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Publication Date

2024-02-01

DOI

10.1016/j.ajo.2023.07.004

Peer reviewed

HHS Public Access

Author manuscript

Am J Ophthalmol. Author manuscript; available in PMC 2024 March 25.

Published in final edited form as:

Am J Ophthalmol. 2024 February ; 258: 139–144. doi:10.1016/j.ajo.2023.07.004.

Risk of herpes zoster ophthalmicus after COVID-19 vaccination in a large US healthcare claims database

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Introduction

One million cases of herpes zoster (HZ) are diagnosed in the United States every year with herpes zoster ophthalmicus (HZO) accounting for 10 to 20 percent of those cases.[1] HZO occurs when latent varicella zoster virus (VZV) reactivates in the ophthalmic branch of the trigeminal nerve, resulting in a range of clinical manifestations including periocular rash, conjunctivitis, keratitis, uveitis, and acute retinal necrosis.[1,2] HZO is associated with significant ocular morbidity and can lead to long-term consequences such as chronic or recurrent disease, postherpetic neuralgia, and blindness.[1,3] Understanding the risk factors for the emergence and recurrence of HZO represents an important component in reducing the burden of this disease.

There have been numerous case reports of HZO following administration of the first, second, and booster doses of the coronavirus 2019 (COVID-19) vaccines, with many of these case reports proposing vaccine-related immunomodulation as the mechanism for this potential relationship.[4–10] Although these reports raise concern for a link between COVID-19 vaccination and HZO, they could represent a reporting bias due to heightened scrutiny of the COVID-19 vaccines rather than a true increase in disease risk. To date, there have been no epidemiologic studies of HZO risk following COVID-19 vaccination, rendering concerned clinicians and patients unable to definitively assess risk. The objective of this study was to determine whether COVID-19 vaccination is associated with an increased risk of HZO.

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Financial Disclosures: Dr. Acharya receives research support in the form of drug donation from AbbVie, Inc. for an NIH-funded clinical trial and has served as a consultant for Roche. No other authors have any financial disclosures.

Meeting Presentations: Poster presentation at the Association for Research in Vision and Ophthalmology's 2022 Annual Meeting.

Supplemental Material available at AJO.com.

Methods

Data Source

This retrospective self-controlled risk interval analysis was conducted using de-identified healthcare claims data from Optum Labs Data Warehouse (OLDW; Optum Labs, Eden Prairie, MN).[11] OLDW contains medical and pharmacy claims from approximately 200 million commercial and Medicare Advantage enrollees in the United States from 1994 to present day. The database includes a mixture of ages, races and ethnicities, and geographical regions across the country. This study was approved by the Institutional Review Board of the University of California, San Francisco and was conducted in adherence with the tenets of the Declaration of Helsinki.

Study Population

The study population consisted of patients who received any dose of a COVID-19 vaccine with emergency use authorization from the US Food and Drug Administration (BNT162b2, Pfizer; mRNA-1273, Moderna; Ad26.COV2.S, Janssen) from December 11, 2020 through June 30, 2021. COVID-19 vaccines were identified by the presence of a Current Procedural Terminology (CPT) or Healthcare Common Procedure Coding System (HCPCS) code in the medical claims, or an 11-digit National Drug Code (NDC) or drug name text search in the pharmacy claims (Supplemental Table 1). Patients with vaccination records inconsistent with CDC guidance at the time of the study (excess doses, vaccination prior to a vaccine's date of emergency use authorization or prior to age-eligibility) were excluded.

Study Design

A self-controlled risk interval (SCRI) design was used to assess whether there was an increased risk of HZO following COVID-19 vaccination. This design involves comparing the incidence of HZO in an exposed risk interval immediately following COVID-19 vaccination to a pre-defined unexposed control interval within the same patient, but remote from vaccination. Self-controlled designs inherently control for time-invariant factors such as demographics and chronic diseases, and are frequently used to study post-licensure vaccine safety.[12,13] However, self-controlled designs require that the probability of experiencing an outcome does not vary over the study period, and that outcome events are independently recurrent or rare. To not violate these assumptions, we excluded patients with a history of HZO prior to the study period, since there is evidence that the probability of HZO recurrence is higher soon after a flare.[14] For similar reasons, we only counted the first occurrence (incident case) of HZO during the study period and disregarded subsequent cases.[12]

We defined the index date as the date of the first recorded COVID-19 vaccination during the study period. We defined the control interval as 90 days to 60 days prior to the index date for each patient, allowing for a 60-day healthy vaccinee effect window between the control and risk periods.[15] Patients were required to be continuously enrolled in both medical and pharmacy coverage from 365 days prior to the start of the control interval through July 31, 2021 to allow for assessment of baseline characteristics, HZO history, and HZO cases after

vaccination. Patients with a history of HZO in the 365 days prior to the control interval were excluded.

