

Do regional geography and race influence management of chronic spontaneous urticaria?



Giselle S. Mosnaim, MD, MS,^{a,b} Matthew Greenhawt, MD, MSc, MBA,^c Polina Imas, BS,^d Loretta Au, PhD,^d Stephanie Mehliis, MD,^{b,e} John Oppenheimer, MD,^f David Lang, MD,^g Jonathan Bernstein, MD,^{h,i} and Marcus Shaker, MD, MS^{j,k,l}
 Evanston and Chicago, Ill; Aurora, Colo; Newark, NJ; Cleveland, Ohio; and Lebanon and Hanover, NH

Chronic spontaneous urticaria is defined as migratory evanescent pruritic blanching wheals that occur with variable frequency for 6 weeks or more, with or without accompanying angioedema. This condition affects approximately 0.1% to 1.4% of persons worldwide. Second-generation H1 antihistamines are the mainstay of management, with refractory cases often managed with an array of options, including H2 antihistamines, leukotriene receptor antagonists, glucocorticosteroids, immunosuppressive agents, and omalizumab. However, the degree of practice variation as to what treatments are prescribed is poorly understood, given that clinical care could be driven by patient preferences or lack of clarity as to best practices for refractory cases. We conducted a small, exploratory study of the role of race, ethnicity, and regional geographic distance to specialist care on chronic spontaneous urticaria prescribing practices. A small-area geographic variation in chronic spontaneous urticaria management in a large Chicago-area health care system was identified. Rates of omalizumab use varied by patient zip code, with more

omalizumab prescriptions being associated with zip codes closer to the main office of an academic medical center-affiliated allergist-immunologist practice. Higher rates of omalizumab use were associated with White race in regional and patient-level analyses, though the reasons for this race-based finding are not clear. (*J Allergy Clin Immunol* 2022;150:1260-4.)

Key words: Chronic urticaria, chronic spontaneous urticaria, chronic idiopathic urticaria, practice variation

Chronic spontaneous urticaria (formerly chronic idiopathic urticarial; CSU) is defined as migratory evanescent pruritic blanching wheals that occur with variable frequency for 6 weeks or more, with or without accompanying angioedema.^{1,2} This condition affects approximately 0.1% (US) to 1.4% (Asian nations) of persons, depending on the country of study.¹⁻³ CSU has significant impact on quality of life.⁴ Although not cost-effective, laboratory testing is often pursued, with limited to no utility.⁵ According to US and the most recent international guidelines

From ^athe Division of Allergy, Asthma and Immunology, Department of Medicine, NorthShore University HealthSystem, Evanston; ^bPritzker School of Medicine, University of Chicago, Chicago; ^cthe Section of Allergy and Immunology, Food Challenge and Research Unit, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora; ^dthe Department of Medicine and ^ethe Division of Dermatology, Department of Medicine, NorthShore University HealthSystem, Evanston; ^fthe Department of Internal Medicine, Rutgers New Jersey Medical School, Newark; ^gthe Department of Allergy and Clinical Immunology, Respiratory Institute, Cleveland Clinic, Cleveland; ^hthe Department of Internal Medicine, Division of Immunology/Allergy Section, University of Cincinnati Medical Center, Cincinnati; ⁱBernstein Allergy Group and Clinical Research Center, Cincinnati; ^jthe Section of Allergy and Immunology, Dartmouth-Hitchcock Medical Center, Lebanon; and the Departments of ^kPediatrics and ^lMedicine, Geisel School of Medicine at Dartmouth, Hanover.

Disclosure of potential conflict of interest: G. S. Mosnaim receives current research grant support from GlaxoSmithKline (GSK), Novartis, Sanofi-Regeneron, and Teva and has received past research grant support from AstraZeneca, Alk-Abello, and Genentech. M. Greenhawt is a consultant for Aquestive; is a member of physician/medical advisory boards for DBV Technologies, Sanofi/Regeneron, Nutricia, Novartis, Aquestive, Allergy Therapeutics, AstraZeneca, ALK-Abello, and Protia; is an unpaid member of the Scientific Advisory Council for the National Peanut Board and the Medical Advisory Board of the International Food Protein Induced Enterocolitis Syndrome Association; is a member of the Brighton Collaboration Criteria Vaccine Anaphylaxis 2.0 Working Group; is the senior associate editor for *the Annals of Allergy, Asthma, and Immunology*; is member of the Joint Taskforce on Allergy Practice Parameters; and has received honorarium for lectures from ImSci, RMSI, MedLearningGroup, and multiple state/local allergy societies. S. Mehliis has received clinical trial support from AbbVie, Akari, Amgen, AstraZeneca, BMS, ChemoCentryx, Dong-A ST, Eli Lilly, Galderma, Incyte, Janssen, Leo Pharma, Menlo, Mayne Pharma, NFlection, Nimbus, Novartis, Pfizer, Regeneron, Sanofi, UCB, Vanda, and VYNE and has been a speaker, advisor, or consultant for AbbVie, Janssen, Novartis, Dermavant, Leo

