Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 72 / No. 30
July 28, 2023

# Health Care Provider Knowledge Regarding Alpha-gal Syndrome — United States, March–May 2022

Ann Carpenter, DVM[1]; Naomi A. Drexler, DrPH[2]; David W. McCormick, MD[2]; Julie M. Thompson, DVM, PhD[2]; Gilbert Kersh, PhD[2]; Scott P. Commins, MD[3]; Johanna S. Salzer, DVM, PhD[2]

## Abstract

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated immunoglobulin E–mediated allergic condition characterized by a reaction to the oligosaccharide galactose-alpha-1,3-galactose (alpha-gal), which is found in mammalian meat and products derived from mammals, including milk, other dairy products, and some pharmaceutical products. Symptoms range from mild (e.g., a rash or gastrointestinal upset) to severe (anaphylaxis); onset typically occurs ≥2 hours after exposure to alpha-gal. No treatment or cure is currently available. Despite the potential life-threating reactions associated with AGS, most patients perceive that health care providers (HCPs) have little or no knowledge of AGS. A U.S. web-based survey of 1,500 HCPs revealed limited knowledge of AGS, identified areas for continuing medical education, and described self-reported diagnostic and management practices. Overall, 42% of surveyed HCPs had never heard of AGS, and among those who had, fewer than one third knew how to diagnose the condition. Two thirds of respondents indicated that guidelines for the diagnosis and management of AGS would be useful clinical resources. Limited awareness and knowledge of AGS among HCPs likely contributes to underdiagnosis of this condition and inadequate patient management, and underestimates of the number of AGS patients in the United States, which currently relies on laboratory testing data alone.

## Introduction

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated, immunoglobulin E (IgE)–mediated allergic condition characterized by a reaction to galactose-alpha-1,3-galactose (alpha-gal), a sugar molecule found in most nonprimate mammals. Evidence suggests that the reaction is primarily associated with the bite of the lone star tick (*Ambylomma americanum*) in the United States. Cases are most prevalent in the southern, midwestern, and mid-Atlantic United States, overlapping the range of the lone star tick (*1*–*3*). No treatment or cure is currently available. Despite the potential life-threatening reactions associated with AGS, patients perceive that health care providers (HCPs) have little or no knowledge of AGS (*4*). Data from a nationwide, web-based survey of HCPs in the United States (DocStyles, Spring 2022), administered by Porter Novelli Public Services, were analyzed to determine HCP knowledge relating to the diagnosis and management of AGS.

INSIDE



**Continuing Education** examination available at https://www.cdc.gov/mmwr/mmwr_continuingEducation.html

**U.S. Department of Health and Human Services**
Centers for Disease Control and Prevention

## Methods

HCPs were identified from the SERMO Global Medical Panel, a physician networking platform with an opt-in, verified panel of medical professionals who receive an honorarium for participating in market research surveys. Panelists were verified using a double opt-in sign up process with telephone confirmation at their place of work.* SERMO identified a random sample of eligible providers from its main database and distributed an electronic invitation to participate in the study, including a link to the web-based survey.† The minimum number of respondents, or survey quota, was set to reach 1,500 primary care practitioners.§ Respondents were providers who actively saw patients; worked in an individual, group, or hospital practice; and had practiced for >3 years.

The analysis was limited to family practitioners, general practitioners, internists, pediatricians, nurse practitioners (NPs), and physician assistants (PAs). Frequencies and percentages were calculated, and Pearson chi-square tests were used to compare categorical variables, using SAS software (version 9.4; SAS Institute).

To assess multifactorial knowledge, a composite knowledge score was calculated for all respondents with a maximum score of 3; one point was awarded for each correct answer to the following three topics: 1) how AGS is acquired, 2) appropriate diagnosis of AGS, and 3) counseling of patients with AGS. Scores ranged from 0 (no answers correct) to 3 (all answers correct). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶

## Results

A total of 1,500 respondents completed the survey, including 1,000 primary care physicians, 250 pediatricians, and 250 PAs and NPs. Overall, 974 (65%) respondents worked in a group outpatient practice or clinic, approximately one third worked in an individual outpatient practice (235; 16%), or in an inpatient practice or a hospital (291; 19%). The largest percentage of respondents worked in the U.S. Census Bureau South Region** (472; 32%), followed by the Northeast Region (377; 25%), and the Midwest Region (337; 22%); approximately one fifth worked in the West Region (314; 21%).

Overall, 635 (42%) respondents had not heard of AGS, and another 530 (35%) reported that they were "not too confident" about their ability to diagnose or manage patients with AGS (Table 1). Only 74 (5%) felt "very confident" in their ability. Among 865 (58%) respondents who were aware of AGS, 674 (78%) had not made a diagnosis of AGS in the previous year;

* https://styles.porternovelli.com/docstyles

† Panelists were verified using a double opt-in sign-up process with telephone confirmation at place of work.

§ A total of 1,000 family or general practitioners and internists, 250 pediatricians, and 250 mid-level health care providers (nurse practitioners and physician assistants).

¶ 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

** https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

The *MMWR* series of publications is published by the Office of Science, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

**Suggested citation:** [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2023;72:[inclusive page numbers].

**TABLE 1. Survey questions and responses by health care providers regarding their practice characteristics and knowledge about alpha-gal syndrome (N = 1,500) — Spring DocStyles survey,* United States, March–May 2022**

| Survey question (total no. of responses) | No. (%) | 95% CI |
|---|---|---|
| **Where do you practice? (1,500)** | | |
| Group outpatient clinic or practice | 974 (65.9) | 63.5–68.3 |
| Individual outpatient practice | 235 (15.9) | 14.1–17.8 |
| Inpatient practice or hospital | 291 (18.2) | 16.3–20.2 |
| **Where is your practice located? (by U.S. Census Bureau region, 1,500)** | | |
| South | 472 (31.5) | 29.1–33.9 |
| Northeast | 377 (25.1) | 22.9–27.3 |
| Midwest | 337 (22.5) | 20.4–24.6 |
| West | 314 (20.9) | 18.8–23.0 |
| **How confident are you in your ability to diagnose and manage patients with AGS? (1,500)** | | |
| Very confident | 74 (4.9) | 3.8–6.0 |
| Somewhat confident | 261 (17.4) | 15.5–19.3 |
| Not too confident | 530 (35.3) | 32.9–33.7 |
| I have not heard of this condition | 635 (42.3) | 39.8–44.8 |
| **You have diagnosed a patient with AGS. Which of the following topics would you counsel them on?† (865)** | | |
| Tick bite prevention | 31 (3.6) | 2.4–4.8 |
| Eliminating red meat from their diet | 148 (17.1) | 15.0–19.6 |
| Caution with new vaccines or medications | 60 (6.9) | 5.2–8.6 |
| Recognizing and managing anaphylaxis | 124 (14.3) | 12.0–16.6 |
| All of the above§ | 502 (58.0) | 54.7–61.3 |
| **Following a detailed patient exam, which of the following tests would you order to confirm an AGS diagnosis?† Select all that apply. (865)** | | |
| sIgE to alpha-gal§ | 252 (29.1) | 26.1–32.1 |
| Allergy skin test | 122 (14.1) | 11.8–16.4 |
| PCR | 107 (12.4) | 10.2-14.6 |
| IgG to alpha-gal | 191 (22.1) | 19.3–24.9 |
| Not sure | 416 (48.1) | 44.8–51.4 |
| **How does a patient get AGS?† (865)** | | |
| From a tick bite§ | 285 (33.0) | 29.9–36.1 |
| Genetic predisposition | 54 (6.2) | 4.6–7.8 |
| Immune complex–mediated | 90 (10.4) | 8.4–12.4 |
| Eating too much red meat | 39 (4.5) | 3.1–5.9 |
| The cause is not yet known | 125 (14.5) | 12.6–16.9 |
| Don't know | 272 (31.5) | 28.4–34.6 |
| **In the past 12 months, how many of your patients reported a recent exposure to ticks? (865)** | | |
| 0 | 142 (16.4) | 13.9–18.9 |
| 1–5 | 343 (39.7) | 36.4–43.0 |
| 6–19 | 242 (28.0) | 25.0–31.0 |
| 20–100 | 125 (14.5) | 12.2–16.9 |
| >100 | 13 (1.5) | 0.1–2.3 |
| **In the past 12 months, how many patients have you diagnosed or managed with AGS? (865)** | | |
| 0 | 674 (77.9) | 75.1–80.7 |
| 1–5 | 136 (15.7) | 13.3–18.1 |
| >5 | 55 (6.4) | 4.7–8.0 |
| 6–19 | 44 (5.1) | 3.6–6.6 |
| 20–100 | 8 (0.9) | 0–2.0 |
| >100 | 3 (0.4) | 0–1.0 |
| **What additional resources would be helpful in treating and managing patients with AGS? Select all that apply. (865)** | | |
| Online training modules | 708 (47.2) | 43.9–50.5 |
| CDC guidelines on diagnosis of AGS | 955 (63.7) | 60.5–66.9 |
| CDC guidelines on management of AGS | 982 (65.5) | 62.3–68.7 |
| List of products containing alpha-gal | 620 (41.3) | 38.0–44.6 |
| Website content for health care providers | 807 (53.8) | 50.5–57.1 |
| No additional resources are needed | 84 (5.6) | 4.1–7.1 |

**Abbreviations:** AGS = alpha-gal syndrome; PCR = polymerase chain reaction; sIgE = alpha-gal–specific serum IgE antibody.
* Administered by Porter Novelli.
† Evaluated together to generate a composite knowledge score.
§ Correct response.

136 (16%) diagnosed or managed one to five patients, and 55 (6%) diagnosed or managed more than five patients.

Among all respondents who were aware of AGS, 416 (48%) reported that they did not know the correct diagnostic tests to order. One third of respondents (285; 33%) correctly reported that patients develop AGS after a tick bite, and approximately one third (272; 32%) reported not knowing how it was acquired. More than one half of the respondents (502; 58%) correctly identified topics on which to counsel AGS patients, such as tick bite prevention, eliminating red meat from their diet, exercising caution when receiving new medications and vaccines, and recognizing and managing anaphylaxis. Overall, 64% and 66% of respondents indicated that guidelines for the diagnosis and management of AGS, respectively, would be helpful clinical resources.

Among the 865 survey respondents who had heard of AGS, only 42 (5%; 95% CI = 3.1%–5.9%) correctly answered all three questions related to etiology, testing, and patient counseling (Table 2). Knowledge scores were higher among pediatricians, 12.3% of whom correctly answered all three questions, than among internists (4.2%), family practitioners (3.7%), PAs (2.6%), and NPs (0%). Knowledge scores were similar across U.S. Census Bureau regions (p = 0.44), and number of years in practice was not significantly associated with provider knowledge scores. There was an inverse relationship in knowledge scores and the number of AGS cases that HCPs reported they had diagnosed and managed (Table 2).

**Summary**

What is already known about this topic?