Outcome Assessment

Individuals who met the inclusion criteria were evaluated for HZO during the 30-day control interval and in the 30 days after receiving a dose of the vaccine or up to the date of the second dose, if the second dose was given less than 30 days after the initial dose. HZO diagnoses were identified during risk periods using International Classification of Disease 10th revision (ICD-10) code B02.3x in the primary or secondary diagnosis position in a medical claim. Both a HZO diagnosis and a systemic antiviral prescription (acyclovir, valacyclovir, or famciclovir) were required to qualify as a HZO outcome event. Among patients who were not on antivirals at the start of the interval, a new antiviral prescription within five days after the first HZO diagnosis was required. Among patients who were on antivirals at the start of the interval, we required either a dose escalation of the antiviral medication, or addition of an oral or ophthalmic steroid within five days following the first HZO diagnosis (Supplemental Table 2). Antiviral dose escalation was identified using the methods described in the Appendix and Supplemental Table 3 (available at AJO.com). In order to identify probable acute HZO episodes, patients were censored at the first qualifying HZO outcome event (i.e. patients could not experience an event after both vaccine doses). ICD-10 codes used to identify comorbidities are shown in Supplemental Table 4.

Statistical Analysis

Conditional Poisson regression models were used to estimate incidence rate ratios (IRR) and corresponding 95% confidence intervals (CI) comparing the risk of HZO in the risk intervals after vaccination to the risk of HZO during the control interval. An offset of the natural log of the entire length of the observed interval was used to account for unequal control and risk interval lengths. Time-varying covariates were assessed, but not adjusted for due to small sample size. Subgroup analyses were conducted by age (less than 50 years vs. 50 years and older) and COVID-19 vaccine type.

Statistical analyses were performed in R (Version 4.1.0, R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/). P-values < 0.05 were considered statistically significant.

Results

A total of 1,959,157 individuals received a COVID-19 vaccine during the study period and were eligible for the SCRI design. The SCRI analysis included 80 patients without a prior history of HZO. The baseline demographics, comorbidities, and vaccination dose characteristics of this group are detailed in Table 1. The mean age was 54.0 (standard deviation [SD] = 12.3), 52.5% were male, and 72.5% were White. The most common comorbidity was diabetes (25.0%). Of the 105 COVID-19 vaccination doses captured in this group, the majority were BNT162b2 (>51.4%).

There were 45 HZO cases in the risk interval following COVID-19 vaccination. The unadjusted incidence rate of HZO following any dose of COVID-19 vaccination was

19.1 cases per 100,000 person-years. The incidence rate ratio comparing the risk of HZO following COVID-19 vaccination to the risk of HZO during the control interval was 0.80 (95% CI: 0.51 – 1.26, p = 0.33).

Subgroup analyses were conducted by age and vaccine type. The incidence rates of HZO in individuals aged <50 years old and ≥50 years old were 13.4 per 100,000 person-years and 27.6 per 100,000 person-years, respectively. Those aged 50 years and older were not at an increased risk of HZO following COVID-19 vaccination (IRR = 0.65, 95% CI: 0.37– 1.15, p = 0.14). We also did not find an increase in HZO risk following vaccination with BNT162b2 (IRR = 0.90, 95% CI: 0.49– 1.69, p = 0.74), mRNA-1273 (IRR = 0.74, 95% CI: 0.36– 1.54, p = 0.42), or Ad26.COV2.S (IRR = 0.50, 95% CI: 0.07–2.56, p = 0.42) (Table 2).