Pharma, and UCB. J. Oppenheimer is a consultant for Amgen, Aimmune, Aquestive, GSK, and Sanofi; member of the Adjudication or Data Safety Monitoring Board for AstraZeneca, Amgen, AbbVie, Novartis, and GSK; is the Executive Editor for *the Annals of Allergy, Asthma, and Immunology*; and a reviewer for UpToDate. D. Lang has carried out clinical research with, served as a consultant for, and/or has received honoraria from AstraZeneca, Sanofi-Regeneron, Genentech, Novartis, and WebMD; is currently serving as Guest Editor, *Journal of Allergy and Clinical Immunology: In Practice*; and is on the editorial boards of *Allergy and Asthma Proceedings* and *DynaMed*. J. Bernstein is an investigator, consultant, and speaker for Sanofi-Regeneron, AstraZeneca, GSK, Novartis, Genentech, Takeda/Shire, CSL-Behring, Pharming, and Biocryst; an investigator and consultant for Amgen, TLL, Celldex, IONIS, Biomarin, Kalvista, and Merck; a consultant for Escient, Cycle, Astria, ONO, and Pharvaris; is the president-elect of the American Academy of Allergy, Asthma & Immunology; is a member of the Joint Task Force of Allergy Practice Parameters, and the Chronic Urticaria Practice Parameter Workgroup cochair; and is on the Medical Advisory Board for HAEA org. M. Shaker has participated in research that has received funding by DBV; is a member of the Joint Task Force on Practice Parameters; serves as an associated editor for *Annals of Allergy, Asthma, and Immunology*; and is an editorial board member for the *Journal of Allergy and Clinical Immunology: In Practice*.

Received for publication July 11, 2022; revised September 21, 2022; accepted for publication October 18, 2022.

Corresponding author: Giselle Mosnaim, MD, MS, 1001 University Place, Evanston, IL 60201. E-mail: Gmosnaim@northshore.org.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

0091-6749/\$36.00

© 2022 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaci.2022.10.017>

Abbreviations used

AMC: Academic medical center

CSU: Chronic spontaneous urticaria (formerly chronic idiopathic urticaria)

OR: Odds ratio

for the management of CSU, step therapy includes (1) monotherapy with second-generation antihistamines up to 4 times the recommended Food and Drug Administration dose with addition of an H2-antagonist or leukotriene receptor antagonist; (2) addition of omalizumab (favored), and (3) cyclosporine.^{1,2}

The degree of practice variation in CSU management is unknown. Some reasonable variation in CSU management may be expected in settings where there is evidence uncertainty or when patient-preference-sensitive approaches are incorporated into clinical decision making. However, variations that are clinician workforce-supply-sensitive, based on economic incentives, tradition, or health care disparities primarily compounded by socioeconomic factors would represent examples of unwarranted practice variation.⁶ The purpose of this study was to evaluate a small geographical area for practice variations in CSU management among different racial and ethnic groups.

METHODS

The study cohort included patients in a large Chicago-area health care system, NorthShore University HealthSystem (a teaching affiliate of the University of Chicago, Pritzker School of Medicine), with CSU defined by the *International Classification of Diseases, Tenth Revision* encounter code of L50.*, between May 2019 and May 2022. Because NorthShore collects patient data on both ethnicity and race, our approach leveraged both of these data items with precedence for ethnicity to categorize patients as White, non-White, or unknown (see Table E1 in this article's Online Repository at www.jacionline.org). Individuals with CSU met 1 of the following 2 criteria to be included in this analysis: (1) 2 separate office visits with a code of L50.* at least 6 weeks apart, or (2) at least 1 office visit with a code of L50.* and diagnostic label of "chronic" urticaria. Abstracted medications included first- and second-generation H1 antihistamines, H2 antihistamines, leukotriene receptor antagonists, oral corticosteroids, cyclosporine, epinephrine, and omalizumab. Historical and external prescriptions were excluded. Comorbid conditions evaluated included the following diagnoses: asthma, allergic rhinitis, venom allergy, food allergy, angioedema, and anaphylaxis, selected by relevant *International Classification of Diseases, Tenth Revision* codes and diagnostic labels (see Table E2 in this article's Online Repository at www.jacionline.org) and validated by the independent review and consensus of 2 practicing allergist-immunologists (G.M. and M.S.). A priori calculations indicated that 378 subjects per group would be required to achieve 80% power to detect a 5% disparity by race in omalizumab prescribing (assuming a clinical preliminary estimate 4% baseline rate of prescribing in the lowest group; assuming a 6% baseline rate, 485 subjects would be required in each group). Statistical analysis included univariate and multivariate odds-ratio (OR) analysis performed at the patient level and was performed using R (version 4.1.0, 2021, Austria, Vienna), with adjustments of multiple comparisons using the Bonferroni correction with the level of statistical significance set at P less than .05. OR analysis was limited to patients with known distances to (1) the academic medical center (AMC)-affiliated allergist-immunologist practice ($n = 475$ or 23% of the cohort) or (2) any prescribing practice ($n = 831$ patients or 41% of the cohort). Figures and data summaries were created with Tableau (version 19.2.358, 2019, Seattle, Wash). The study was approved by the NorthShore University HealthSystem Institutional Review Board.