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated allergic condition characterized by a hypersensitivity to an oligosaccharide found in most mammalian meat and products derived from it. Symptoms can be life-threatening and can include anaphylaxis. Cases are increasing, although patients report limited health care provider (HCP) awareness of AGS.

What is added by this report?

HCP respondents (N = 1,500) to a nationwide survey had limited AGS knowledge: 42% were not aware of AGS, and another 35% were not confident in their ability to diagnose or manage AGS patients.

What are the implications for public health practice?

Limited HCP knowledge about AGS is concerning, especially because the number of suspected cases is increasing, and the range of the tick primarily associated with this condition is expected to expand. Improved HCP education might facilitate a rapid diagnosis of AGS, improve patient care, and support public health understanding of this emerging condition.

## Discussion

This analysis indicated a low level of knowledge among U.S. HCPs regarding the diagnosis and management of AGS, with 78% of providers having little to no knowledge of AGS. Previous assessments of AGS knowledge among HCPs in the United States were limited to small studies within individual jurisdictions but found similar patterns of an overall lack of knowledge among those surveyed (*5*,*6*).

Few HCPs reported diagnosing AGS or managing patients with AGS within the previous year, despite an annual increase in the number of tests performed and suspected AGS cases identified nationally and the number of persons who received positive test results increasing from 13,371 in 2017 to 18,885 in 2021[††] (*1*,*3*). Provider knowledge of AGS etiology, testing, and patient counseling decreased as the number of patients they reported diagnosing or managing with AGS increased. This inverse association suggests that some HCPs might be incorrectly diagnosing AGS, possibly on the basis of symptoms or testing alone, and subsequently recommending dietary modifications where none are warranted. This limited provider knowledge might also lead to delayed or missed diagnosis and incorrect patient management. A growing number of resources are available for HCPs seeking additional education related to the evaluation, diagnosis, and management of patients with AGS (*7*,*8*). Diagnosis of AGS requires careful elicitation of a history in a patient with compatible symptoms, and diagnostic testing for alpha-gal–specific IgE antibodies (≥0.1 kU/L is considered a positive test result) (*8*). A 2015 study found that approximately one fifth (21%) of patients received a diagnosis within their first year of signs and symptoms, whereas the remaining 79% received a diagnosis in an average of 7.1 years (*9*). Repeated visits to HCPs and referrals to specialists might be necessary for patients to receive a proper diagnosis and care, creating a disadvantage to those patients who face challenges seeking health care in general or who lack access to specialty practitioners, such as allergists.

### Limitations

The findings in this report are subject to at least two limitations. First, the findings might not be generalizable to all practicing HCPs in the United States since respondents were part of a provider panel. Second, providers might have interpreted

[††] The national standardized case definition accepted in 2021 by the Council of State and Territorial Epidemiologists defined a confirmed case of AGS as being in a person who met the clinical criteria and confirmatory laboratory evidence (serum or plasma sIgE specific to alpha-gal ≥0.1 IU/mL or ≥0.1 kU/L). A suspected case of AGS was defined as being in a person who had confirmatory laboratory evidence with no clinical information available. https://ndc.services.cdc.gov/case-definitions/alpha-gal-syndrome-ags/

**TABLE 2. Knowledge about alpha-gal syndrome among health care providers, overall and by region and provider characteristics (N = 865) — Spring DocStyles survey,* United States, March–May 2022**

| Characteristic | No. (%) of questions answered correctly | | | | Mean (SD) | Total | Chi-square, p-value |
|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | | | |
| **Overall composite knowledge score** | **213 (24.62)** | **417 (48.21)** | **193 (22.31)** | **42 (4.86)** | **1.07 (0.81)** | **865** | — |
| **U.S. Census Bureau region†** | | | | | | | |
| Northeast | 48 (24.49) | 97 (49.49) | 44 (22.45) | 7 (3.57) | 1.05 (0.78) | **196** | 0.15 |
| Midwest | 50 (24.27) | 99 (48.06) | 47 (22.82) | 10 (4.85) | 1.08 (0.81) | **206** | 0.31 |
| South | 64 (21.99) | 135 (46.39) | 74 (25.43) | 18 (6.19) | 1.16 (0.84) | **291** | Ref |
| West | 51 (29.65) | 86 (50.00) | 28 (16.28) | 7 (4.07) | 0.95 (0.79) | **172** | <0.05 |
| **Total** | **213** | **417** | **193** | **42** | **1.07 (0.81)** | **865** | **0.44** |
| **No. of yrs in practice** | | | | | | | |
| <5 | 18 (16.8) | 62 (57.9) | 22 (20.6) | 5 (4.7) | 1.13 (0.74) | **107 (12.4)** | 0.57 |
| 6–10 | 51 (24.3) | 100 (47.6) | 50 (23.8) | 9 (4.3) | 1.08 (0.81) | **210 (24.3)** | 0.19 |
| 11–15 | 52 (29.9) | 80 (46.0) | 37 (21.3) | 5 (2.9) | 0.97 (0.79) | **174 (20.1)** | <0.05 |
| 16–20 | 42 (33.1) | 54 (42.5) | 27 (21.3) | 4 (3.2) | 0.94 (0.82) | **127 (14.7)** | <0.05 |
| >20 | 50 (20.2) | 121 (49.0) | 57 (23.1) | 19 (7.7) | 1.18 (0.84) | **247 (28.6)** | Ref |
| **Total** | **213** | **417** | **193** | **42** | **1.07 (0.81)** | **865** | **0.06** |
| **Provider type** | | | | | | | |
| Pediatrician | 28 (21.5) | 49 (37.7) | 37 (28.5) | 16 (12.3) | 1.32 (0.95) | **130 (15.0)** | Ref |
| FP | 68 (25.0) | 137 (50.5) | 57 (21.0) | 10 (3.7) | 1.03 (0.78) | **272 (31.5)** | <0.01 |
| Internist | 87 (26.4) | 161 (48.8) | 68 (20.6) | 14 (4.2) | 1.03 (0.80) | **330 (38.2)** | <0.01 |
| NP | 12 (21.1) | 31 (54.4) | 14 (24.6) | 0 (—) | 1.04 (0.68) | **57 (6.6)** | 0.02 |
| PA | 18 (23.7) | 39 (51.3) | 17 (22.4) | 2 (2.6) | 1.04 (0.76) | **76 (8.8)** | 0.02 |
| **Total** | **213** | **417** | **193** | **42** | **1.07 (0.81)** | **865** | **<0.05** |
| **No. of cases diagnosed or no. of patients managed** | | | | | | | |
| 0 | 154 (22.9) | 346 (51.3) | 148 (22.0) | 26 (3.9) | 1.07 (0.77) | **674 (77.9)** | 0.05 |
| 1–5 | 29 (21.3) | 58 (42.7) | 38 (27.9) | 11 (8.1) | 1.22 (0.88) | **136 (15.7)** | Ref |
| 6–19 | 22 (50.0) | 12 (27.3) | 5 (11.4) | 5 (11.4) | 0.84 (1.03) | **44 (5.1)** | 0.03 |
| 20–100 | 6 (75.0) | 0 (—) | 2 (25.0) | 0 (—) | 0.50 (0.93) | **8 (0.9)** | 0.06 |
| >100 | 2 (66.7) | 1 (33.3) | 0 (—) | 0 (—) | 0.33 (0.58) | **3 (0.4)** | 0.11 |
| **Total** | **213** | **417** | **193** | **42** | **1.07 (0.81)** | **865** | **<0.05** |

**Abbreviations:** FP = family practitioner; NP = nurse practitioner; PA = physician assistant; Ref = referent group.
* Administered by Porter Novelli.
† https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

response options differently. For example, when asked about how a patient acquires AGS, one response option was "the cause is not yet known." Although tick bites have been widely recognized as triggering the hypersensitivity to alpha-gal (*2*), and "tick bites" was considered the correct response, the detailed immunologic aspects of the tick bite etiology of AGS are still being investigated. These possible differences in interpretation, as well as the nature of self-reporting, might have contributed to misclassification of responses as being correct or incorrect.

## Implications for Public Health Practice

Considering the recent description of a continued increase in the number of persons receiving positive alpha-gal–specific IgE (sIgE) antibody test results, growing numbers of suspected AGS cases (*3*), and expanding North American ranges of the lone star tick (*10*), the knowledge gap found in this survey of HCPs is concerning. Currently, AGS is not a nationally notifiable condition, and understanding epidemiologic trends relies on laboratory-based surveillance (*1*,*3*). The lack of HCP knowledge of AGS is likely to lead to undertesting, further hampering knowledge of the national prevalence of AGS.[§§] Increased HCP education and awareness of AGS are needed to hasten and improve the accuracy of AGS diagnoses, patient care, and the understanding of the epidemiology of this emerging condition.

[§§] https://www.cdc.gov/ticks/alpha-gal/index.html

## Acknowledgments

Eleanor Farley Saunders, Fred Fridinger, Lyle Petersen.

Corresponding author: Ann Carpenter, pzy4@cdc.gov.

[1]Epidemic Intelligence Service, CDC; [2]Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [3]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Scott P. Commins reports institutional support from the National Institute of Allergy and Infectious Diseases, National Institutes of Health; royalties from UpToDate, Inc.; payment or honoraria from Genentech for participation in educational events and from Regeneron for participation in an advisory meeting; and an unpaid position as president-elect of the Southeastern Allergy, Asthma, and Immunology Society. No other potential conflicts of interest were disclosed.

