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## Letters Trends in racial disparities of emergency department utilization for asthma in coronavirus disease 2019



Annals

CONS

Racial disparities between White and non-White patients with asthma in the United States have been documented before the coronavirus disease 2019 (COVID-19) pandemic.<sup>1,2</sup> During the pandemic, non-White populations experienced disproportionately higher rates of COVID-19 infection, hospitalization, and mortality.<sup>3</sup> Survey data of patients and providers also suggest that the pandemic worsened the ability of non-White patients with asthma' to afford asthma medications and control their symptoms.<sup>4</sup> The pandemic did, however, hasten the adoption of several societal and health care system changes, including mask use, social distancing, remote work and schooling, and expansion of telemedicine. These interventions are potentially protective to patients with asthma by means of decreased exposure to respiratory pathogens, and telemedicine can improve provider access among the socioeconomically disadvantaged.<sup>5</sup> There is currently a paucity of large-scale studies regarding the impact of the pandemic on racial disparities in health care use for patients with asthma. To address this, we leveraged data from a large externally validated multisite data aggregation initiative to evaluate how the pandemic affected known disparities in emergency department (ED) use between White and non-White patients with asthma.<sup>6</sup>

This was an interrupted time-series (ITS) analysis of retrospective data from a large, nationwide data aggregation collaboration. Epic Corporation's Aggregate Data Program (ADP) combines deidentified electronic health record data monthly from the Epic sites across all 50 states. Variables collected by ADP include total patient counts, asthma prevalence, and relative monthly incidence of asthma-related ED visits. The ADP defines patients with asthma as nondeceased patients with an active diagnosis of asthma on their problem lists, or patients with encounters or billing diagnoses of asthma in the past year based on International Classification of Diseases, Tenth Revision. Asthma ED visits are defined as ED encounters with an associated visit diagnosis of asthma on the basis of International Classification of Diseases, Tenth Revision. Asthma prevalence and ED visits are stratified by race, ethnicity, age groups (pediatric vs adult), sex, and location (ie, state). For our analysis, we evaluated data from January 1, 2017 to February 1, 2021.

We determined the monthly incidence of asthma ED visits (calculated as the number of asthma ED visits divided by the number of patients with asthma) for non-White (combined black, Asian, Native American/Alaskan Native, and Hawaiian/Pacific Islander) and White patients with asthma separately. We then calculated the monthly risk ratio by dividing the incidence among non-White patients with asthma by the incidence among White patients with asthma. This risk ratio served as our measure for racial disparity. We defined the

**Disclosures:** The authors have no conflicts of interest to report. **Funding:** The authors have no funding sources to report. start of the pandemic as March 11, 2020, based on the World Health Organization's declaration. We compared the prepandemic and pandemic risk ratio by means of an unpaired *t* test. We performed an ITS analysis by constructing a linear regression model of risk ratio as predicted by time and onset of a pandemic. All analyses were done in R version 4.0.3 (The R Foundation, Vienna, Austria).<sup>7</sup> Institutional review was not sought as the data were deidentified and aggregated at the population level.

The ADP included a monthly average of 77.3 ( $\pm$  32.4) million patients, with 22.4 million patients in January 2017 (beginning) and 102.2 million in February 2021 (end). The monthly average of patients with asthma was 4.6  $(\pm 1.9)$  million patients, starting with 1.3 million and ending with 6.0 million. Monthly asthma prevalence was 5.9% ( $\pm$  0.2%), with 5.9% at the beginning and 6.0% at the end. Adult patients with asthma (ie,  $\geq 20$  years) comprised 76.4% of our population, and women comprised 59.1%. Our data included a total of 15.4 million asthma ED visits, 59.0% of which were by non-White patients with asthma. The number of asthma ED visits per month on average was 0.31 ( $\pm$  0.12) million, with 0.087 million in January 2017 and 0.25 million in February 2021. The pandemic risk ratio was statistically significantly lower than prepandemic risk ratio (prepandemic mean 2.61, pandemic mean 2.54, P <.01). An ITS analysis revealed a prepandemic risk ratio trend of 0.006/month (95% confidence interval [CI], [0.003-0.009], P <.01). During the pandemic, the change in the risk ratio trend was -0.027 per month (95% CI [-0.043 to -0.012], P <.01). Prepandemic and pandemic trends in risk ratio are detailed in Figure 1. This shifting trend in risk ratio was reflected in adults (prepandemic: 0.008 per month, 95% CI [0.005-0.012]; pandemic: -0.034, 95% CI [-0.051 to -0.015]) but not in children (prepandemic: -0.005 per month, 95% CI [-0.009 to -0.001]; pandemic: 0.028, 95% CI [0.009-0.046]).