Among the 45 patients that developed HZO following vaccination, the median time to HZO was 12 days (interquartile range [IQR]: 7–16 days following any dose of COVID-19 vaccination. The median time to HZO was 11 days (IQR: 7–15 days) following dose one of the COVID-19 vaccination. Following dose two of the COVID-19 vaccination, the median time to HZO was 15 days (IQR: 7–23.2 days).

Discussion

In this SCRI analysis, we found no increased risk of HZO following COVID-19 vaccination with BNT162b2, mRNA-1273, or Ad26.COV2.S. Stratification by age did not show any difference in risk. The incidence of HZO after COVID-19 vaccination in individuals without a prior history of HZO was 19.1 per 100,000 person-years.

Prior research on the incidence of HZO conducted by our group using the same claims database has shown that HZO incidence is overall slowly increasing in the United States. In particular, the risk of HZO has increased in middle-aged patients who are not yet eligible for the zoster vaccination, while the incidence of HZO has decreased in individuals older than 60 since the introduction of the first zoster vaccine, Zostavax, in 2006. The overall incidence rate of HZO from this previous study was 38.9 per 100,000 person-years, with incidence rates of 17.8 per 100,000 person-years for those age <50 and 79.0 per 100,000 person-years for those age ≥50.[16] In another study utilizing data from Kaiser Permanente Hawaii, the overall incidence of HZO was found to be 30.9 per 100,000 person-years.[17] Compared to our current study, the incidence rates found in these previous studies are higher; this may be explained by the younger population included in this study. However, the low incidence of HZO following COVID-19 vaccination observed in our study compared to the estimated incidence in the general population supports our study's findings of no increased risk of HZO following COVID-19 vaccination.[16,17]

HZO following COVID-19 vaccination has been reported in multiple case reports since the widespread distribution of the COVID-19 vaccines.[4–10] In general, reactivation of VZV is associated with states of diminished cell-mediated immunity, as arises from older age and immunosuppression.[18] HZO has been described following administration of the zoster virus live vaccine and the recombinant zoster virus vaccine,[19,20] though a mechanism for this potential relationship has not been determined. In the case of the mRNA COVID-19

vaccines, it has been hypothesized that stimulation of toll-like receptors, a pathway implicated in the reactivation of VZV from latency, could explain the development of HZ and HZO after vaccination.[21–23]

Results from studies on HZ following COVID-19 vaccination have been mixed.[24–27] Our group has published the largest cohort study analyzing occurrence of HZ after COVID-19 vaccination and found no increase in risk following a full or single dose of the COVID-19 primary vaccination series.[28] This report, however, did not examine risk of HZO following COVID-19 vaccination.

To date, characterization of the nature of HZO cases following COVID-19 vaccination has been limited by the small number of cases reported. Our study is the first known report monitoring the real-world safety of COVID-19 vaccination and HZO risk, providing reassurance to patients and providers concerned about the safety profile of the COVID-19 vaccines.

There are several limitations to this study. One limitation is the potential for misclassification of exposure or outcome due to the limited granularity of claims-based data. Incomplete capture of COVID-19 vaccine records is an established limitation of insurance claims data.[29] Therefore, we could not be certain that an individual without record of COVID-19 vaccination in the database was truly unvaccinated. However, use of the SCRI design is a strength as it allowed us to prevent misclassification of COVID-19 vaccination status; by using an SCRI design, we were able to use patients with a record of COVID-19 vaccination as their own control to avoid this known issue. Use of the SCRI design, however, is limited in that we cannot study patients with a prior history of HZO as the timing of the original event may influence the risk of recurrence. To avoid misclassification of HZO outcome in our claims-based data, we required an ICD-10 code and a prescription or escalation of antivirals within five days of diagnosis. We considered the possible impact of the recombinant zoster vaccine. However, less than 11 patients (exact number not presented to protect patient privacy) had a change in zoster vaccine status during the study period. Therefore, due to sparse numbers, this could not be reasonably adjusted for as a covariate in the models. Additionally, we would expect similar immunity from prior vaccination during the control and risk intervals given the proximity of these time periods as immunity would not be expected to change quickly enough to impact results in the study period. Another limitation of this study is patients with basic insurance plans or no insurance coverage are not captured in OLDW, and thus our study may represent a more economically advantaged population. Lastly, as the outcome is rare, our sample size prevents us from studying important subgroups that may be at higher risk such as immunosuppressed or older individuals. Future research on these subgroups and in patients with a prior history of HZO would provide additional valuable information.