## References

1. Binder AM, Commins SP, Altrich ML, et al. Diagnostic testing for galactose-alpha-1,3-galactose—United States, 2010–2018. Ann Allergy Asthma Immunol 2021;126:411–16.e1. PMID:33422649 https://doi.org/10.1016/j.anai.2020.12.019
2. Macdougall JD, Thomas KO, Iweala OI. The meat of the matter: understanding and managing alpha-gal syndrome. ImmunoTargets Ther 2022;11:37–54. PMID:36134173 https://doi.org/10.2147/ITT.S276872
3. Thompson J, Carpenter A, Kersh GJ, Wachs T, Commins SP, Salzer JS. Geospatial distribution of suspected alpha-gal syndrome cases—United States, January 2017–December 2022. MMWR Morb Mortal Wkly Rep 2023;72: 815–20. https://www.cdc.gov/mmwr/volumes/72/wr/mm7230a2.htm?s_cid=mm7230a2_w
4. Flaherty MG, Threats M, Kaplan SJ. Patients' health information practices and perceptions of provider knowledge in the case of the newly discovered alpha-gal food allergy. J Patient Exp 2020;7:132–9. PMID:32128382 https://doi.org/10.1177/2374373518808310
5. Carson DA, Kopsco H, Gronemeyer P, et al. Knowledge, attitudes, and practices of Illinois medical professionals related to ticks and tick-borne disease. One Health 2022;15:100424. PMID:36277108 https://doi.org/10.1016/j.onehlt.2022.100424
6. Hedberg C, Kaler A, Bell M. P110 knowledge and perceptions of alpha-gal syndrome among primary care physicians in Arkansas 8166. Annals of Allergy, Asthma & Immunology 2021; 127(Suppl 4):S42. https://doi.org/10.1016/j.anai.2021.08.128
7. McGill SK, Hashash JG, Platts-Mills TA. AGA clinical practice update on alpha-gal syndrome for the GI clinician: commentary. Clin Gastroenterol Hepatol 2023;21:891–6. PMID:36958889 https://doi.org/10.1016/j.cgh.2022.12.035
8. Commins SP. Diagnosis & management of alpha-gal syndrome: lessons from 2,500 patients. Expert Rev Clin Immunol 2020;16:667–77. PMID:32571129 https://doi.org/10.1080/1744666X.2020.1782745
9. Flaherty MG, Kaplan SJ, Jerath MR. Diagnosis of life-threatening alpha-gal food allergy appears to be patient driven. J Prim Care Community Health 2017;8:345–8. PMID:28447914 https://doi.org/10.1177/2150131917705714
10. Raghavan RK, Peterson AT, Cobos ME, Ganta R, Foley D. Current and future distribution of the lone star tick, *Amblyomma americanum* (L.) (Acari: Ixodidae) in North America. PLoS One 2019;14:e0209082. PMID:30601855 https://doi.org/10.1371/journal.pone.0209082

# Geographic Distribution of Suspected Alpha-gal Syndrome Cases — United States, January 2017–December 2022

Julie M. Thompson, DVM, PhD[1]; Ann Carpenter, DVM[1]; Gilbert J. Kersh, PhD[1]; Tyler Wachs[2]; Scott P. Commins, MD[3]; Johanna S. Salzer, DVM, PhD[1]

## Abstract

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated allergic condition characterized by a potentially life-threatening immunoglobulin E (IgE)–mediated hypersensitivity to galactose-alpha-1,3-galactose (alpha-gal), an oligosaccharide found in most nonprimate mammalian meat and products derived from these mammals. Specific symptoms and severity of AGS vary among persons, and no treatment or cure is currently available. During 2010–2018, more than 34,000 suspected cases of AGS were identified in the United States, but current knowledge of where cases occur is limited. This study examined alpha-gal–specific IgE (sIgE) antibody testing results submitted to the commercial laboratory responsible for nearly all testing in the United States before 2022 to assess the geographic distribution and magnitude of this emerging condition. During January 1, 2017–December 31, 2022, a total of 357,119 tests were submitted from residences in the United States, corresponding to 295,400 persons. Overall, 90,018 (30.5%) persons received a positive test result in the study period, and the number of persons with positive test results increased from 13,371 in 2017 to 18,885 in 2021. Among 233,521 persons for whom geographic data were available, suspected cases predominantly occurred in counties within the southern, midwestern, and mid-Atlantic U.S. Census Bureau regions. These data highlight the evolving emergence of AGS and can be used to help state and local health agencies initiate surveillance and target public health outreach and health care provider education to high-risk localities.

## Introduction

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated allergic condition characterized by a potentially life-threatening immunoglobulin E (IgE)–mediated hypersensitivity to galactose-alpha-1,3-galactose (alpha-gal), an oligosaccharide found in most nonprimate mammalian tissue and products derived from these mammals, such as milk, other dairy products, and some pharmaceutical products (*1*). Specific signs and symptoms and severity of AGS vary among persons (*2*), and no treatment or cure is currently available (*1*). More than 34,000 suspected AGS cases* were identified in the United States during 2010–2018 (*3*), but knowledge of where cases occurred is limited. This study examined alpha-gal–specific IgE (sIgE) antibody testing results submitted to the commercial laboratory responsible for nearly all testing in the United States before 2022† to describe the geographic distribution and magnitude of this emerging condition in the United States.

## Methods

Deidentified data from sIgE tests§ and panels¶ submitted in the United States during January 1, 2017–December 31, 2022, were obtained from Eurofins Viracor, the clinical testing laboratory responsible for nearly all testing in the United States before 2022 (www.eurofins-viracor.com), and contained the following variables: patient identification number, age, sex (male, female, or unknown), date of testing, test result provided in kilounits of alpha-gal sIgE per liter (kU/L), and patient state of residence and zip code. No clinical data or travel histories of persons receiving testing were provided. Observations with invalid state entries or entries from outside the United States were excluded. An alpha-gal sIgE test result ≥0.1 kU/L was considered positive. For persons who received one test, a person was suspected to have AGS if they received a positive test, and a person was considered to not have AGS if a negative test was received. For persons who received multiple tests, a person who received at least one positive test result was suspected to have AGS, and a person who received all negative

* The national standardized case definition accepted in 2021 by the Council of State and Territorial Epidemiologist defined a confirmed case of AGS as being in a person who met the clinical criteria and had confirmatory laboratory evidence (serum or plasma sIgE to alpha-gal ≥0.1 international unit per milliliter or ≥0.1 kU/L). A suspected case of AGS was defined as being in a person who had confirmatory laboratory evidence with no clinical information available. https://ndc.services.cdc.gov/case-definitions/alpha-gal-syndrome-ags/

† Until August 2021, Eurofins Viracor was the primary commercial laboratory offering alpha-gal sIgE testing. Few academic institutions and specialty allergy clinics offered testing before August 2021. Several commercial laboratories began offering alpha-gal sIgE testing in August 2021.

§ Alpha-gal sIgE tests (Eurofins Viracor testing code 30039).

¶ Alpha-gal panels included alpha-gal IgE, beef IgE, pork IgE, and lamb or mutton IgE (Eurofins Viracor testing code 403196P).

** For zip codes that crossed county boundaries, the county with the greatest proportion of residential addresses was selected according to the U.S. Department of Housing and Urban Development's Office of Policy Development and Research.

test results was considered to not have AGS. The date and location of residence at the time of the first positive test result (among persons with suspected AGS) or the first negative test result (among those who did not have AGS) were recorded. Means and SDs were calculated for continuous variables, and frequencies and percentages were calculated for categorical and ordinal variables. Risk ratios (RRs), 95% CIs, and p-values were calculated to determine associations with positive test results. Pearson's chi-square tests, Cochran-Armitage test for trend, and student's *t* tests with unequal variances were used to compare categorical, ordinal, and continuous variables, respectively. All analyses were performed using SAS software (version 9.4; SAS Institute).

Counties of patient residences were derived from original zip code data.** The number of persons with positive test results per 1 million (1M) population per year (PPY) were calculated for counties using population estimates from the U.S. Census Bureau.†† Counties with suspected AGS cases were assigned to one of three equal proportioned categories: low (<11 suspected AGS cases per 1M PPY), medium (11–87), and high (>87). Counties without suspected AGS cases were assigned to a zero category. QGIS (version 3.28.2; QGIS Project) was used for map generation. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§

## Results

During January 1, 2017–December 31, 2022, a total of 357,119 tests were submitted from U.S. residences¶¶, corresponding to 295,400 persons who were included in this analysis. Among these, 235,752 (80%) reported state of residence, and 233,521 (79%) reported zip code of residence. The majority of persons who received testing received one test during the study period, but 36,257 persons (12.3%) received more than one test. Overall, 188,532 (63.8%) persons receiving testing were female, but 42% of men received a positive test result, compared with 24% of women (Table). Persons who received a positive test result were significantly older (mean = 48 years; SD = 19.9) than were those who received a negative test result (mean = 41 years; SD = 19.6) (p<0.001); among persons aged ≥70 years, 44.6% received a positive test result.

During the study period, 90,018 (30.5%) persons received a positive test result and were classified as having suspected AGS. Each year during the study, approximately 30,000–70,000 persons received testing, although testing peaked at 66,106 persons in 2021, before other commercial laboratories began providing alpha-gal sIgE testing. The percentage of persons who received a positive test result remained at nearly 30% nationally during the study period, and an increasing number of positive test results were received each year until 2022. Each year, 13,371–18,885 persons received a positive test result (mean = 15,003; SD = 3,385.7).

Test results from 79% of persons with available geographic data were used for map generation. The highest numbers of suspected AGS cases were identified in counties within New York (Suffolk [3,746]) and Virginia (Bedford [1,511]); 4% of all suspected cases nationwide resided in Suffolk County, New York. The highest number of suspected AGS cases per 1M PPY were in counties in Virginia (Charlotte [12,273]) and Kentucky (Muhlenberg [6,107]). The highest prevalences of suspected cases (per 1M PPY) were found throughout a nearly contiguous region of the southern, midwestern, and mid-Atlantic United States, particularly parts of Oklahoma, Kansas, Arkansas, Missouri, Mississippi, Tennessee, Kentucky, Illinois, Indiana, North Carolina, Virginia, Maryland, and Delaware (Figure). Counties with moderate and high numbers of suspected cases per 1M PPY were detected in Minnesota and Wisconsin, corresponding to 238 total suspected cases (238 of 2,456 persons tested; 9.7%) during the 6-year study period, and were distinct from this contiguous region. Suspected AGS cases were predominantly located in areas where the lone star tick (*Amblyomma americanum*) is known to be established or reported.

## Discussion

During 2017–2021, there was an annual increase in positive test results for AGS in the United States. More than 90,000 suspected AGS cases were identified during the study period, and the number of new suspected cases increased by approximately 15,000 each year during the study.

Health care providers (HCPs) in the United States have low awareness of AGS. Among surveyed providers, 42% had never heard of AGS, and 35% reported they were "not too confident" in their ability to diagnose AGS or to manage patients with AGS (*4*). In this study, it was presumed that HCPs submitting alpha-gal sIgE tests had a reasonably high index of clinical suspicion of AGS. Alpha-gal sIgE testing conducted by HCPs with knowledge of AGS and with a high index of suspicion has been shown to have 98% sensitivity (*5*,*6*) and 92% specificity (*6*). Because no clinical data were available in the current study to correlate positive test results with the

†† https://data.census.gov/table?q%20=%20b01003&g%20=%20010XX00US$0500000,&tid%20=%20ACSDT1Y2021.B01003 (Accessed December 1, 2022).

§§ 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

¶¶ Test results from 10 specimens were excluded from the analysis. These reported invalid state entries or were reported from outside the United States.

