical care for upper respiratory infection, bronchitis, sinusitis, or allergic rhinitis was determined by whether there was an IP or OT claim with a primary *ICD-9* diagnostic code for that condition in the 30 days prior to the index date.

ZIP code-specific areas

The unit of analysis for the geographic variation in this study was a ZIP code-specific area determined using the methodology by Fang et al [22]. ZIP code-specific areas were chosen over counties or census tracts because variation can occur within a county or census tract. The area for a ZIP code, called the original ZIP code, was the combination of that ZIP code and the next closest ZIP codes in terms of driving time between the ZIP codes, until at least 10 eligible children resided in the area. We hold a database containing driving times and distances between ZIP codes in the United States, which was used to determine the next closest ZIP codes in terms

of driving time to the original ZIP code. The areas for all ZIP codes in our database were determined except for Arizona, Maine, Alaska, and Hawaii ZIP codes. Areas for Arizona and Maine ZIP codes were not determined because none of the children in these areas would have been from these states. Because driving times cannot be calculated between all ZIP codes in Alaska and Hawaii, no areas were created for ZIP codes in these states.

Data analysis

Descriptive statistics of patient characteristics for patients using and not using ICS were produced. A t-test was used to compare the mean age between the ICS and no ICS groups. Chi-squared tests were used to compare the use of ICS between levels of patient characteristics.

For each ZIP code-specific area, the unadjusted ICS rate and the area treatment ratio for ICS were calculated. The numerator for the area treatment ratio was the number of children residing in the area that used ICS. The denominator for the area treatment ratio was the sum of the predicted probabilities of using ICS for all the children residing in the area. An area treatment ratio greater than one indicates higher than expected use of ICS in that area given the demographic and clinical characteristics of the children residing there. Using the full cohort, ICS use was regressed on demographic and clinical characteristics using logistic regression to get predicted probabilities.

The descriptive statistics for the unadjusted ICS rates and area treatment ratios for ICS were minimum, maximum, and 25th, 50th, and 75th percentiles. Area treatment ratios for the original ZIP codes were mapped for visual comparison. All analyses were conducted using SAS

9.4. Microsoft MapPoint North America 2013 was used to map ZIP code-specific area treatment ratios. The study was approved by the University of Iowa Institutional Review Board.

Results

Of 15,917 children, 13% used an ICS (Table 1). Nearly half of the children filled more than 200 SABA treatments in the 30-day window. Twenty-seven percent had at least one outpatient visit for asthma, and 14% had at least one asthma exacerbation in the 90 days prior to the frequent SABA usage. Upper respiratory infection was the most common condition for which children received care in the 30 days immediately prior to the frequent SABA usage.

The demographic characteristic of race/ethnicity was related to ICS use (Table 1). With regard to the characteristics of the frequent SABA usage, both timing and intensity of SABA usage were associated with ICS use. Asthma exacerbations both 30 and 90 days prior to frequent SABA usage were associated with ICS use. Allergic rhinitis was the only condition associated with ICS use. Eighteen percent of children with allergic rhinitis used an ICS while only 13% of children without allergic rhinitis used an ICS.

The unadjusted ICS rates ranged between areas from 0--64% with a median rate of 10% (Table 2). The area treatment ratios for ICS ranged from 0--4.9, meaning in some areas ICS use was nearly five times what was expected based on the characteristics of the children residing in the area. The median area treatment ratio was 0.8, meaning ICS use was less than expected in more than half of the areas.

Area treatment ratios for all ZIP code-specific areas were mapped by original ZIP code, but only the southern United States is included in Figure 2 to permit greater detail in the illustration. The southern states are displayed because the geographic variation in ICS use observed in these states is representative of the geographic variation observed in the nation. The map highlights the substantial difference in ICS use that existed between some adjoining areas. Some areas of higher than expected ICS use were contiguous to areas with lower than expected ICS use. For example, this was observed in western Arkansas.

Discussion

Thirteen percent of children with persistent asthma in Medicaid used ICS in this study. ICS use was associated with race/ethnicity, timing and intensity of SABA use, visits for asthma, asthma exacerbations, and allergic rhinitis. There was variation in the unadjusted ICS rates between areas. ICS use was minimal in some areas and reached as high as 64% in one area. Geographic variation remained after adjusting for the demographic and clinical characteristics of children residing in an area. Some higher ICS use areas were adjacent to lower use areas.