This study is the first epidemiologic assessment of the relationship between any vaccination and HZO. Although the sample size that developed HZO during the study period was small, our study is much larger than what can be captured in single hospital centers and likely other claims databases. Therefore, although rare, this study allowed us to examine this clinically significant outcome. We found the risk of HZO was not increased following COVID-19

vaccination using a rigorous SCRI design which allows us to control for time-invariant factors. Our study adds to the existing body of literature monitoring the real-world safety of the COVID-19 vaccines and provides reassurance to patients and providers concerned about the safety profile of the COVID-19 vaccines.

Conclusion

This study found no evidence of an increased risk of HZO following COVID-19 vaccination. This result supports the safety of the COVID-19 vaccines from an ophthalmic standpoint and can provide reassurance for patients and providers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Funding/Support:

This study was funded by the National Eye Institute and Office of Research on Women's Health at the National Institutes of Health (R01 EY028739, PI Acharya) and an Optum Labs Data Warehouse research credit. The UCSF Department of Ophthalmology is supported by a core grant from the NEI (EY06190) and an unrestricted grant from the Research to Prevent Blindness Foundation. The sponsors of this study had no role in the study design, data collection, analysis, interpretation, manuscript preparation, or decision to submit this manuscript.

References

1. Liesegang TJ. Herpes Zoster Ophthalmicus. Natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008;115(2 SUPPL.):3–12. doi:10.1016/j.ophtha.2007.10.009 [PubMed: 17997486]
2. Shaikh S, Ta CN. Evaluation and management of herpes zoster ophthalmicus. Am Fam Physician. 2002;66(9). https://pubmed-ncbi-nlm-nih-gov.ucsf.idm.oclc.org/12449270/
3. Tran KD, Falcone MM, Choi DS, et al. Epidemiology of herpes zoster ophthalmicus: recurrence and chronicity. Ophthalmology. 2016;118(24):6072–6078. doi:10.1016/j.ophtha.2016.03.005
4. Lazzaro DR, Ramachandran R, Cohen E, Galetta SL. COVID-19 vaccination and possible link to herpes zoster. Am J Ophthalmol Case Rep. 2022;25:101359. doi:10.1016/j.ajoc.2022.101359 [PubMed: 35097240]
5. Bernardini N, Skroza N, Mambrin A, et al. Herpes zoster ophthalmicus in two women after Pfizer-BioNTech (BNT162b2) vaccine. J Med Virol. Published online September 29, 2021. doi:10.1002/jmv.27366
6. Thimmanagari K, Veeraballi S, Roach D, Al Omour B, Slim J. Ipsilateral zoster ophthalmicus post COVID-19 vaccine in healthy young adults. Cureus. 2021;13(7):e16725. doi:10.7759/cureus.16725 [PubMed: 34471577]
7. Papasavvas I, de Courten C, Herbort CP. Varicella-zoster virus reactivation causing herpes zoster ophthalmicus (HZO) after SARS-CoV-2 vaccination - report of three cases. J Ophthalmic Inflamm Infect. 2021;11(1):28. doi:10.1186/s12348-021-00260-4 [PubMed: 34529153]
8. Rallis KI, Fausto R, Ting DSJ, Al-Aqaba MA, Said DG, Dua HS. Manifestation of herpetic eye disease after COVID-19 vaccine: a UK Case Series. Ocul Immunol Inflamm. Published online April 12, 2022:1–6. doi:10.1080/09273948.2022.2046795
9. Ryu KJ, Kim DH. Recurrence of varicella-zoster virus keratitis after SARS-CoV-2 vaccination. Cornea. 2022;41(5):649–650. doi:10.1097/ICO.0000000000002999 [PubMed: 35383620]
10. Martora F, Fabbrocini G, Picone V. A case of herpes zoster ophthalmicus after third dose of Comirnaty (BNT162b2 mRNA) vaccine. Dermatol Ther. 2022;35(5). doi:10.1111/dth.15411