**TABLE. Characteristics of persons who received testing for alpha-gal–specific immunoglobulin E — United States, January 1, 2017–December 31, 2022**

| Characteristic | No. (%) | | | RR (95% CI) | p-value[§] |
|---|---|---|---|---|---|
| | Total (N = 295,400) | Positive test result* (n = 90,018) | Negative test result† (n = 205,382) | | |
| **Age, yrs, mean (SD)** | **43.1 (19.9)** | 48.2 (19.9) | 40.8 (19.6) | NA | <0.001 |
| **Age group, yrs** | | | | | |
| 0–9 | **12,332** | 2,478 (2.8) | 9,854 (4.8) | Ref | <0.001 |
| 10–19 | **32,421** | 8,007 (8.9) | 24,414 (11.9) | 1.3 (1.2–1.4) | |
| 20–29 | **36,852** | 7,682 (8.5) | 29,170 (14.2) | 1.0 (1.0–1.1) | |
| 30–39 | **46,520** | 10,929 (12.1) | 35,591 (17.3) | 1.2 (1.2–1.3) | |
| 40–49 | **49,297** | 13,837 (15.4) | 35,460 (17.3) | 1.6 (1.4–1.6) | |
| 50–59 | **47,975** | 17,157 (19.1) | 30,818 (15.0) | 2.2 (2.1–2.3) | |
| 60–69 | **40,690** | 16,858 (18.7) | 23,832 (11.6) | 2.8 (2.7–3.0) | |
| >70 | **29,304** | 13,064 (14.5) | 16,240 (7.9) | 3.2 (3.0–3.4) | |
| **Sex** | | | | | |
| Female | **188,532** | 45,257 (50.3) | 143,275 (69.7) | Ref | <0.001 |
| Male | **104,629** | 43,874 (48.7) | 60,755 (29.6) | 2.3 (2.2–2.3) | |
| Unknown | **2,239** | 887 (1.0) | 1,352 (0.7) | 2.1 (1.9–2.3) | |
| **Year** | | | | | |
| 2017[¶] | **35,869** | 13,371 (14.9) | 22,498 (11.0) | Ref | <0.001 |
| 2018 | **43,195** | 13,821 (15.4) | 29,374 (14.3) | 0.8 (0.8–0.8) | |
| 2019 | **57,327** | 17,372 (19.3) | 39,955 (19.5) | 0.7 (0.7–0.8) | |
| 2020 | **56,726** | 16,936 (18.8) | 39,790 (19.4) | 0.7 (0.7–0.7) | |
| 2021 | **66,106** | 18,885 (21.0) | 47,221 (23.0) | 0.7 (0.7–0.7) | |
| 2022 | **36,177** | 9,633 (10.7) | 26,544 (12.9) | 0.6 (0.6–0.6) | |

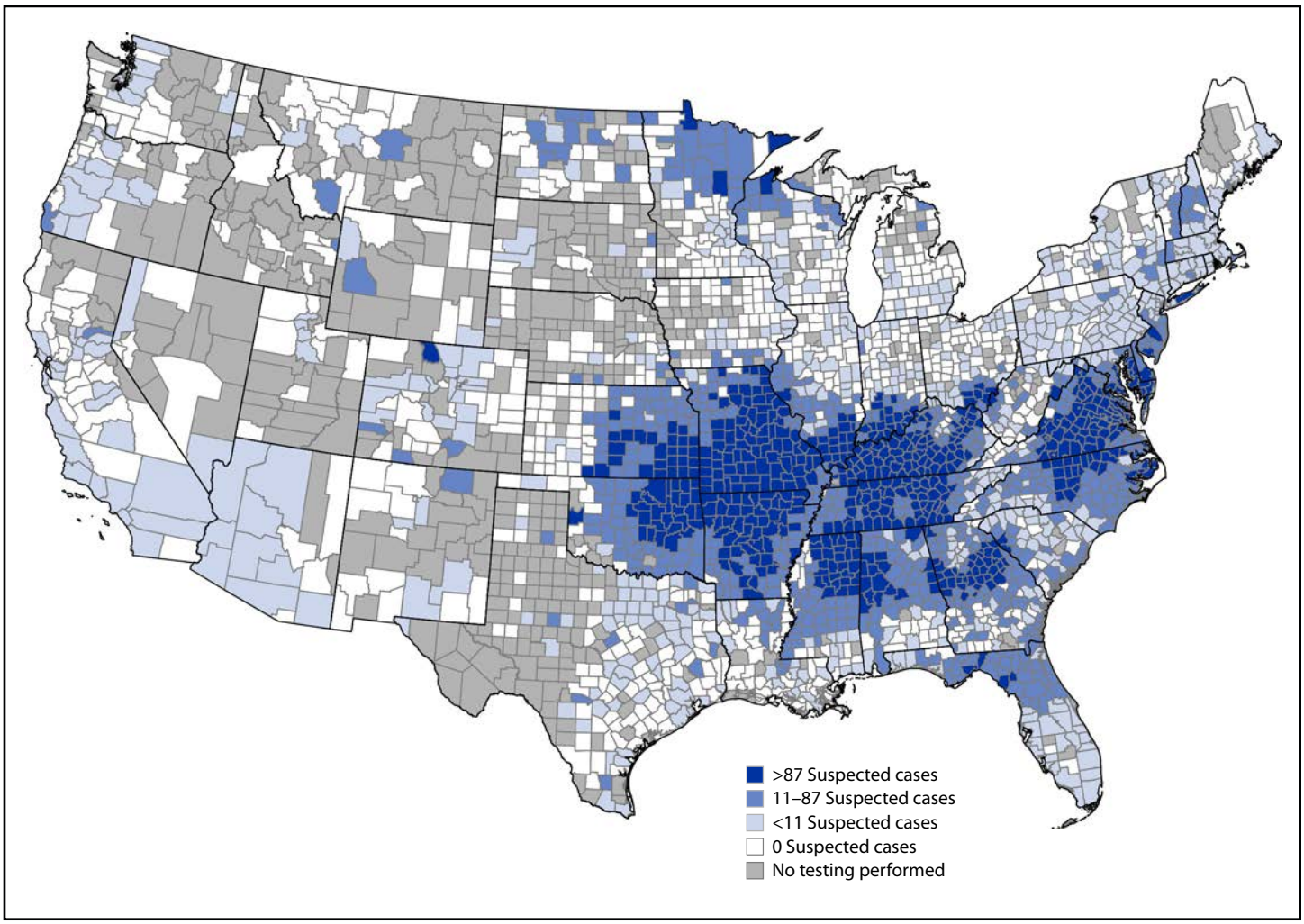
**Abbreviations:** IgE = immunoglobulin E; kU = kilounit; NA = not applicable; Ref = referent group; RR = risk ratio.
* At least one alpha-gal–specific IgE test result ≥0.1 kU/L in a patient was considered positive.
† All alpha-gal–specific IgE test results <0.1 kU/L in a patient were considered negative.
§ P-values were calculated to identify significant difference in trends (age group or year) or interactions (sex) between those who received positive and negative test results; p<0.05 were considered statistically significant.
¶ Year was abstracted for the date of the first positive test result (for persons who received at least one positive test result) and the first negative test (for persons who only received negative test results).

presence of clinical symptoms consistent with AGS, all cases were considered suspected. However, recent unpublished surveillance data that examined positive alpha-gal sIgE test results at commercial laboratories showed that approximately 90% of persons with a positive test result did have clinical symptoms consistent with AGS (K Cervantes, New Jersey Department of Health, personal communication, July 2023) and that they were classified as having confirmed AGS.

Persons with suspected AGS were predominantly located in areas where the lone star tick is known to be established or reported, particularly throughout Arkansas, Kentucky, Missouri, and Suffolk County, New York. The geographic distribution of AGS is very similar to that of ehrlichiosis, caused by *Ehrlichia chaffeensis* and *E. ewingii*, disease agents also known to be transmitted by the lone star tick. These data therefore support the association previously observed between lone star ticks and alpha-gal sensitization among patients in the United States. This study also identified focal clusters of cases in areas where there are no known established populations of lone star ticks, such as Minnesota and Wisconsin, although these data are relatively sparse, and more information is needed to validate these as cases acquired in those areas. A small retrospective review in Iowa, Minnesota, and Wisconsin found that of 47 AGS patients who received positive alpha-gal sIgE test results, 11 (23%) lived in areas where the lone star tick was not previously known to be present, and some persons reported bites from blacklegged ticks (four; 9%) or lone star ticks (three; 6%), although when these bites occurred relative to symptom onset or how the ticks were identified is not described (*7*). Nevertheless, alpha-gal has been identified in the saliva of other tick species (*8*,*9*), and bites from other tick species are associated with AGS in other parts of the world (*8*). In this investigation, the geography suggests that lone star ticks remain the primary species associated with AGS in the United States, and cases outside the established range of this tick species need to be further investigated to better understand exposure history and contributing factors associated with the onset of this allergic condition.

The results of the current study can aid in initiating national surveillance efforts for this emerging allergic condition and for geographically targeting high-risk populations for public health outreach and HCP education. Whether the increasing numbers of suspected AGS cases seen in this study are an indication of increased awareness, increasing emergence, or both remains unclear. Further, these results support including AGS in community outreach regarding tickborne disease

**FIGURE. Geographic distribution of suspected alpha-gal syndrome cases* per 1 million population per year — United States, 2017–2022**




**Abbreviations:** IgE = immunoglobulin E; IU = international unit; kU = kilounit.
* A suspected case of alpha-gal syndrome was defined as being in a person who had confirmatory laboratory evidence (serum or plasma alpha-gal–specific IgE ≥0.1 IU/mL or ≥0.1 kU/L) with no clinical information available.

prevention efforts, especially because the health consequences of tick exposures leading to AGS could ultimately be lifelong.

## Limitations

The findings in this report are subject to at least four limitations. First, it is known that other specialty laboratories within academic institutions and allergy clinics have conducted alpha-gal sIgE testing before 2022. In addition, other commercial laboratories have conducted testing since August 2021, which are not reflected in these results and likely contributes to the decrease in suspected AGS cases in 2022. Thus, these results almost certainly underestimate the number of persons seeking testing and persons receiving positive test results. Second, localities associated with patient test results do not necessarily reflect the geographic area where the tick bites or first onset of AGS symptoms occurred, and travel-associated cases certainly are possible. Third, test specificity for AGS is 92% among symptomatic persons (*6*), and false positives are possible. Finally, some of the original data were excluded from the study because of invalid state entries or entries from outside the United States, though this represented <1% of the total sample.

## Implications for Public Health Practice

Because numerous barriers affect access to testing, these test results do not equitably reflect the U.S. populations affected by AGS. Studies have documented that most patients seeking and receiving sIgE testing were more likely to report being non-Hispanic White, with higher incomes, and higher educational attainment (*5*,*10*). The need for repeated clinical visits and access to specialized practitioners, which might span several

**Summary**

What is already known about this topic?

Alpha-gal syndrome (AGS) is an emerging, tick bite–associated allergic condition characterized by potentially life-threatening hypersensitivity to an oligosaccharide found in most mammalian meat and products derived from it; however, in the absence of national surveillance, the geographic distribution and number of cases are largely unknown.

What is added by this report?

The number of suspected AGS cases in the United States has increased substantially since 2010, and states with established populations of lone star ticks are most affected, although suspected AGS cases were also identified in areas outside of this tick's range.

What are the implications for public health practice?

These data can facilitate initiating AGS surveillance, improve health care provider education in high-risk areas, and enhance targeted public health outreach and prevention.

years before a diagnosis is made (*10*), also creates a testing barrier for patients. These known challenges are likely the reason that only a portion of persons with AGS are tested for alpha-gal sIgE antibodies. The suspected health equity gaps associated with AGS warrant further examination.