Our study found that, during the pandemic, the racial disparity in ED use among people with asthma did not worsen. In fact, the pandemic reversed a marginally positive prepandemic trend, although this trend visually appeared to begin normalizing in 2021. Despite the now well-described reduction in overall ED visits for asthma during COVID-19, the racial disparity in ED use between non-White and White patients with asthma remains substantial.<sup>8</sup>

It is possible that any number of the changes during the pandemic (ie, mask use, social distancing, remote work and schooling, telemedicine) caused this shifting trend. Recent data found that non-White patients with asthma who work outside the home experienced a significant reduction in asthma exacerbations during the pandemic, suggesting that COVID-associated precautions reduced respiratory infections and other environmental triggers of asthma exacerbation.<sup>5</sup> Phone and video conferencing allow providers, patients, employees,



Effect of COVID-19 Pandemic on Racial Disparity in Incidence of Asthma ED Visits

**Figure 1.** RR on the incidence of asthma-related ED visits among non-White to White patients with asthma before and during COVID-19 pandemic beginning March 11, 2020 (shaded area). The prepandemic RR trend was 0.006 per month, (95% CI, 0.003-0.009, *P* <.01); the pandemic RR trend was -0.027 per month, (95% CI, -0.043 to -0.012, *P* <.01). CI, confidence interval; COVID-19, coronavirus disease 2019; ED, emergency department; RR, risk ratio.

educators, and students to connect without the risk of airborne or droplet transmission, theoretically mitigating virus-induced exacerbations. These technologies could also enable the socioeconomically disadvantaged—who are disproportionately non-White—to readily access their primary care providers without barriers such as transportation limitations or missed workdays.<sup>9</sup>

The primary strength of our study arises from the volume of patients we were able to include across the national landscape by means of Epic's ADP data set, which has been validated against national survey data.<sup>6</sup> Our study has several limitations. The dearth of variables collected by the ADP data set prevented us from further investigating the specific etiology underlying the change in trend. In addition, the ADP data set does not deduplicate across Epic sites. Some patients may seek care at multiple Epic sites and so may be double-counted in asthma prevalence reporting. Other data sets with deidentified, aggregated data have struggled with similar duplication issues but have still yielded valuable insights.<sup>10</sup> Ultimately, more research is needed to investigate the factors underlying the observed trend change so we learn how to address racial disparities going forward.

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## References

- Fitzpatrick AM, Gillespie SE, Mauger DT, et al. Racial disparities in asthma-related health care use in the National Heart, Lung, and Blood Institute's Severe Asthma Research Program. J Allergy Clin Immunol. 2019;143(6):2052–2061.
- Zook HG, Payne NR, Puumala SE, Ziegler KM, Kharbanda AB. Racial/ethnic variation in emergency department care for children with asthma. *Pediatr Emerg Care*. 2019;35(3):209–215.
- Mackey K, Ayers CK, Kondo KK, et al. Racial and ethnic disparities in COVID-19related infections, hospitalizations, and deaths: a systematic review. Ann Intern Med. 2021;174(3):362–373.
- Baptist AP, Lowe D, Sarsour N, et al. Asthma disparities during the COVID-19 pandemic: a survey of patients and physicians. J Allergy Clin Immunol Pract. 2020;8 (10):3371–3377.e1.
- Salciccioli JD, She L, Tulchinsky A, Rockhold F, Cardet JC, Israel E. Effect of COVID-19 on asthma exacerbation. J Allergy Clin Immunol Pract. 2021;9(7):2896–2899.e1.
- Tarabichi Y, Goyden J, Liu R, Lewis S, Sudano J, Kaelber DC. A step closer to nationwide electronic health record-based chronic disease surveillance: characterizing asthma prevalence and emergency department utilization from 100 million patient records through a novel multisite collaboration. J Am Med Inform Assoc. 2020;27(1):127–135.

- R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2020. Available at: https://www.R-project.org/. Accessed May 1, 2021.
- Taquechel K, Diwadkar AR, Sayed S, et al. Pediatric asthma health care utilization, viral testing, and air pollution changes during the COVID-19 pandemic. J Allergy Clin Immunol Pract. 2020;8(10):3378–3387.e11.
- Williams DR, Priest N, Anderson NB. Understanding associations among race, socioeconomic status, and health: patterns and prospects. *Health Psychol*. 2016;35 (4):407–411.
- Newton-Dame R, McVeigh KH, Schreibstein L, et al. Design of the New York City macroscope: innovations in population health surveillance using electronic health records. *EGEMS (Wash DC)*. 2016;4(1):1265.

## Coronavirus disease 2019 vaccine hypersensitivity evaluated with vaccine and excipient allergy skin testing



Since the coronavirus disease 2019 (COVID-19) messenger RNA (mRNA) vaccines became available, Vaccine Adverse Event Reporting System data and early reports identified rare cases of anaphylaxis.<sup>1</sup> Banerji et al<sup>2</sup> proposed a suggested approach to skin test for COVID-19 vaccine excipients, specifically polyethylene glycol, polysorbate 80, and polysorbate 20. Using this algorithm, and skin testing with COVID-19 mRNA vaccine leftover from vial overfill, we report findings in a case series of 39 patients referred to an allergy and immunology practice for possible COVID-19 vaccine hypersensitivity from January to May 2021.