11. OptumLabs. OptumLabs and OptumLabs Data Warehouse (OLDW) descriptions and citation. OptumLabs OptumLabs Data Wareh OLDW Descr Cit.
12. Petersen I, Douglas I, Whitaker H. Self controlled case series methods: an alternative to standard epidemiological study designs. BMJ. 2016;354:i4515. doi:10.1136/BMJ.I4515 [PubMed: 27618829]
13. Whitaker HJ, Farrington CP, Spiessens B, Musonda P. Tutorial in biostatistics: the self-controlled case series method. Stat Med. 2006;25(10):1768–1797. doi:10.1002/sim.2302 [PubMed: 16220518]
14. Lee SM, Han J, Yang CM, et al. Chronic and recurrent herpes zoster ophthalmicus. Med Kaunas Lith. 2021;57(10):999. doi:10.3390/medicina57100999
15. Rowhani-Rahbar A, Klein NP, Dekker CL, et al. Biologically plausible and evidence-based risk intervals in immunization safety research. Vaccine. 2012;31(1):271–277. doi:10.1016/j.vaccine.2012.07.024 [PubMed: 22835735]
16. Kong CL, Thompson RR, Porco TC, Kim E, Acharya NR. Incidence rate of herpes zoster ophthalmicus: a retrospective cohort study from 1994 through 2018. Ophthalmology. 2020;127(3):324–330. doi:10.1016/J.OPHTHA.2019.10.001 [PubMed: 31668889]
17. Borkar DS, Tham VM, Esterberg E, et al. Incidence of herpes zoster ophthalmicus: results from the Pacific Ocular Inflammation Study. PLoS ONE. 2017;32(7):736–740. doi:10.1371/journal.pone.0178059
18. Weinberg A, Levin MJ. VZV T cell-mediated immunity. Curr Top Microbiol Immunol. 2010;342:341–357. doi:10.1007/82_2010_31 [PubMed: 20473790]
19. Hwang CW, Steigleman WA, Saucedo-Sanchez E, Tuli SS. Reactivation of herpes zoster keratitis in an adult after varicella zoster vaccination. Cornea. 2013;32(4):508–509. doi:10.1097/ICO.0b013e318277acae [PubMed: 23187165]
20. Lu TJ, Ta CN. Reactivation of herpes zoster keratitis following Shingrix vaccine. Case Rep Ophthalmol. 2022;13:104–108. doi:10.1159/000522272 [PubMed: 35431886]
21. A C KL. Immune responses induced by mRNA vaccination in mice, monkeys and humans. Vaccines. 2021;9(1):1–14. doi:10.3390/VACCINES9010061
22. Zhang C, Maruggi G, Shan H, Li J. Advances in mRNA vaccines for infectious diseases. Front Immunol. 2019;10. Accessed February 21, 2022. https://www.frontiersin.org/article/10.3389/fimmu.2019.00594
23. West JA, Gregory SM, Damania B. Toll-like receptor sensing of human herpesvirus infection. Front Cell Infect Microbiol. 2012;2:122. doi:10.3389/fcimb.2012.00122 [PubMed: 23061052]
24. Birabaharan M, Kaelber DC, Karris MY. Risk of herpes zoster reactivation after messenger RNA COVID-19 vaccination: A cohort study. J Am Acad Dermatol. Published online November 23, 2021. doi:10.1016/j.jaad.2021.11.025
25. Brosh-Nissimov T, Sorek N, Yeshayahu M, et al. Oropharyngeal shedding of herpesviruses before and after BNT162b2 mRNA vaccination against COVID-19. Vaccine. 2021;39(40):5729–5731. doi:10.1016/j.vaccine.2021.08.088 [PubMed: 34481701]
26. Shasha D, Bareket R, Sikron FH, et al. Real-world safety data for the Pfizer BNT162b2 SARS-CoV-2 vaccine: historical cohort study. Clin Microbiol Infect. 2022;28(1):130–134. doi:10.1016/j.cmi.2021.09.018 [PubMed: 34592420]
27. Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. N Engl J Med. 2021;385(12):1078–1090. doi:10.1056/NEJMoa2110475 [PubMed: 34432976]
28. Akpandak I, Miller DC, Sun Y, Arnold BF, Kelly JD, Acharya NR. Assessment of herpes zoster risk among recipients of COVID-19 vaccine. JAMA Netw Open. 2022;5(11):e2242240. doi:10.1001/jamanetworkopen.2022.42240 [PubMed: 36383382]
29. Centers for Medicare & Medicaid Services (CMS). Assessing the completeness of Medicare claims data for measuring COVID-19 vaccine administration. Centers for Medicare & Medicaid Services (CMS). Accessed March 22, 2022. https://www.cms.gov/files/document/assessing-completeness-medicare-claims-data-measuring-covid-19-vaccine-administration.pdf

Table 1.