AGS is a growing clinical and public health concern for persons in the United States, yet in the absence of a national surveillance system, the prevalence of this condition is largely unknown. More than 34,000 suspected AGS cases were previously identified during 2010–2018, and 20,211 of these were identified during 2010–2016 from alpha-gal sIgE test results (*3*). Together with suspected AGS cases identified from alpha-gal sIgE tests and panels in this study, a total of 110,229 suspected cases were documented during 2010–2022. Assuming 70%–90% of these suspected cases (77,161–99,207) are clinically compatible AGS cases, and assuming that 22%–80% of all persons with AGS have access to knowledgeable HCPs who submit a specimen for alpha-gal sIgE testing, 96,000–450,000 persons in the United States might have been affected by AGS since 2010. A recent survey (*4*) found that approximately 22% of HCPs in the United States were somewhat or very confident that they would be able to diagnose or manage patients with AGS. However, it has been estimated that approximately 80% of AGS patients at specialty clinics received alpha-gal sIgE testing as part of their clinical diagnosis. If testing trends continue, and the geographic range of the lone star tick continues to expand, the number of AGS cases in the United States is predicted to increase during the coming years, presenting a critical need for synergistic public health activities including 1) community education targeting tick bite prevention to reduce the risk for acquiring AGS, 2) HCP education to improve timely diagnosis and management, and 3) improved surveillance to aid public health decision-making.

## Acknowledgments

Bryan Ayres, Brad Biggerstaff, Alison Binder, Alison Hinckley, R. Ryan Lash, William Nicholson, Lyle Petersen, CDC; Kim Cervantes, Mervin Cuadera, Julie Murphy, Rebecca Osborn, Elizabeth Schiffman, other public health officials, Surveillance Working Group for Alpha-gal Syndrome.

Corresponding author: Johanna S. Salzer, hio7@cdc.gov.

[1]Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [2]Eurofins Viracor, Lenexa, Kansas; [3]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Scott P. Commins reports institutional support from the National Institute of Allergy and Infectious Diseases, National Institutes of Health; royalties from UpToDate, Inc.; payment or honoraria from Genentech for participation in educational events and from Regeneron for participation in an advisory meeting; and an unpaid position as president-elect of the Southeastern Allergy, Asthma, and Immunology Society. No other potential conflicts of interest were disclosed.

## References

1. Commins SP, Jerath MR, Cox K, Erickson LD, Platts-Mills T. Delayed anaphylaxis to alpha-gal, an oligosaccharide in mammalian meat. Allergol Int 2016;65:16–20. PMID:26666477 https://doi.org/10.1016/j.alit.2015.10.001
2. Commins SP, Satinover SM, Hosen J, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. J Allergy Clin Immunol 2009;123:426–33.e2. PMID:19070355 https://doi.org/10.1016/j.jaci.2008.10.052
3. Binder AM, Commins SP, Altrich ML, et al. Diagnostic testing for galactose-alpha-1,3-galactose, United States, 2010 to 2018. Ann Allergy Asthma Immunol 2021;126:411–16.e1. PMID:33422649 https://doi.org/10.1016/j.anai.2020.12.019
4. Carpenter A, Drexler NA, McCormick DW, et al. Health care provider knowledge regarding alpha-gal syndrome—United States, March–May 2022. MMWR Morb Mortal Wkly Rep 2023;72:809–14. https://www.cdc.gov/mmwr/volumes/72/wr/mm7230a1.htm?s_cid=mm7230a1_w
5. Kersh GJ, Salzer J, Jones ES, et al. Tick bite as a risk factor for alpha-gal-specific immunoglobulin E antibodies and development of alpha-gal syndrome. Ann Allergy Asthma Immunol 2023;130:472–8. PMID:36574585 https://doi.org/10.1016/j.anai.2022.11.021
6. Commins SP. Diagnosis & management of alpha-gal syndrome: lessons from 2,500 patients. Expert Rev Clin Immunol 2020;16:667–77. PMID:32571129 https://doi.org/10.1080/1744666X.2020.1782745
7. Chacon Osorio GR, Palraj R, van Nunen S, White MJ. Newly recognized α-gal syndrome in the upper midwestern United States. Mayo Clin Proc 2022;97:1754–5. PMID:36058588 https://doi.org/10.1016/j.mayocp.2022.07.003

8. Platts-Mills TAE, Commins SP, Biedermann T, et al. On the cause and consequences of IgE to galactose-α-1,3-galactose: a report from the National Institute of Allergy and Infectious Diseases workshop on understanding IgE-mediated mammalian meat allergy. J Allergy Clin Immunol 2020;145:1061–71. PMID:32057766 https://doi.org/10.1016/j.jaci.2020.01.047
9. Crispell G, Commins SP, Archer-Hartman SA, et al. Discovery of alpha-gal–containing antigens in North American tick species believed to induce red meat allergy. Front Immunol 2019;10:1056. PMID:31156631 https://doi.org/10.3389/fimmu.2019.01056
10. Flaherty MG, Kaplan SJ, Jerath MR. Diagnosis of life-threatening alpha-gal food allergy appears to be patient driven. J Prim Care Community Health 2017;8:345–8. PMID:28447914 https://doi.org/10.1177/2150131917705714

# Travel-Associated Dengue Cases — United States, 2010–2021

Joshua M. Wong, MD[1]; Aidsa Rivera, DrPH[1]; Hannah R. Volkman, PhD[1]; Brenda Torres-Velasquez, PhD[1]; Dania M. Rodriguez, MSc[1]; Gabriela Paz-Bailey, MD, PhD[1]; Laura E. Adams, DVM[1]

## Abstract

Dengue, the leading cause of arboviral disease worldwide, can be fatal without appropriate treatment. Among 7,528 confirmed or probable travel-associated U.S. dengue cases reported during 2010–2021, one in five (1,474, 20%) was reported in 2019. This is 168% higher than the annual average number of cases reported during 2010–2018 and 2020–2021 (approximately 550 per year) and 61% higher than the 913 cases reported in 2016, the second highest year on record. The number of cases as a fraction of air traffic volume to international destinations outside North America or Europe was also highest in 2019, with 41.9 cases per million trips, compared with 21.0 per million in other years during 2010–2021. This report compares the number and characteristics of travel-associated dengue cases reported to national surveillance in the United States in 2019 with cases reported during 2010–2018 and 2020–2021. Areas with conditions suitable for dengue transmission as well as the population at risk for dengue are expected to increase, placing U.S. travelers at higher risk for infection. Health care providers should be aware that dengue is a common cause of fever in the returning traveler and be familiar with its signs and symptoms, testing, and management. Dengue vaccines are not currently recommended for U.S. travelers; therefore, persons should review areas of dengue risk and follow guidance for preventing mosquito bites.

## Introduction

Dengue is the leading cause of arboviral disease in the world (*1*) and can be fatal without appropriate treatment. In 2019, the World Health Organization (WHO) reported the highest number of dengue cases worldwide compared with cases reported in previous years (*2*).

Dengue is caused by four distinct but closely related dengue virus (DENV) types (1–4) and is transmitted by *Aedes* mosquitos. Infection with a DENV confers long-term immunity to that specific type but only short-term immunity to other types. Dengue causes approximately 400 million annual infections, one quarter of which lead to symptomatic disease, and results in more than 40,000 deaths.* In U.S. states, most dengue cases are associated with travel to areas with endemic dengue transmission (*3*), although endemic transmission does occur in six U.S. territories† and freely associated states§ (*4*).

## Methods

Dengue has been a nationally notifiable disease since 2010. State health departments report dengue cases to CDC through CDC's National Arbovirus Surveillance System (ArboNET), which maintains data on human disease and arboviral infections among presumptively viremic blood donors, veterinary disease cases, mosquitoes, dead birds, and sentinel animals.¶ This report includes confirmed and probable cases reported to ArboNET and associated with travel outside of the reporting jurisdiction within the 2 weeks preceding the onset of an acute febrile illness.

Confirmed or probable cases must have appropriate testing** and a clinically compatible case of dengue-like illness, dengue, or severe dengue.†† Cases per million air trips§§ by region of travel¶¶ were calculated using data on international air travelers from the National Travel and Tourism Office, as has

* https://www.cdc.gov/dengue/about/index.html
† American Samoa, Puerto Rico, and U.S. Virgin Islands.
§ Federated States of Micronesia, Marshall Islands, and Palau.

¶ https://www.cdc.gov/mosquitoes/mosquito-control/professionals/ArboNET.html
** Case classification was performed according to the Council of State and Territorial Epidemiologists' (CSTE) 2015 case definition (https://ndc.services.cdc.gov/case-definitions/dengue-virus-infections-2015/). Confirmed or probable cases must have a clinically compatible case of dengue-like illness, dengue, or severe dengue. The laboratory criterion for a probable case is defined as detection of immunoglobulin M (IgM) anti-DENV antibody in serum, if the person lived in or traveled to an area with transmission of another flavivirus or was recently vaccinated against a flavivirus (e.g., yellow fever virus or Japanese encephalitis virus). The laboratory criteria for a confirmed case are detection of 1) DENV nucleic acid by reverse transcription–polymerase chain reaction in any body fluid or tissue, 2) DENV antigen in tissue by a validated assay, 3) DENV nonstructural protein 1 (NS1) antigen by a validated assay, or 4) IgM anti-DENV antibody if exposure occurred in an area without evidence of other flavivirus transmission.
†† Clinical syndrome classification was updated in the 2015 CSTE case definition. Reported cases previously classified as "dengue hemorrhagic fever" and "dengue shock" before reporting changed were reclassified as "severe dengue," and cases classified as "dengue fever with hemorrhage" were reclassified as "dengue" for this analysis. Annual trends might not be comparable.
§§ Individual travelers might take multiple international air trips every year, each of which is counted separately in the total number of air trips. Because data on total number of international air travelers and their region of travel are not available, true incidence (cases per number of international air travelers per year) cannot be calculated.
¶¶ The following cases were excluded: 1) those associated with travel to U.S. states or territories (481), because data from the Customs and Border Protection Advance Passenger Information System (APIS) excludes domestic travel; 2) those associated with travel to multiple regions (96) or where the country was unknown (306); 3) those associated with travel to North America (882), because travel between the continental United States and other North American countries commonly occurs by land borders, and the mode of travel for travel-associated cases is not reported to ArboNET; and 4) those associated with travel to Europe (six).

been previously described*** (*3*). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†††

## Results

During 2010–2021, a total of 7,528 confirmed or probable travel-associated dengue cases were reported to ArboNET. Among these, 1,474 (20%) occurred in 2019, representing a 168% increase over the annual average of 550 cases during 2010–2018 and 2020–2021, and a 61% increase over the 913 cases reported in 2016, the year with the second highest number of cases (Figure 1). The lowest annual number of cases reported (205) was in 2021, when travel patterns were substantially altered because of the COVID-19 pandemic. During all three analysis periods, cases were evenly distributed among females and males, and age distribution remained consistent, with median ages of 41, 42, and 42 years during 2010–2018, 2019, and 2020–2022, respectively (Table).