RESULTS

A total of 2007 subjects were identified ($n = 1077$ White, 541 non-White, and 389 unknown) with variations identified in insurance coverage by race (see Table E3 in this article's Online Repository at www.jacionline.org). The plurality of subjects (48%) did not have an allergic comorbidity (Table I). Second-generation H1 antihistamines were dispensed by prescription in 9.3% of subjects, without significant differences noted between groups. Of the 6.5% of subjects prescribed omalizumab, a greater proportion of White subjects were prescribed this therapy than non-White individuals (White, 9.7% vs non-White, 3.7% vs unknown 1.8%; $P < .001$) (Table II).

Regional analyses

Significant small-area geographic practice variations were identified in omalizumab use. Fewer patients living in regions at greater physical distance from an AMC-affiliated allergist-immunologist practice received omalizumab (Fig 1, A). Negative correlations were identified for both non-White (Fig 1, B, Spearman $\rho = -0.42$; $P = .0930$) and White subjects (Fig 1, C, Spearman $\rho = -0.29$, $P = .0260$, combined Spearman $\rho = -0.25$, $P = .0215$).

Patient-level analyses

To better understand regional variation in omalizumab use, patient-level univariate and multivariate OR analyses were performed. In multivariate analysis adjusted for geographic region, number of allergic comorbidities, race, and insurance type, the geographic distance from the AMC affiliate was not a significant contributor to omalizumab use. We found that greater distance from the AMC-affiliated allergist-immunologist was paradoxically associated with a nonsignificant increased odds of omalizumab use in the adjusted analysis (1.028; $P = .066$; see Tables E4 and E5 in this article's Online Repository at www.jacionline.org), and when distance from any prescribing practice was considered, this effect persisted (OR, 1.029; $P = .046$; see Tables E6 and E7 in this article's Online Repository at www.jacionline.org). In the adjusted analysis, far fewer patients of non-White (AMC adjustment: OR, 0.246, $P < .001$; any practice adjustment: OR, 0.243, $P < .001$) and unknown race (AMC adjustment: OR, 0.173, $P < .001$; any practice adjustment: OR, 0.066, $P < .001$) received omalizumab. In the model considering distance from any prescribing practice, patients with additional allergic comorbidities (OR, 1.251; $P = .045$) and Medicaid patients had increased odds for receiving omalizumab (OR, 1.025; $P = .976$) (Tables E6 and E7). We did not observe any significant differences in the use of cyclosporine or oral corticosteroid with race.

DISCUSSION

We identified small-area geographic practice variations in CSU management in a large Chicago-area health care system. Regional rates of omalizumab use varied by patient zip code, and a greater proportion of omalizumab prescriptions were found in zip codes closer to the main office of an AMC-affiliated allergist-immunologist practice (Fig 1, A). Further investigation with a subsample using patient-level analysis that explicitly considered distance from this practice did not confirm this finding. Notably, higher rates of omalizumab use were associated with White versus

TABLE I. Number of comorbidities

No. of comorbidities	White (N = 1077)	Non-White (N = 541)	Unknown (N = 389)	Total (N = 2007)
0	47.2%	46.6%	52.4%	48.0%
1	27.8%	27.9%	32.1%	28.6%
2	16.3%	19.2%	11.6%	16.2%
3	7.5%	4.8%	3.1%	5.9%
4	1.2%	1.3%	0.8%	1.1%
5	0	0.1%	0.0%	0.0%

Comorbidities evaluated included asthma, allergic rhinitis, venom allergy, food allergy, angioedema, and anaphylaxis, selected by relevant *ICD-10* codes and diagnostic label (Table E1) and validated by the independent review and consensus of 2 practicing allergist-immunologists.

ICD-10, International Classification of Diseases, Tenth Revision.

TABLE II. Prescribed medications for CSU

Medication	White (N = 1077)	Non-White (N = 541)	Unknown (N = 389)	Total (N = 2007)	P value
Rx 1stGENAH1 only	11.2%	10.0%	5.4%	9.8%	.0039
Rx 2ndGENAH1 only	7.9%	11.1%	10.8%	9.3%	.0605
Rx 1stGENAH1 and 2ndGENAH1	3.1%	5.4%	4.1%	3.9%	.0762
No AH1 Rx	77.8%	73.6%	79.7%	77.0%	.0610
OCS	22.9%	24.4%	21.3%	23.0%	.5468
Cyclosporine	0.4%	0.6%	0.5%	0.4%	.7375
Epinephrine	14.9%	16.3%	12.1%	14.7%	.2014
Omalizumab	9.7%	3.7%	1.8%	6.5%	<.001
Rx AH2	12.1%	12.8%	12.9%	12.4%	.8854
LTRA	18.0%	16.8%	15.7%	17.2%	.5543

P values in bold are statistically significant.

LTRA, Leukotriene receptor antagonist; No AH1 Rx, No oral antihistamine H1 prescribed (but patients may have nonprescribed over-the-counter agents); OCS, oral corticosteroid; Rx 1stGENAH1, prescribed first-generation oral H1 antihistamine; Rx 2ndGENAH1, prescribed second-generation oral H1 antihistamine; Rx 1stGENAH1 and 2ndGENAH2, prescribed first- and second-generation oral H1 antihistamines; Rx AH2, prescribed H2 antihistamine (note that patients may have nonprescribed over-the-counter agents).

non-White race both in regional and in patient-level analyses, within the limits of our data. The reasons for this race-based finding are not clear.