The proportion of children that did not use ICS (87%) was unexpectedly high for children with persistent asthma who are candidates for daily ICS according to national guidelines [3]. One study found 65.9% of Medicaid children with persistent asthma had a physician visit at which they had persistent asthma but were not prescribed a controller medication at that visit [23]. Our results reflect those who were not prescribed ICS and those who did not fill ICS after it was prescribed, and this may explain why the percentage of children that did not use ICS was so high in our study. In a study of adults and children with asthma, 14--20% did not fill the controller

medication they were prescribed within 30 days, depending on the class of controller medication prescribed [24].

Children exhibiting certain clinical characteristics were more likely to use ICS. Children filling more than 200 SABA treatments in the index 30-day window were more likely to use ICS than children filling exactly 200 treatments. If children were depleting one fill before initiating the next fill, the children filling more than 200 SABA treatments likely used more than 100 SABA treatments (e.g. more than a single 200-puff albuterol inhaler) in that month. Children filling exactly 200 SABA treatments may have been closer to using only one 200-puff inhaler or 100 vials that month. Use of more than one 200-puff albuterol inhaler per month on average increases patients' risk of death from asthma [25]. Substantial reliance on SABA in the children filling more than 200 treatments likely prompted stronger beliefs about the appropriateness of ICS, resulting in the association seen in our study. Children in our study with a recent asthma exacerbation were more likely to use ICS. A past exacerbation predisposes a patient to a future exacerbation [26]. A recent exacerbation probably stimulated the use of an ICS to prevent another exacerbation.

We found wider geographic variation in unadjusted ICS rates than another study. Garcia and Lyon-Callo found a range of 43 percentage points in ICS rates between areas in one state [15], while our range was 64 percentage points. Our inclusion of nearly all states rather than a single state likely explains the discrepancy. Demographic and clinical characteristics were not solely responsible for the geographic variation we found, as there was still substantial variation in the area treatment ratios for ICS after adjusting for these characteristics. The remaining

variation signals differences between areas in their preference for using ICS. Higher ICS use areas were not always separated from lower use areas by intermediate use areas, meaning area preference for ICS does not necessarily change gradually from one area to the next.

Preference for using ICS could differ between areas for multiple reasons. One reason is prescribers in some areas may be more inclined to prescribe ICS to children than prescribers in other areas. Willingness to prescribe ICS for children is likely influenced by experience treating asthma and familiarity with the evidence regarding its treatment and outcomes. Differences in prescribing between prescribers are expected to be greatest when there is a lack of scientific evidence directly relevant to the patients being treated. For example, children with asthma and allergic rhinitis, a common asthma comorbidity, may be treated with ICS and intranasal corticosteroids [27, 28]. The effects of concomitant use of these drugs on growth is unknown [29]. Prescribers in some areas may be more comfortable prescribing ICS in the face of uncertainty than others. Another reason is differences in parent willingness to use ICS in their children. Some parents have strong concerns about the adverse effects of ICS but still allow their children to use them [12]. At least a portion of children and adults prescribed ICS for asthma never fill the medication [24]. Parents in some areas may be more willing to allow their children to use ICS than parents in other areas. A third reason is differences in access to controller medications stemming from Medicaid policy. For example, a state Medicaid program may have restricted access to montelukast, a non-ICS controller medication, through prior authorization [30]. Obtaining montelukast would be more difficult in such a state. Subsequently, ICS use in that state may be higher than expected based on the characteristics of the area residents if prescribers prescribe ICS because they believe montelukast will not be approved. Conversely, if

the particular ICS a prescriber wants to prescribe is restricted, that prescriber may opt to prescribe a non-ICS controller instead, which would result in lower than expected ICS use.

We acknowledge several limitations exist. Frequency of SABA use is only one indicator of asthma impairment health care providers are encouraged by guidelines to consider when determining treatment [3]. Other indicators are activity limitations, nighttime awakenings, and lung function. None of these indicators are available in administrative claims data. We were unable to account for these clinical characteristics in our analysis, so geographic differences in these characteristics could be contributing to the geographic variation in ICS use. While we could not exclude patients who were using SABA exclusively for prevention of exercise-induced bronchospasm (EIB), we suspect the number of children in our cohort who did not have persistent asthma was small. The substantial SABA use required for inclusion in our study (≥ 100 treatments in 30 days) makes it difficult for a child to be using SABA exclusively for prevention of EIB and still qualify. Furthermore, the geographic variation in ICS use we observed would only be influenced by the inclusion of children without persistent asthma if those children were unevenly distributed across areas. We do not have reason to believe they were unevenly distributed. With regard to the included cohort, we were unable to include children enrolled in comprehensive managed care plans and prepaid health plans covering inpatient or outpatient medical services. We included children in fee-for-service arrangements as well as those in primary care case management and managed care plans for behavioral health and dental. While this reduced the size of our cohort, the rate of asthma episodes does not differ between children enrolled in comprehensive managed care and fee-for-service Medicaid [31]. Finally, we assumed a subsequent SABA fill indicated the medication dispensed in the previous fill had been

depleted. An example of when this assumption is not correct is if the subsequent SABA is filled to have an inhaler on-hand at school. However, if action is taken to ensure a SABA is readily available at home and at school, this potentially indicates a child is experiencing frequent symptoms, has persistent asthma, and is a candidate for controller medication.