The proportions of cases classified as dengue-like illness, dengue, and severe dengue were similar in 2019, 2010–2018, and 2020–2021. The proportions of cases among patients who were hospitalized and who had an unknown disposition were similar during 2010–2018 (42% and 2%, respectively) and in 2019 (42% and 5%, respectively), whereas a smaller proportion of patients was hospitalized (33%) and a higher proportion had an unknown disposition (22%) during 2020–2021. Fewer than 1% of dengue patients died during 2010–2018 (18) and in 2019 (one), and no deaths occurred during 2020–2021. DENV-1 was the most frequently reported type across the three periods; however, the dengue type was unknown for 95% of cases during 2010–2018, 93% in 2019, and 83% during 2020–2021.

During the entire period, most cases (90%) were associated with travel outside U.S. states or territories. The most frequently visited region among travel-associated cases in 2019 was the Caribbean (39%), followed by Asia (27%) and North America§§§ (14%). Travel patterns were similar during 2010–2018, with 33%, 29%, and 10% of patients reporting travel to those three regions, respectively. However, during 2020–2021, a period with major disruptions to travel because of the COVID-19 pandemic, the most frequently visited region was North America (30%), followed by the Caribbean (27%) and Asia (19%). The number of dengue cases per million air trips to destinations outside North America or Europe in 2019 (41.9 per million) was nearly twice that during other years during 2010–2021 (21.0 per million). These rates varied by region of travel across the periods analyzed. During 2010–2018, the highest number of cases per million air trips was associated with travel to Central America (32.1), followed by Asia (22.9) and the Caribbean (20.5). (Figure 2) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/131003). In 2019, the highest rates were associated with travel to the Caribbean (56.8), Central America (49.7), and Asia (39.6); during 2020–2021, the highest number of cases per million trips (37.3) was associated with travel to Oceania, followed by Asia (23.5) and South America (15.8).

Travelers returning from the top 10 countries of acquisition during 2010–2021 accounted for more than two thirds (69%) of cases reporting an international travel history (Supplementary Figure; https://stacks.cdc.gov/view/cdc/131002). Seven countries (Cuba, the Dominican Republic, El Salvador, India, Jamaica, Mexico, and the Philippines) were among the top 10 countries of acquisition across all three periods (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/131004). Seasonality among travel-associated cases was similar during 2010–2018 and 2019, with most cases occurring during July–November. Seasonal trends were less apparent during 2020–2021, when fewer cases were reported relative to previous periods.

## Discussion

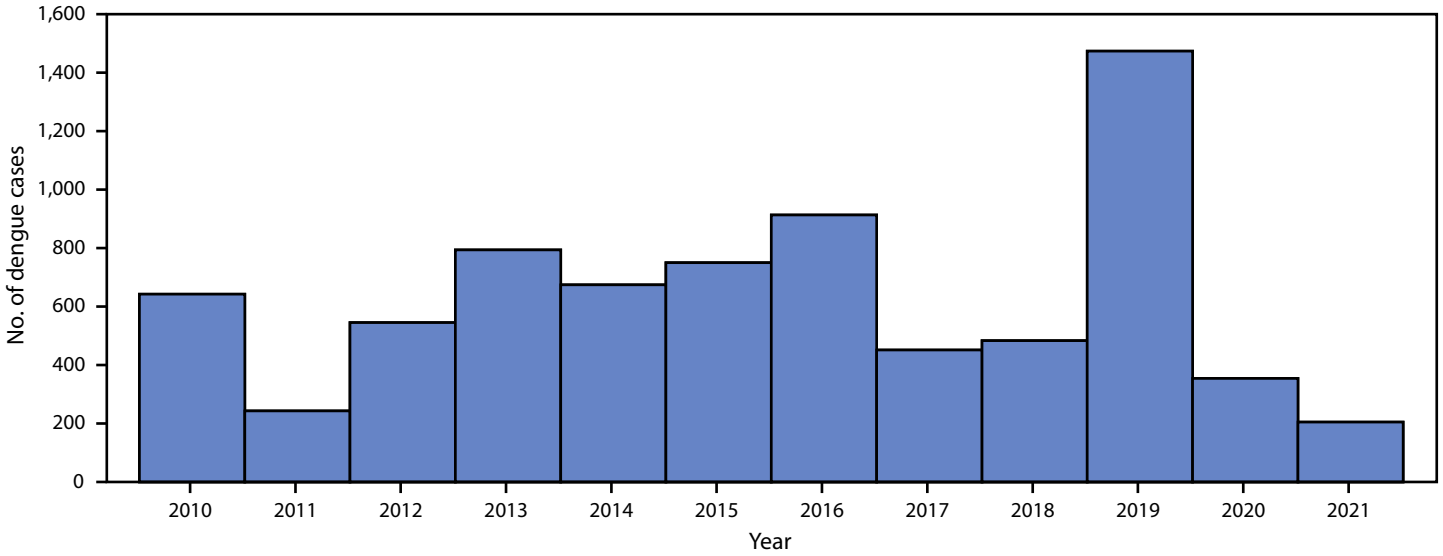
U.S. jurisdictions reported more travel-associated dengue cases in 2019 than in any other year since dengue in the United States became nationally notifiable in ArboNET in 2010. The lowest number of cases reported occurred in 2021, during a period marked by unprecedented travel restrictions and a decline in overall travel because of the COVID-19 pandemic. The characteristics of persons with dengue, including age, sex, clinical syndromes, and outcomes, were similar in 2019 to those reported in other years during 2010–2021. The Caribbean, Asia, and North America were the top regions of acquisition, respectively, during 2010–2018 and 2019. However, during 2020–2021, the proportion of cases associated with travel to North America surpassed both the Caribbean and Asia, and the proportion of cases associated with travel to Asia decreased relative to the Caribbean, possibly reflecting a decline in overall travel because of the COVID-19 pandemic, with the largest regional decrease in air trips to Asia, or variations in regional dengue activity during those periods. The number of cases per million international air trips was higher in 2019 than that

*** International air traffic volume information (denominator) is from the APIS/I-92 Monitor (https://www.trade.gov/us-international-air-travel-statistics-i-92-data) and from the Survey of International Air Travelers (https://www.trade.gov/survey-international-air-travelers-siat), both managed by the U.S. Department of Commerce, National Travel and Tourism Office.

††† 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

§§§ Travel-associated cases from North America include cases associated with travel to Mexico (882) and the United States (nine). Among cases associated with travel to the United States, four were reported during 2010–2018, three in 2019, and two during 2020–2021.

**FIGURE 1. Reported confirmed and probable travel-associated dengue cases, by year (N = 7,528) — National Arbovirus Surveillance System, United States, 2010–2021**




during 2010–2018 or 2020–2021, which varied by year and region of travel. The sharp overall increase in 2019 mirrors global dengue activity, with the highest number of dengue cases worldwide reported to WHO in 2019 (*2*) and in the Region of the Americas (*5*) since reporting to the Pan American Health Organization/WHO began in 1980.[¶¶¶]

## Limitations

The findings in this report are subject to at least four limitations. First, case counts are underestimated because many travelers with dengue do not seek medical care, are not tested for dengue when evaluated, or do not receive a correct diagnosis. Second, incomplete reporting of clinical data might lead to misclassification of the clinical syndrome, likely underestimating severe dengue cases among reported cases. Third, changes to the clinical syndrome classification in the 2015 case definition required reclassification of cases reported before this change for this analysis, complicating its comparison among the three periods. Finally, the dataset does not include cases among U.S. travelers who contracted dengue while traveling and whose cases were not reported to U.S. surveillance.

## Implications for Public Health Practice

Global dengue is expected to increase in disease prevalence and geographic range, placing U.S. travelers at increased risk for infection (*1*). As travel returns to levels similar to those before the COVID-19 pandemic, clinicians should consider dengue in the differential diagnosis of fever in the returning traveler and understand its signs and symptoms, appropriate testing, and disease management[****] for two reasons: 1) early recognition of dengue and prompt intravenous fluid management, when indicated, reduces mortality to <1%, whereas untreated dengue can have a case-fatality ratio as high as 13% (*1*) and 2) travelers infected with dengue returning to the United States can introduce the virus to local *Aedes* mosquito populations, present in one half of U.S. counties (*6*), potentially leading to local DENV transmission.[††††] It is important for jurisdictions

**Summary**

**What is already known about this topic?**

Dengue is the most common arboviral disease worldwide and a common cause of fever in travelers returning from areas with endemic disease. More dengue cases were reported to the World Health Organization in 2019 than in any other year. Vaccines are not currently recommended for travelers to areas with endemic dengue.

**What is added by this report?**

In 2019, the number of reported travel-associated dengue cases in the United States was 168% higher than the annual average during 2010–2018 and 2020–2021.

**What are the implications for public health practice?**

As dengue incidence increases globally, the risk for U.S. travelers will increase. Clinicians should be prepared to recognize, test for, and treat dengue. Travelers should follow CDC guidelines to prevent mosquito bites and vectorborne diseases.

[¶¶¶] https://www3.paho.org/data/index.php/en/mnu-topics/indicadores-dengue-en.html

[****] https://www.cdc.gov/dengue/healthcare-providers/index.html

[††††] Local dengue outbreaks were recently reported in Texas in 2013, Hawaii in 2015, and Florida in 2013 and 2020. https://www.cdc.gov/dengue/areaswithrisk/in-the-us.html