The impact of socioeconomic and demographic group membership on patterns of prescribed pharmacotherapy has not been previously evaluated in the context of geographic variation within a single health care system for patients with CSU. The degree to which distance from allergist-immunologist care explains disparities identified in omalizumab utilization in CSU is uncertain; however, a recent retrospective analysis suggested that disparities in general biologic use for asthma may relate to age, race/ethnicity, income, geographic region, commercial insurance, and specialist access.⁷ Although access barriers may be one factor that impact care, our study suggests that CSU treatment with omalizumab may be linked to race.

Prevalence of CSU is not increased in White compared with non-White patients.⁸ In a cross-sectional analysis of diverse populations across 4 census regions, Wertenteil et al⁸ found that the adjusted prevalence of chronic urticaria was highest in non-White patients (Black patients: 292 [95% CI, 285-298] per 100,000 adults; other races: 331 [95% CI, 323-328] per 100,000) compared with White patients (262 [95% CI, 260-264] per 100,000, $P < .001$). For this reason, a higher overall rate of CSU in White patients would not explain the difference in omalizumab use according to race in our study. The factors that influence the association of race and omalizumab use may involve other socioeconomic population differences and/or health disparities that could include access to transportation, wealth, employment, and childcare obligations. Additional explanations

could relate to underlying responsiveness of CSU to antihistamine treatments, patient preference, adherence, other health maintenance behaviors, or patient-clinician communication and engagement. Our findings are consistent with previous studies that have reported that non-White patients are less likely to receive biologic therapy in a number of medical conditions, including psoriasis and rheumatoid arthritis.^{9,10} Takeshita et al⁹ found that odds of biologic use in psoriasis were 69% lower among Black patients (OR, 0.31; 95% CI, 0.16-0.6), and in another study,⁹ Black patients with rheumatoid arthritis had 53% lower odds of receiving a biologic agent. Our findings suggest that this pattern may persist in CSU, and the underlying reasons should be explored.

Access-based influences of health care utilization may be amenable to innovative models to help improve health care delivery and optimize treatment. One example of such an innovation is the recent Food and Drug Administration approval (April 2021) allowing self-administration of omalizumab at home for patients who have tolerated at least 3 in-office supervised doses uneventfully. This strategy has been shown to be cost-effective and has the potential to improve health equity, particularly in those patients with more limited access to specialist care. Telemedicine visits are another innovation that could help to overcome access barriers related to distance from the allergy and immunology office, though the effect of office distance was not consistently a significant factor, depending on the analysis and adjustment variables. In addition, the ability of patients and clinicians to have 2-way communication via the electronic medical record (eg, patients' use of their electronic medical record portals to upload signed consent forms that would