Characteristics of COVID-19 vaccinated patients and COVID-19 vaccine doses included in the self-controlled risk interval analysis

Patient-level Characteristics	**N patients (%) (N=80)**
Age	
Mean (SD)	54.0 (12.3)
Median [Q1, Q3]	56.5 [46.0, 62.0]
Gender	
Female	38 (47.5%)
Male	42 (52.5%)
Race	
White	58 (72.5%)
Non-White	22 (27.5%)
Healthcare utilization	
Ambulatory visit count	
Mean (SD)	14.2 (14.6)
Median [Q1, Q3]	9.0 [5.0, 18.0]
Inpatient visit ever	18 (22.5%)
Medical history[†]	
Autoimmune disease	<11 (<13.8%)
Cardiovascular disease	<11 (<13.8%)
Diabetes (any type)	20 (25.0%)
Immunocompromised[a]	<11 (<13.8%)
Received zoster vaccine	<11 (<13.8%)
Medication use[†]	
Systemic corticosteroids	<11 (<13.8%)
Other immunosuppressive drugs	<11 (<13.8%)
Antivirals	<11 (<13.8%)
Dose-level Characteristics	**N doses (%) (N=105)**
Type of vaccination[†]	
BNT162b2	>54 (>51.4%)
mRNA-1273	40 (38.1%)
Ad26.COV2.S	<11 (<10.5%)
Dose administered	
1st	58 (55.2%)
2nd	47 (44.8%)
Observation time after dose (days)	

Patient-level Characteristics	N patients (%) (N=80)
Mean (SD)	27.8 (3.6)
Median [Q1, Q3]	30.0 [27.0, 30.0]
Site of vaccination	
Office	26 (24.8%)
Outpatient hospital	22 (21.0%)
Pharmacy	46 (43.8%)
Other	11 (10.5%)
Date of vaccination	
Dec 2020 through Feb 2021	11 (10.5%)
Mar 2020 through Apr 2021	75 (71.4%)
May 2021 through Jun 2021	19 (18.1%)

[a]Immunocompromising conditions included HIV/AIDS, cancer, solid organ transplantation, and immunosuppressive medication use.

[†]OptumLabs requires cell counts of less than 11 to be reported as less than 11, rather than reporting true values, to protect patient privacy. To prevent back-calculation, the value in a corresponding cell of the same subgroup is lowered and reported with a greater-than sign to ensure that the total case count within the subgroup stays the same. Each affected subgroup's count and proportion were reported with greater-than and less-than signs.

Table 2.

Incidence rate ratios of HZO in overall self-controlled analysis and subgroup self-controlled analyses

Subgroup[†]	Total patients in subgroup	HZO cases in risk interval	Incidence Rate Ratio[a] (95% CI)	p
Overall	80	45	0.80 (0.51, 1.26)	0.329
Age < 50 years	30	19	1.14 (0.55, 2.48)	0.738
Age ≥ 50 years	50	26	0.65 (0.37, 1.15)	0.136
BNT162b2	>38	See footnote[b]	0.90 (0.49, 1.69)	0.741
mRNA-1273	31		0.74 (0.36, 1.54)	0.418
Ad26.COV2.S	<11		0.50 (0.07, 2.56)	0.423

Abbreviations: HZO = herpes zoster ophthalmicus; CI = confidence interval.

[a]Incidence rate ratios compare the incidence of HZO in exposed (risk) intervals after vaccination to unexposed (control) interval within the same individual.

[b]To protect patient privacy, HZO case counts cannot be displayed within these small subgroups.

[†]OptumLabs requires cell counts of less than 11 to be reported as less than 11, rather than reporting true values, to protect patient privacy. To prevent back-calculation, the value in a corresponding cell of the same subgroup is lowered and reported with a greater-than sign to ensure that the total case count within the subgroup stays the same. Each affected subgroup's count and proportion were reported with greater-than and less-than signs.