**TABLE. Characteristics of reported confirmed and probable travel-associated dengue cases (N = 7,528) — National Arbovirus Surveillance System, United States, 2010–2018, 2019, and 2020–2021**

| Characteristic | No. (%) | | |
|---|---|---|---|
| | 2010–2018 | 2019 | 2020–2021 |
| **Total** | **5,495 (100)** | **1,474 (100)** | **559 (100)** |
| **Case status*** | | | |
| Probable | 1,708 (31) | 793 (46) | 229 (41) |
| Confirmed | 3,787 (69) | 681 (54) | 330 (59) |
| **Sex** | | | |
| Female | 2,748 (50) | 743 (50) | 275 (49) |
| Male | 2,746 (50) | 729 (49) | 284 (51) |
| Unknown | 1 (<1) | 2 (<1) | 0 (—) |
| **Age group, yrs** | | | |
| Median (IQR) | 41 (27–55) | 42 (26–56) | 42 (28–57) |
| 0–9 | 143 (3) | 68 (5) | 21 (4) |
| 10–19 | 557 (10) | 178 (12) | 60 (11) |
| 20–29 | 962 (17) | 196 (13) | 80 (14) |
| 30–39 | 936 (17) | 238 (16) | 88 (16) |
| 40–49 | 991 (18) | 254 (17) | 107 (19) |
| 50–59 | 986 (18) | 256 (18) | 94 (17) |
| ≥60 | 910 (17) | 284 (19) | 108 (19) |
| Unknown | 10 (<1) | 0 (—) | 1 (<1) |
| **Race†** | | | |
| American Indian or Alaska Native | 17 (<1) | 2 (<1) | 3 (<1) |
| Asian or Pacific Islander | 843 (15) | 216 (15) | 71 (13) |
| Black or African American | 301 (6) | 77 (5) | 24 (4) |
| White | 2,439 (44) | 646 (44) | 247 (44) |
| Other or unknown | 1,895 (34) | 533 (36) | 214 (38) |
| **Ethnicity†** | | | |
| Hispanic or Latino | 1,616 (30) | 599 (41) | 245 (44) |
| Non-Hispanic | 2,538 (46) | 504 (34) | 189 (34) |
| Unknown | 1,341 (24) | 371 (25) | 125 (22) |
| **Dengue clinical syndrome§** | | | |
| Dengue-like illness | 297 (5) | 56 (4) | 18 (3) |
| Dengue | 5,030 (92) | 1,388 (94) | 532 (95) |
| Severe dengue | 55 (1) | 29 (2) | 4 (1) |
| Unknown | 113 (2) | 1 (<1) | 5 (1) |
| **Hospitalized** | | | |
| No | 2,912 (53) | 820 (56) | 251 (45) |
| Yes | 2,325 (42) | 625 (42) | 185 (33) |
| Unknown | 258 (5) | 29 (2) | 123 (22) |
| **Outcome** | | | |
| Survived | 5,310 (97) | 1,405 (95) | 521 (93) |
| Died | 18 (<1) | 1 (<1) | 0 (—) |
| Unknown | 167 (3) | 68 (5) | 38 (7) |
| **DENV type** | | | |
| DENV-1 | 131 (2) | 51 (3) | 43 (8) |
| DENV-2 | 79 (1) | 32 (2) | 35 (6) |
| DENV-3 | 51 (1) | 23 (2) | 16 (3) |
| DENV-4 | 29 (1) | 1 (<1) | 3 (<1) |
| Unknown | 5,205 (95) | 1,367 (93) | 462 (83) |
| **Origin of acquisition** | | | |
| Outside of U.S. states or territories | 4,830 (88) | 1,414 (96) | 497 (89) |
| Within a U.S. state or territory | 443 (8) | 13 (1) | 25 (4) |
| Unknown | 222 (4) | 47 (3) | 37 (7) |
| **Region of acquisition** | | | |
| Africa | 97 (2) | 18 (1) | 12 (2) |
| Asia | 1,615 (29) | 401 (27) | 107 (19) |
| Caribbean | 1,794 (33) | 570 (39) | 149 (27) |
| Central America | 684 (12) | 158 (11) | 34 (6) |
| Europe | 5 (<1) | 0 (—) | 1 (<1) |
| North America¶ | 520 (10) | 206 (14) | 165 (30) |
| Oceania | 127 (2) | 35 (2) | 13 (2) |
| South America | 341 (6) | 33 (2) | 41 (7) |
| Multiple | 90 (2) | 6 (<1) | 0 (—) |
| Unknown | 222 (4) | 47 (3) | 37 (7) |

**Abbreviations:** CSTE = Council of State and Territorial Epidemiologists; DENV = dengue virus; IgM = immunoglobulin M; NS1 = nonstructural protein 1.

* Case classification was performed according to the CSTE 2015 case definition (https://ndc.services.cdc.gov/case-definitions/dengue-virus-infections-2015/). Confirmed or probable cases must have a clinically compatible case of dengue-like illness, dengue, or severe dengue. The laboratory criterion for a probable case is defined as detection of IgM anti-DENV antibody in serum, if the person lived in or traveled to an area with transmission of another flavivirus or was recently vaccinated against a flavivirus (e.g., yellow fever virus or Japanese encephalitis virus). The laboratory criteria for a confirmed case are 1) DENV nucleic acid by reverse transcription–polymerase chain reaction in any body fluid or tissue, 2) DENV antigen in tissue by a validated assay, 3) DENV NS1 antigen by a validated assay, or 4) IgM anti-DENV antibody if exposure occurred in an area without evidence of other flavivirus transmission.

† Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

§ Clinical syndrome classification was updated in the CSTE 2015 case definition. Reported cases previously classified as "dengue hemorrhagic fever" and "dengue shock" before reporting changed were reclassified as "severe dengue," and cases classified as "dengue fever with hemorrhage" were reclassified as "dengue" for this analysis. Annual trends might not be comparable.

¶ Travel-associated cases from North America include cases associated with travel to Mexico (882) and U.S. states (nine). Among cases associated with travel to U.S. states, four were reported during 2010–2018, three in 2019, and two during 2020–2021.

to strengthen surveillance for dengue and consider ways to increase the identification and reporting of type.[§§§§] Because persons build immunity against each specific DENV type, surveillance that can reliably detect the introduction of new types will guide epidemic risk potential and the impact of vaccine and vector control interventions in areas where dengue is endemic.

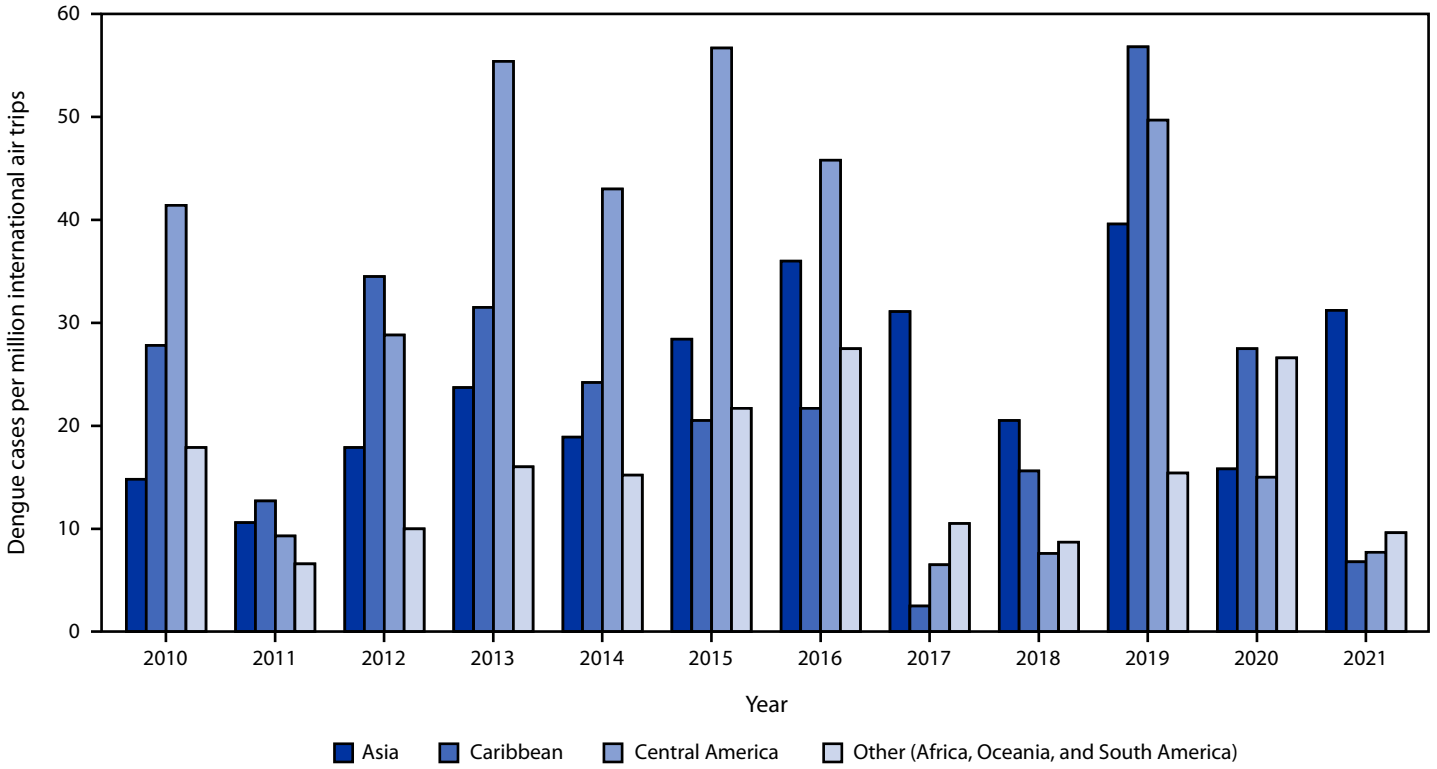
Although a dengue vaccine is recommended for routine use in children and adolescents aged 9–16 years with laboratory-confirmed previous DENV infection who live in areas of the United States where dengue is endemic (*7*,*8*), vaccination is not recommended for travelers.[¶¶¶¶] Dengue and other vectorborne diseases such as Zika and malaria[*****] can be prevented while

[§§§§] CDC Dengue Branch provides free dengue testing to public health laboratories requesting confirmatory testing and virus typing (https://www.cdc.gov/ncezid/dvbd/specimensub/dengue-shipping.html). Reporting DENV type is preferred, but not required. https://ndc.services.cdc.gov/mmgpage/arboviral-message-mapping-guide/

[¶¶¶¶] https://www.cdc.gov/dengue/vaccine/index.html

[*****] https://www.cdc.gov/malaria/travelers/index.html

**FIGURE 2. Reported confirmed and probable travel-associated dengue cases (N = 5,757)* per million international air trips, by region of acquisition — multiple data sources,† United States, 2010–2021**




**Abbreviations:** APIS = Customs and Border Protections Advance Passenger Information System; ArboNET = National Arbovirus Surveillance System.

* The following cases were excluded: 1) those associated with travel to U.S. states or territories (481), because data from APIS excludes domestic travel; 2) those associated with travel to multiple regions (96) or where the country was unknown (306); 3) those associated with travel to North America (882), because travel between the continental United States and other North American countries commonly occurs by land borders, and the mode of travel for travel-associated cases is not reported to ArboNET; and 4) those associated with travel to Europe (six).

† International air traffic volume information (denominator) is from the APIS/I-92 Monitor (https://www.trade.gov/us-international-air-travel-statistics-i-92-data) and from the Survey of International Air Travelers (https://www.trade.gov/survey-international-air-travelers-siat), both managed by the U.S. Department of Commerce, National Travel and Tourism Office.

traveling by taking measures to prevent mosquito bites,†††† including using Environmental Protection Agency–registered insect repellent, wearing protective clothing,§§§§§ and staying in lodging that has air conditioning or window screens. New interventions are emerging, including new dengue vaccines in clinical trials and novel vector control methods that do not rely on chemical control of mosquitoes (*1*,*9*). Effective and scalable public health measures to prevent dengue will be needed to reduce risk among residents of and travelers to areas where dengue is endemic.

†††† https://www.cdc.gov/dengue/prevention/plan-for-travel.html

§§§§§ Protective clothing includes loose-fitting, long-sleeved shirts and pants.