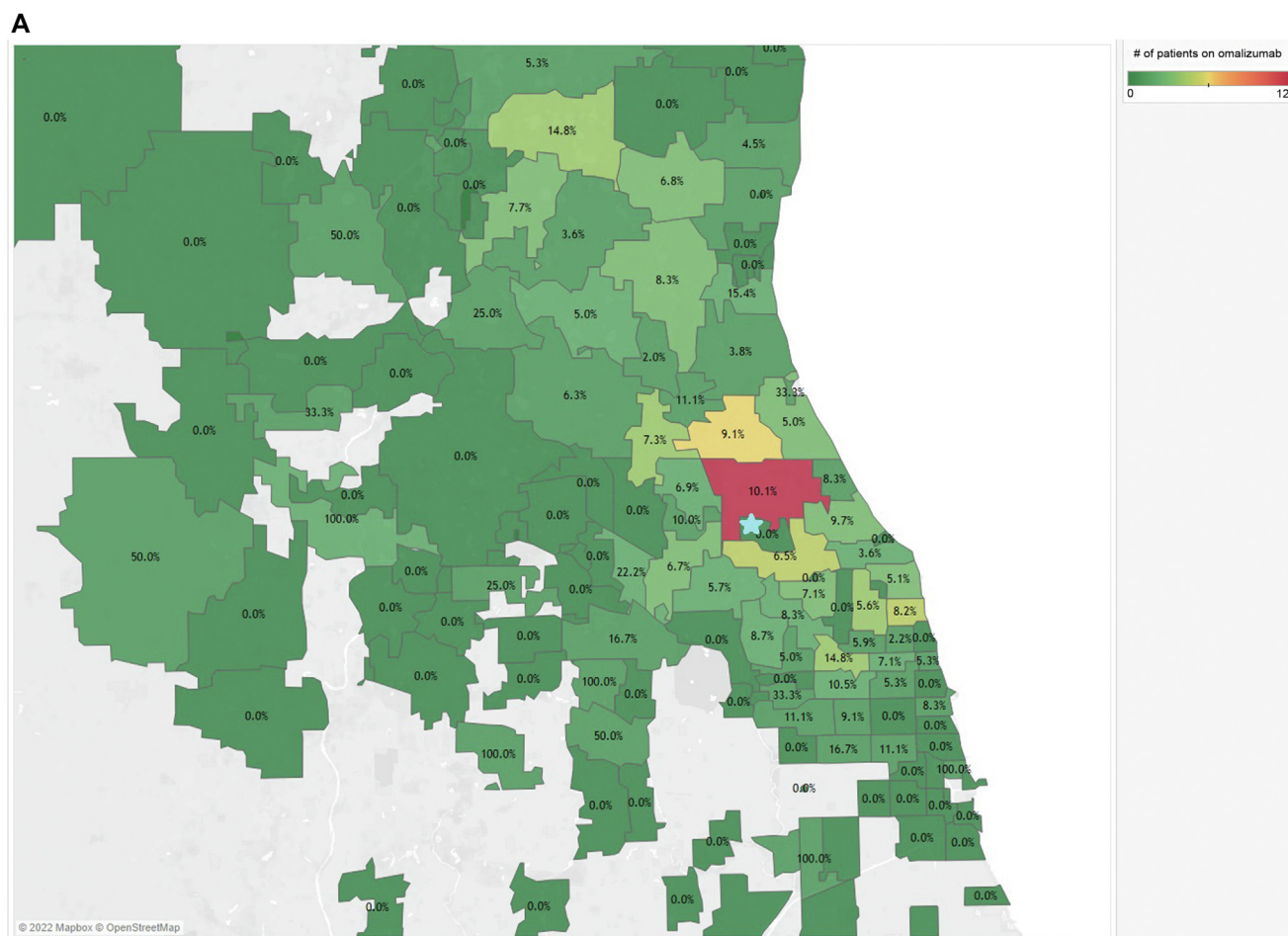


FIG 1. A, Heat map by number of patients who received omalizumab prescription. Zip codes where fewer patients received a prescription for omalizumab are a darker shade of green (absolute). Zip codes in yellow and red are associated with a higher number of patients who received an omalizumab prescription (absolute). The star marks the location of the AMC-affiliated allergist-immunologist practice. Percentages shown represent the relative percentage of patients in each area receiving omalizumab. **B,** Utilization of omalizumab for non-White patients by distance from prescriber. The relationship between distance from prescriber and rate of omalizumab prescription for non-White patients living in different zip codes is shown. Each circle represents a zip code. The label shows the rate of omalizumab prescriptions in a given zip code (Spearman $\rho = -0.42$; $P = .0930$). **C,** Utilization of omalizumab for White patients by distance from prescriber. The relationship between distance from prescriber and rate of omalizumab prescription for White patients living in different zip codes is shown here. Each circle represents a zip code. The label shows the rate of omalizumab prescriptions in a given zip code (Spearman $\rho = -0.29$; $P = .0260$).

permit clinicians to submit prior authorization documents for insurance coverage) further supports these options. Our findings in this exploratory study, intended to promote hypothesis generation rather than generalizability, warrant further assessment of wider geographically distributed CSU populations to better understand how race and geography may influence disparities of health care delivery for this chronic disease. It would also be beneficial to consider longitudinal patient data to address additional confounding factors, including how long a patient has been seeking care, whether they clinically qualify for omalizumab, or whether an alternative treatment was sufficient.

This study has several limitations. First, we evaluated records from a single hospital system. The data evaluated include the NorthShore legacy system and its 4 original hospitals. Three of these hospitals are located in the northwest suburbs of Illinois: Glenview, Highland Park, and Skokie. The fourth legacy hospital

is in Evanston, which services a more ethnically diverse area. The AMC-affiliated allergist-immunologist practice is within a predominantly White practice service area. Although the hospital system serves a diverse population, 54% of the CSU population was White and about half of the 95% of patients who had commercial insurance were White. Second, because our medication data were derived from orders rather than physician notes, we were not able to evaluate use of first- and second-generation H1 receptor antihistamines obtained over the counter for the treatment of CSU, differentiate the use of H1-receptor or H2-receptor antihistamines for the treatment of other comorbid conditions (eg, allergic rhinitis, atopic dermatitis, and gastroesophageal reflux), or infer severity of the underlying CSU diagnosis. The use of natural language processing technology to extract free text from clinician notes would potentially increase the ability to capture real-world over-the-counter antihistamine