Conclusions

Geographic variation in ICS use exists for children with persistent asthma in Medicaid, with some areas using ICS substantially more or less than expected given the characteristics of the children in the area. Concrete evidence identifying the drivers of this variation is needed, as is an understanding of how asthma outcomes such as rates of exacerbations and adverse effects correspond to rates of ICS use.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Table 1. Characteristics by use of inhaled corticosteroids (ICS).

	Total ^a (N = 15917)	ICS ^b (N = 2032)	No ICS ^b (N = 13885)	P value ^c
Age, mean and standard deviation (in years)	11.5 (3.8)	11.4 (3.9)	11.5 (3.8)	0.28
Sex				
Male	9259 (58%)	1210 (13%)	8049 (87%)	0.18
Female	6658 (42%)	822 (12%)	5836 (88%)	
Race/ethnicity				
White	6104 (38%)	721 (12%)	5383 (88%)	0.025
Black	6041 (38%)	798 (13%)	5243 (87%)	
Hispanic	2031 (13%)	286 (14%)	1745 (86%)	
Other	1741 (11%)	227 (13%)	1514 (87%)	
Season of index date				
Winter	3743 (24%)	476 (13%)	3267 (87%)	<0.001
Spring	4167 (26%)	459 (11%)	3708 (89%)	
Summer	4426 (28%)	619 (14%)	3807 (86%)	

Fall	3581 (23%)	478 (13%)	3103 (87%)	
Year of index date				
2006	9911 (62%)	1246 (13%)	8665 (87%)	0.35
2007	6006 (38%)	786 (13%)	5220 (87%)	
SABA treatments filled in index 30-day window				
200 treatments	8627 (54%)	973 (11%)	7654 (89%)	<0.001
>200 treatments	7290 (46%)	1059 (15%)	6231 (85%)	
Visits for asthma in 90 days prior to index date				
0	11501 (72%)	1445 (13%)	10056 (87%)	0.004
1	3736 (23%)	472 (13%)	3264 (87%)	
≥ 2	680 (4%)	115 (17%)	565 (83%)	
Asthma exacerbations in 90 days prior to index date				
0	13637 (86%)	1669 (12%)	11968 (88%)	<0.001
≥ 1	2280 (14%)	363 (16%)	1917 (84%)	
Visits for asthma in 30 days prior to index date				
0	13756 (86%)	1765 (13%)	11991 (87%)	0.056
1	2009 (13%)	239 (12%)	1770 (88%)	

≥2	152 (1%)	28 (18%)	124 (82%)	
Asthma exacerbations in 30 days prior index date				
0	14871 (93%)	1874 (13%)	12997 (87%)	0.019
≥1	1046 (7%)	158 (15%)	888 (85%)	
Upper respiratory infection in 30 days prior to index date				
No	15145 (95%)	1947 (13%)	13198 (87%)	0.13
Yes	772 (5%)	85 (11%)	687 (89%)	
Bronchitis in 30 days prior to index date				
No	15748 (99%)	2009 (13%)	13739 (87%)	0.74
Yes	169 (1%)	23 (14%)	146 (86%)	
Sinusitis in 30 days prior to index date				
No	15737 (99%)	2002 (13%)	13735 (87%)	0.11
Yes	180 (1%)	30 (17%)	150 (83%)	
Allergic rhinitis 30 days prior to index date				
No	15517 (97%)	1962 (13%)	13555 (87%)	0.004
Yes	400 (3%)	70 (18%)	330 (83%)	

^aExpressed as column percentages.

^bExpressed as row percentages.

^cP values for t-test and chi-squared tests. Values below 0.05 for chi-squared tests indicate there is an association between ICS use and the tested characteristic.

Table 2. Descriptive statistics for unadjusted inhaled corticosteroid (ICS) rate and area treatment ratio for ICS.