Expanded skin testing for COVID-19 vaccine excipients was performed as previously published.<sup>2</sup> In addition, percutaneous and intradermal skin tests (1:10 dilution and full strength both for pricks and intradermals) with Moderna and Pfizer COVID-19 vaccines were completed. We recorded whether premedication was used and analyzed available laboratory data (serum tryptase, soluble terminal complement complex, complete blood cell count with differential). Premedication could consist of H<sub>1</sub> blockers, H2 blockers, and leukotriene antagonists. An example regimen was cetirizine 20 mg, famotidine 40 mg, and montelukast 10 mg daily starting 3 days before the vaccine. Patient outcome or vaccine tolerance was assessed through follow-up and chart review.

Patient characteristics and atopic conditions are illustrated in Table 1. Notably, 77% (n = 30) of the patients were referred for reactions to COVID-19 mRNA vaccine. The remaining 23% (n = 9) were referred for other high-risk history for potential reaction to the vaccine. The most common clinical presentation (Table 1) was urticaria and angioedema, immediate (within 4 hours) in 36% of the patients (n = 14) and delayed (beyond 4 hours) in 28% of the patients (n = 11). Overall, 46% of the reactions were immediate (n = 18), and the mean time to occurrence was 32 minutes. Furthermore, 31% of the reactions was 3.8 days. Such designation was not applicable in 23% (n = 9) patients referred for other high-risk history.

None of the patients demonstrated positive percutaneous or intradermal skin test results for COVID-19 vaccine excipients. Furthermore, 11% of the patients (n = 4) had positive intradermal skin testing result to COVID-19 vaccines of unclear clinical significance (3 patients with immediate positive intradermal skin testing result to Moderna vaccine, 1 patient with delayed full-strength positive intradermal result to Pfizer vaccine). The patients with positive skin test results also tolerated the subsequent vaccine.

Of the patients, 95% (n = 37) tolerated their succeeding COVID-19 vaccine without serious allergic reaction. Furthermore, 92% (n = 36) have received 2 doses of COVID-19 vaccines. There was 1 patient

who was prescreened owing to severe chronic idiopathic urticaria and angioedema who elected to receive the Janssen vaccine. Of the patients who tolerated their subsequent COVID-19 vaccine, 62%(n = 23) received premedication.

One patient with initial reaction to Moderna experienced nausea and pruritus during skin testing, similar but milder than initial reaction. Despite negative skin test results, this necessitated

## Table 1

Patient Characteristics and COVID-19 Vaccine Hypersensitivity

Characteristic	Value
Age, mean (SD), y	56(16)
Sex, n (%)	
Female	34 (87)
Male	5(13)
Ethnicity, n (%)	
White	34 (87)
African American	3 (8)
Hispanic	2(5)
Vaccine, n (%)	
Moderna	19 (47.5
Pfizer	19 (47.5
Janssen	$2(5)^{a}$
Patients on baseline antihistamine, n (%)	14 (36)
Patients on baseline montelukast, n (%)	8 (21)
Peripheral eosinophilia, n (%)	3 (8)
Elevated serum tryptase, n (%)	2(5)
Atopic, n (%)	37 (95)
Concomitant allergic disorders, n (%) <sup>b</sup>	
Allergic rhinitis	21 (54)
Antibiotics allergy	21 (54)
Asthma or COPD	12 (31)
Food allergy	8 (21)
Chronic idiopathic urticaria and angioedema	16 (41)
Mastocytosis	1(3)
Most common reactions, n (%)	. ,
Immediate urticaria and angioedema (<4 h after vaccine)	14 (36)
Delayed urticaria and angioedema (>4 h after vaccine)	11 (28)
Asthma, COPD chest tightness, or shortness of breath	3 (8)
Syncopal or vasovagal	2(5)
Concerning high-risk history for potential to have allergic reaction on receipt of vaccine	
Allergy to meds or other high-risk allergy history (includes latex and hymenoptera)	5(13)
Reaction to other vaccines or injectables	6 (15) <sup>c</sup>
Clinical history of concern for polyethylene glycol allergy	2(5)
Treatments of acute vaccine reactions requiring intramuscular	. ,
epinephrine and systemic corticosteroids	
Received intramuscular epinephrine and systemic corticoste-	2(5)
roids, n (%)	2 (5)
Received systemic corticosteroids only, n (%)	2(5)

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; meds, medications.

<sup>a</sup>A total of 40 vaccines, 39 patients (1 received Moderna and then Janssen).

<sup>b</sup>Total percentages exceeded 100% owing to overlap.

<sup>c</sup>4 patients had reaction to influenza vaccine. 2 patients had reaction to omalizumab.

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