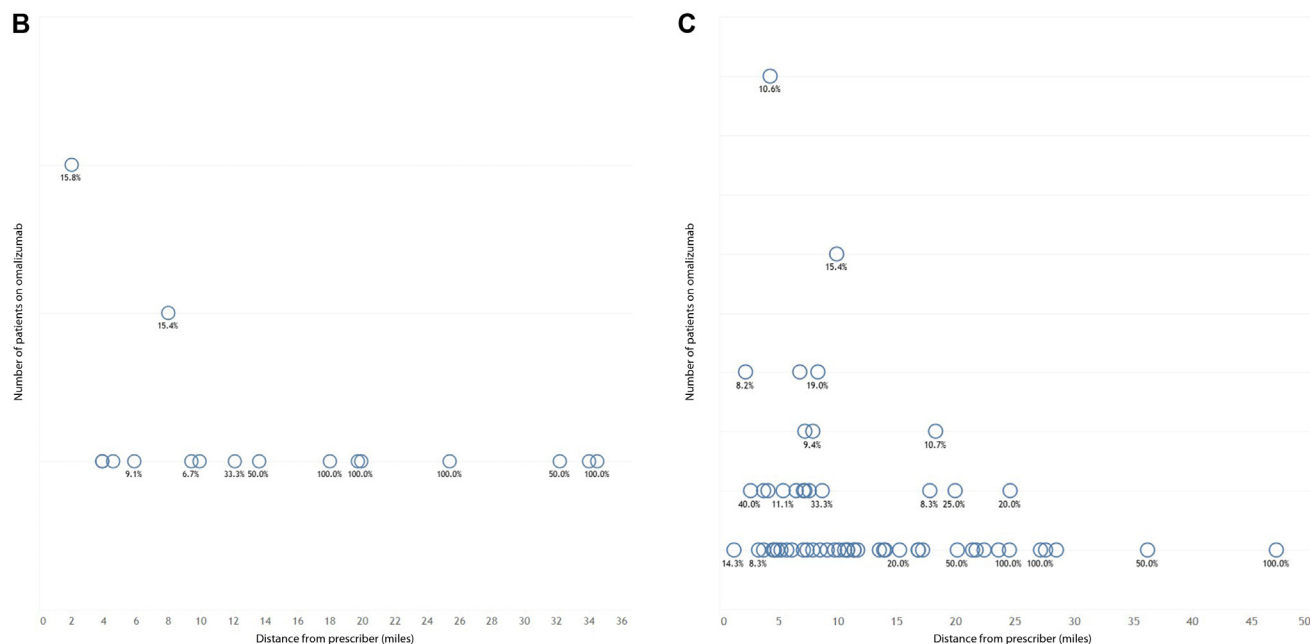


FIG 1. (Continued).

use and better understand whether patients are receiving guideline-directed care for CSU management. Third, medication adherence was not assessed. Fourth, patient-level assessment of distance from prescribers was unavailable in many patients, which may explain divergent findings in the subgroup patient-level analysis compared with rates of omalizumab prescriptions based on patient zip code. Fifth, we were unable to account for clinician dispensing of drug samples. Lastly, this was a cross-sectional analysis that spanned a significant portion of the coronavirus disease 2019 pandemic, and there are limitations common to these types of studies, including an inability to determine causal inferences.

CONCLUSIONS

Although distance between a patient's home and the allergist-immunologist's office may affect best practices for CSU management and lead to health disparities, our analysis suggests that race may be a significant factor influencing omalizumab use in a large Midwestern hospital system. Although implementing innovations in care delivery (including new Food and Drug Administration approvals for at-home administration of biologic therapies when appropriate, telemedicine, and electronic medical record bidirectional communication between patients and clinicians to process prior authorizations) may help to overcome these barriers, additional research is needed to better understand the influence of geography and race on CSU treatment.

REFERENCES

- Bernstein JA, Lang DM, Khan DA, Craig T, Dreyfus D, Hsieh F, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol* 2014;133:1270-7.
- Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA(2)LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy* 2022; 77:734-66.
- Fricke J, Avila G, Keller T, Weller K, Lau S, Maurer M, et al. Prevalence of chronic urticaria in children and adults across the globe: systematic review with meta-analysis. *Allergy* 2020;75:423-32.
- Ates H, Firat S, Buhari GK, Keren M, Cifci B, Erkeköl FO. Relationships between quality of life, sleep problems, and sleep quality in patients with chronic idiopathic urticaria. *J Cosmet Dermatol* 2022;21:4072-9.
- Shaker M, Oppenheimer J, Wallace D, Lang DM, Rambasek T, Dykewicz M, et al. Optimizing value in the evaluation of chronic spontaneous urticaria: a cost-effectiveness analysis. *J Allergy Clin Immunol Pract* 2020;8:2360-9.e1.
- Moen A, Goodman DC. Unwarranted geographic variation in paediatric health care in the United States and Norway. *Acta Paediatr* 2022;111:733-40.
- Inselman JW, Jeffery MM, Maddux JT, Shah ND, Rank MA. Trends and disparities in asthma biologic use in the United States. *J Allergy Clin Immunol Pract* 2020;8: 549-54.e1.
- Wertenteil S, Strunk A, Garg A. Prevalence estimates for chronic urticaria in the United States: a sex- and age-adjusted population analysis. *J Am Acad Dermatol* 2019;81:152-6.
- Takeshita J, Gelfand JM, Li P, Pinto L, Yu X, Rao P, et al. Psoriasis in the US Medicare population: prevalence, treatment, and factors associated with biologic use. *J Invest Dermatol* 2015;135:2955-63.
- Chu LH, Portugal C, Kawatkar AA, Stohl W, Nichol MB. Racial/ethnic differences in the use of biologic disease-modifying antirheumatic drugs among California Medicaid rheumatoid arthritis patients. *Arthritis Care Res (Hoboken)* 2013;65: 299-303.