	Minimum	25 th percentile	50 th percentile	75 th percentile	Maximum
Unadjusted ICS rate	0%	7%	10%	20%	64%
Area treatment ratio for ICS	0	0.5	0.8	1.5	4.9

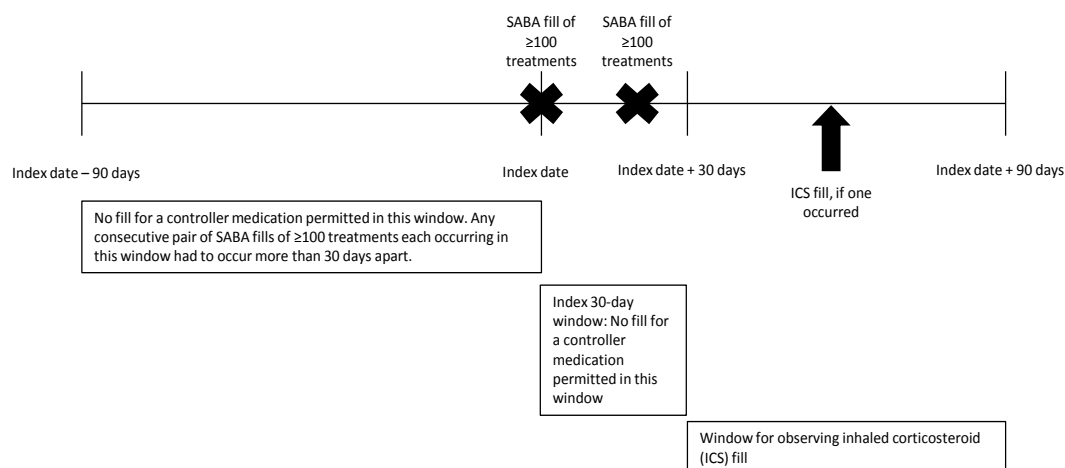


Figure 1. Illustration of select inclusion criteria and window of inhaled corticosteroid observation. SABA, short-acting beta₂-agonist.

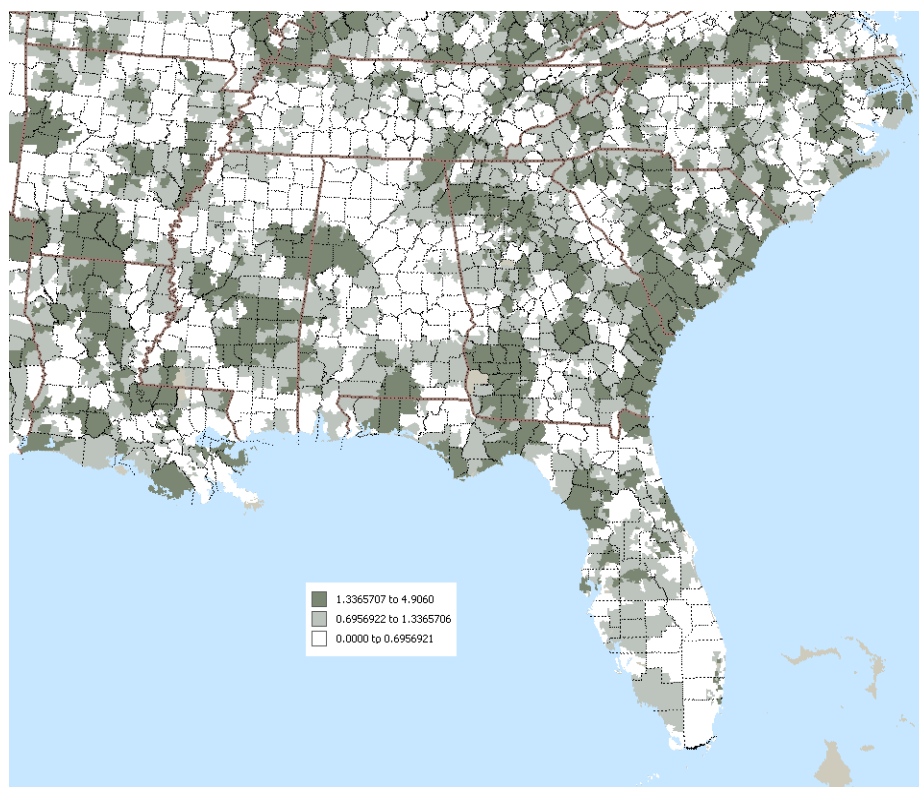


Figure 2. Map of area treatment ratio for inhaled corticosteroids specific to each ZIP code in the southern United States. Each shade represents a range of area treatment ratios. For example, area treatment ratios from 1.3365707 to 4.9060 are shown in dark gray. Area treatment ratios in excess of one indicate higher than expected ICS use based on the characteristics of the children living in the area.