TABLE E1. Race and ethnicity of study population

Classification	Ethnicity	Race	Total
White	Non-Hispanic	White	1076
White	Non-Hispanic	Total	1076
White	Declined/unknown	White	1
White	Declined/unknown	Total	1
White	Total	Total	1077
Non-White	Hispanic/Latino	White	31
Non-White	Hispanic/Latino	Other	126
Non-White	Hispanic/Latino	Asian	2
Non-White	Hispanic/Latino	Declined/unknown	7
Non-White	Hispanic/Latino	African American or Black	2
Non-White	Hispanic/Latino	Total	168
Non-White	Non-Hispanic	Asian	249
Non-White	Non-Hispanic	African American or Black	114
Non-White	Non-Hispanic	American Indian or Alaska Native	5
Non-White	Non-Hispanic	Pacific Islander/Hawaiian Native	4
Non-White	Non-Hispanic	Total	372
Non-White	Declined/unknown	Asian	1
Non-White	Declined/unknown	Total	1
Non-White	Total	Total	541
Unknown	Non-Hispanic	Other	320
Unknown	Non-Hispanic	Declined/unknown	10
Unknown	Non-Hispanic	Total	330
Unknown	Declined/unknown	Other	16
Unknown	Declined/unknown	Declined/unknown	43
Unknown	Declined/unknown	Total	59
Unknown	Total	Total	389

Base population
Encounter criteria
Encounter <i>ICD</i> code: L50*
Encounter date: within the past 36 mo
Encounter type: Office visit
Select encounter DX only
Service area 200
One row per patient is selected
An indicator for patients with at least 2 visits, 6 or more weeks apart <i>or</i> the diagnosis name contains “Chronic”
Medication criteria
Patient fulfills the encounter criteria above
Medication list provided by requestor
Order was placed, but patient may not currently be on the medication
Med order date is within 3 mo before or after any relevant encounter
MED_THERA_CLASS is not “Analgesics & Anesthetics” or “Topical Products”
MED_PHARM_CLASS is not “Decongestants” or “Cough/Cold”
Allergist seen indicators
Visit physician primary specialty contains “Allergy”
Comorbidities
ALLERGIC_RHINITIS_IND—when the <i>ICD</i> contains J30 then 1 else 0
ASTHMA_IND—when the <i>ICD</i> contains J45 then 1 else 0
ANAPHYLAXIS_IND—when the <i>ICD</i> is on the list below and the ENC_DX_NAME contains “ANAPHYLA” then 1 else 0
“T78.2XXA,” “T78.2XXD,” “T78.2XXS,” “T78.3XXA,” “T78.3XXD,” “T78.3XXS”
These <i>ICDs</i> are classified under multiple categories: anaphylaxis, angioedema, food
“T78.00XA,” “T78.00XD,” “T78.00XS,” “T78.01XA,” “T78.01XD,” “T78.02XA,” “T78.02XD,” “T78.03XD,” “T78.05XA,” “T78.05XD,” “T78.05XS”
“T78.07XA,” “T78.07XD,” “T78.09XA,” “T78.09XD,” “T78.09XS,” “T78.1XXA”
ANGIOEDEMA_IND—when the <i>ICD</i> is on the list below and the ENC_DX_NAME contains “EDEMA” then 1 else 0
“T78.2XXA,” “T78.2XXD,” “T78.2XXS,” “T78.3XXA,” “T78.3XXD,” “T78.3XXS”
These <i>ICDs</i> are classified under multiple categories: anaphylaxis, angioedema, food
“T78.00XA,” “T78.00XD,” “T78.00XS,” “T78.01XA,” “T78.01XD,” “T78.02XA,” “T78.02XD,” “T78.03XD,” “T78.05XA,” “T78.05XD,” “T78.05XS”
“T78.07XA,” “T78.07XD,” “T78.09XA,” “T78.09XD,” “T78.09XS,” “T78.1XXA”
FOOD_ALLERGY_IND—when the <i>ICD</i> is on the list below then 1 else 0
“Z91.010,” “Z91.011,” “Z91.012,” “Z91.013,” “Z91.018,” “Z91.02,” “T78.1XXA,” “T78.1XXD,” “T78.1XXS”
These <i>ICDs</i> are classified under multiple categories: anaphylaxis, angioedema, food
“T78.00XA,” “T78.00XD,” “T78.00XS,” “T78.01XA,” “T78.01XD,” “T78.02XA,” “T78.02XD,” “T78.03XD,” “T78.05XA,” “T78.05XD,” “T78.05XS,”
“T78.07XA,” “T78.07XD,” “T78.09XA,” “T78.09XD,” “T78.09XS,” “T78.1XXA”
VENOM_ALLERGY_IND—when the <i>ICD</i> is 1 of the following “Z91.038,” “Z91.030” then 1 else 0

ICD, International Classification of Diseases.

TABLE E3. Variation in insurance by race and use of antihistamine therapy

Prescription	Insurance	White (N = 1077)	Unknown (N = 389)	Non-White (N = 541)	Total (N = 2007)
First-generation only	Commercial/Medicare	62.60%	10.50%	26.80%	100.00%
First-generation only	Commercial/Medicare	119	20	51	190
First-generation only	Medicaid	50.00%	25.00%	25.00%	100.00%
First-generation only	Medicaid	2	1	1	4
First-generation only	No Insurance			100.00%	100.00%
First-generation only	No Insurance			2	2
Second-generation only	Commercial/Medicare	46.80%	22.00%	31.20%	100.00%
Second-generation only	Commercial/Medicare	81	38	54	173
Second-generation only	Medicaid	28.60%	28.60%	42.90%	100.00%
Second-generation only	Medicaid	2	2	3	7
Second-generation only	No insurance	28.60%	28.60%	42.90%	100.00%
Second-generation only	No insurance	2	2	3	7
First- and second-generation	Commercial/Medicare	42.00%	18.80%	39.10%	100.00%
First- and second-generation	Commercial/Medicare	29	13	27	69
First- and second-generation	Medicaid	57.10%	14.30%	28.60%	100.00%
First- and second-generation	Medicaid	4	1	2	7
First- and second-generation	No insurance		100.00%		100.00%
First- and second-generation	No insurance		2		2
No H1 antihistamine	Commercial/Medicare	55.50%	20.00%	24.50%	100.00%
No H1 antihistamine	Commercial/Medicare	823	296	364	1,483
No H1 antihistamine	Medicaid	25.00%	20.50%	54.50%	100.00%
No H1 antihistamine	Medicaid	11	9	24	44
No H1 antihistamine	No insurance	21.10%	26.30%	52.60%	100.00%
No H1 antihistamine	No insurance	4	5	10	19
Total		53.70%	19.40%	27.00%	100.00%
Total		1077	389	541	2007

TABLE E4. Summary statistics for AMC-affiliated allergist-immunologist practice subpopulation

Variable	Count	Percent of sample (N = 475)	Percent of CSU cohort (N = 2007)
NUMBER OF PATIENTS	475	100%	24%
OUTCOMES	124	26%	6%
FEMALE	327	69%	16%
DIST_CLIN_MEAN	10.7	2%	1%
DIST_CLIN_MEDIAN	8.3	2%	0%
COMORB_0	140	29%	7%
COMORB_1	134	28%	7%
COMORB_2	126	27%	6%
COMORB_3	60	13%	3%
COMORB_4	14	3%	1%
COMORB_5	1	0%	0%
WHITE	273	57%	14%
NON_WHITE	133	28%	7%
UNKNOWN	69	15%	3%
INSURE_COMMERCIAL	450	95%	22%
INSURE_MEDICAID	14	3%	1%
INSURE_NONE	11	2%	1%
WHITE_COMMERCIAL	267	56%	13%
NON_WHITE_COMMERCIAL	121	25%	6%
UNKNOWN_COMMERCIAL	62	13%	3%

TABLE E5. Multivariate OR analysis results of omalizumab utilization for AMC-affiliated allergist-immunologist practice subpopulation

Variable	Coefficient	P value	OR	Lower CI	Upper CI
(Intercept)	−0.885	.051	0.413	0.167	0.995
AGE	0.006	.323	1.006	0.994	1.018
PAT_GENDER_F	−0.236	.371	0.789	0.471	1.331
ALLERGY_COMORBIDITIES	0.030	.789	1.030	0.827	1.281
DIST_CLIN	0.028	.066	1.028	0.998	1.059
INSURANCE_Medicaid	−0.920	.400	0.398	0.021	2.368
INSURANCE_No_Insurance	−14.861	.983	0.000	NA	2.06×10^{17}
RACE_ETH_Non_White	−1.401	<.001	0.246	0.125	0.457
RACE_ETH_Unknown	−1.756	<.001	0.173	0.058	0.418

NA, Not applicable/available.

TABLE E6. Summary statistics for patients with known distances to any prescriber

Variable	Count	Percent of sample (N = 831)	Percent of CSU cohort (N = 2007)
TOTAL_n	831	100%	41%
OUTCOMES	118	14%	6%
FEMALE	585	70%	29%
DIST_MEDIAN_MEAN	9.5	1%	0%
DIST_MEDIAN_MEDIAN	7.3	1%	0%
COMORB_0	350	42%	17%
COMORB_1	230	28%	11%
COMORB_2	164	20%	8%
COMORB_3	69	8%	3%
COMORB_4	17	2%	1%
COMORB_5	1	0%	0%
WHITE	448	54%	22%
NON_WHITE	229	28%	11%
UNKNOWN	154	19%	8%
INSURE_COMMERCIAL	794	96%	40%
INSURE_MEDICAID	24	3%	1%
INSURE_NONE	13	2%	1%
WHITE_COMMERCIAL	437	53%	22%
NON_WHITE_COMMERCIAL	213	26%	11%
UNKNOWN_COMMERCIAL	144	17%	7%

TABLE E7. Multivariate OR analysis results of omalizumab utilization for patients with known distances to any prescriber

Variable	Coefficient	P value	OR	Lower CI	Upper CI
(Intercept)	−1.748	.000	0.174	0.074	0.396
AGE	0.001	.932	1.001	0.989	1.012
PAT_GENDER_F	−0.213	.422	0.808	0.485	1.375
ALLERGY_COMORBIDITIES	0.224	.045	1.251	1.003	1.555
DIST_MEDIAN	0.028	.046	1.029	1.000	1.057
INSURANCE_Medicaid	0.024	.976	1.025	0.153	4.057
INSURANCE_No_Insurance	−13.538	.985	0.000	NA	1.67×10^{22}
RACE_ETH_Non_White	−1.416	<.001	0.243	0.118	0.456
RACE_ETH_Unknown	<0.001	<.001	0.066	0.011	0.218

NA, Not applicable/available.