Corresponding author: Joshua M. Wong, nof9@cdc.gov.

[1]Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

## References

1. Wong JM, Adams LE, Durbin AP, et al. Dengue: a growing problem with new interventions. Pediatrics 2022;149:e2021055522. PMID:35543085 https://doi.org/10.1542/peds.2021-055522
2. World Health Organization. Dengue and severe dengue. Geneva, Switzerland: World Health Organization; 2022. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue
3. Rivera A, Adams LE, Sharp TM, Lehman JA, Waterman SH, Paz-Bailey G. Travel-associated and locally acquired dengue cases—United States, 2010–2017. MMWR Morb Mortal Wkly Rep 2020;69:149–54. PMID:32053577 https://doi.org/10.15585/mmwr.mm6906a1
4. Ryff KR, Rivera A, Rodriguez DM, et al. Epidemiologic trends of dengue in U.S. territories, 2010–2020. MMWR Surveill Summ 2023;72(No. SS-4):1–12. PMID:37192141 https://doi.org/10.15585/mmwr.ss7204a1
5. Pan American Health Organization. Epidemiological update: dengue. Washington, DC: World Health Organization; Pan American Health Organization; 2019. https://www.paho.org/en/documents/epidemiological-update-dengue-11-november-2019

6. Johnson TL, Haque U, Monaghan AJ, et al. Modeling the environmental suitability for *Aedes (Stegomyia) aegypti* and *Aedes (Stegomyia) albopictus* (Diptera: Culicidae) in the contiguous United States. J Med Entomol 2017;54:1605–14. PMID:29029153 https://doi.org/10.1093/jme/tjx163
7. Mac VV, Wong JM, Volkman HR, et al. Notes from the field: prevalence of previous dengue virus infection among children and adolescents—U.S. Virgin Islands, 2022. MMWR Morb Mortal Wkly Rep 2023;72:288–9. PMID:36927833 https://doi.org/10.15585/mmwr.mm7211a4
8. Paz-Bailey G, Adams L, Wong JM, et al. Dengue vaccine: recommendations of the Advisory Committee on Immunization Practices, United States, 2021. MMWR Recomm Rep 2021;70(No. RR-6):1–16. PMID:34978547 https://doi.org/10.15585/mmwr.rr7006a1
9. Hernandez-Romieu AC, Adams LE, Paz-Bailey G. Opportunities for improved dengue control in the US territories. JAMA 2023;330:19–20. PMID:37192216 https://doi.org/10.1001/jama.2023.8567

# Demographic Disparities in Mpox Vaccination Series Completion, by Route of Vaccine Administration — California, August 9, 2022–March 31, 2023

Tarek Salih, MD[1,*]; Josh Vance, MPH, MEd[1,2,*]; Joshua Quint, PhD[1]; Brenda Meza, MPP[1]; Louise McNitt, MD[1]; Webster U. Lincoln[1]; Robert Schechter, MD[1]

## Abstract

In August 2022, the Food and Drug Administration authorized JYNNEOS vaccine (modified vaccinia Ankara vaccine, Bavarian Nordic), a 2-dose series used for the prevention of *Monkeypox virus* infection, to be administered via a dose-sparing intradermal route, in addition to the previously authorized subcutaneous route. The California Department of Public Health investigated whether demographic disparities in vaccination series completion varied by route of administration of the recipient's first dose. Among California residents who received their first dose during August 9, 2022–March 31, 2023, a total of 59.8% received a second dose. Series completion was highest among non-Hispanic White persons (64.1%), persons aged ≥65 years (72.6%), and adults with male sex assignment at birth (62.1%); series completion was lowest among non-Hispanic Black or African American persons (51.3%), persons aged 18–24 years (42.9%), and adults assigned female sex at birth (42.8%). When the first dose was received by subcutaneous administration, overall series completion was 58.8% compared with 60.2% when the first dose was administered intradermally. Odds of series completion across all race and ethnicity groups, persons aged 18–64 years, community health conditions, and persons assigned male sex at birth were not greater when the first dose was administered subcutaneously compared with intradermally. Intradermal use of JYNNEOS vaccine did not lower overall 2-dose series completion rates. Continued efforts are needed to ensure persons at risk for *Monkeypox virus* infection receive both recommended doses.

## Introduction

In response to the 2022 U.S. mpox outbreak, CDC and the Administration for Strategic Preparedness and Response initiated distribution of JYNNEOS smallpox and mpox vaccine, licensed in the United States as a 2-dose series, with doses administered 28 days apart (*1*). During May 26, 2022–August 8, 2022, the vaccine was exclusively administered via subcutaneous (SC) injection of a 0.5 mL dose (*2*). On August 9, 2022, the Food and Drug Administration authorized a dose-sparing 0.1 mL intradermal (ID) injection (*3*). Despite increased availability resulting from ID administration and efforts to improve access while the outbreak evolved, 2-dose vaccination series completion among California residents was 64.5% overall[†] and varied across demographic groups (*2*). Concerns were raised that ID administration of the first dose might lead to lower series completion among persons at risk for scarring or keloid formation (*4*).

## Methods

Persons aged ≥18 years with documentation of receipt of ≥1 dose of JYNNEOS vaccine reported to the California Immunization Registry during August 9, 2022–March 31, 2023, were included. The starting date of August 9, 2022, was used to restrict the analysis to the period after authorization of ID administration of JYNNEOS. Descriptive statistics were calculated for persons who had received ≥1 reported dose of JYNNEOS for which the route of administration of the first dose was recorded, and results were stratified by demographic groups. Persons who had received 2 doses of JYNNEOS vaccine were included if a minimum of 24 days[§] separated the first and second dose and the second dose was reported on or before April 30, 2023. Odds ratios (ORs) and 99% Wald CIs were estimated using logistic regression to assess differences in series completion overall and by route of administration of the first dose[¶] stratified by race and ethnicity, age group, community health conditions (using Healthy Places Index [HPI] quartiles

[*] These authors contributed equally to this report.

[†] Among California residents who received a first dose of JYNNEOS during May 26, 2022–March 31, 2023, 64.5% completed the vaccination series by April 30, 2023. During the study period (August 9, 2022–March 31, 2023), 59.8% completed the vaccination series by April 30, 2023.

[§] JYNNEOS is licensed as a 2-dose vaccine, with doses recommended to be given 28 days apart; however, a minimum interval of 24 days between doses is acceptable. https://www.cdc.gov/poxvirus/mpox/interim-considerations/jynneos-vaccine.html#dosing

[¶] Data collected in the California Immunization Registry do not differentiate between patients returning for their second dose who 1) might have requested one route of administration versus the other, 2) were recommended by their provider to receive one route versus the other, or 3) visited a provider exclusively offering one route type. Because of these limitations, this analysis did not consider route of administration of the second dose when assessing whether administration route of the first dose acted as a deterrent to vaccine series completion.

ranked from 1 [least healthy] to 4 [healthiest])** (5), and sex assignment at birth.†† Similarly, to ascertain whether series completion was affected by policy changes, vaccine supply, and mpox incidence over time, completion rates by month of receipt of the first dose were assessed. SAS statistical software (version 9.4; SAS Institute) was used for all analyses. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§

## Results

Among 119,345 California residents who received their first JYNNEOS dose during August 9, 2022–March 31, 2023, a total of 71,317 (59.8%) completed the 2-dose series (Table). Persons who were assigned female sex at birth (42.8%) had lower odds of returning for a second dose than did those assigned male sex at birth (62.1%). Compared with the odds of completing the series among non-Hispanic White (White)

** HPI quartiles are based on data from 25 identified key drivers of health and life expectancy at birth. Each county and zip code are assigned to a quartile based on these 25 measures, ranked from 1 (least healthy) to 4 (healthiest). https://map.healthyplacesindex.org

†† Data submitted to the California Immunization Registry do not currently include sexual orientation or gender identity information and are generally based on the sex or gender entered at the time of the person's first dose of any vaccine; however, some records have been updated to reflect a person's gender identity as being "other" or "nonbinary."

§§ 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

**TABLE. Percentage and odds ratios for completing the mpox vaccine series, by route of administration of first dose and demographic subgroup — California, August 9, 2022–March 31, 2023**

| Characteristic | First doses, route of administration, no. | | | Completed series, route of first dose administration, no. (%)* | | | Odds ratio (99% CI)¶,** |
|---|---|---|---|---|---|---|---|
| | Total† | SC | ID | Total (SC or ID)§ | SC | ID | |
| **Total** | **119,345** | **35,862** | **83,483** | **71,317 (59.8)** | **21,084 (58.8)** | **50,233 (60.2)** | **NA** |
| **Sex assigned at birth** | | | | | | | |
| Female | **13,446** | 4,086 | 9,360 | **5,759 (42.8)** | 1,503 (36.8) | 4,256 (45.5) | 0.69 (0.66–0.72) |
| Male | **105,366** | 31,614 | 73,752 | **65,387 (62.1)** | 19,521 (61.7) | 45,866 (62.2) | Ref |
| Unknown or other†† | **533** | 162 | 371 | **171 (32.0)** | 60 (37.0) | 111 (29.9) | NA§§ |
| **Race and ethnicity** | | | | | | | |
| Asian, NH | **14,284** | 4,729 | 9,555 | **8,686 (60.8)** | 2,845 (60.2) | 5,841 (61.1) | 0.95 (0.91–0.99) |
| Black or African American, NH | **8,828** | 3,010 | 5,818 | **4,531 (51.3)** | 1,536 (51.0) | 2,995 (51.5) | 0.80 (0.76–0.84) |
| White, NH | **53,059** | 15,237 | 37,822 | **33,992 (64.1)** | 9,655 (63.4) | 24,337 (64.3) | Ref |
| Hispanic or Latino | **31,270** | 9,204 | 22,066 | **17,691 (56.6)** | 5,081 (55.2) | 12,610 (57.1) | 0.88 (0.86–0.91) |
| Multiracial/Other | **9,698** | 3,003 | 6,695 | **5,632 (58.1)** | 1,742 (58.0) | 3,890 (58.1) | 0.91 (0.87–0.95) |
| Unknown | **2,206** | 679 | 1,527 | **785 (35.6)** | 225 (33.1) | 560 (36.7) | NA§§ |
| **Age group, yrs** | | | | | | | |
| 18–24 | **8,950** | 2,607 | 6,343 | **3,838 (42.9)** | 1,069 (41.0) | 2,769 (43.7) | 0.59 (0.55–0.63) |
| 25–34 | **32,963** | 10,588 | 22,375 | **17,032 (51.7)** | 5,427 (51.3) | 11,605 (51.9) | 0.71 (0.68–0.74) |
| 35–44 | **26,453** | 8,384 | 18,069 | **15,568 (58.9)** | 5,013 (59.8) | 10,555 (58.4) | 0.81 (0.77–0.85) |
| 45–54 | **19,767** | 6,017 | 13,750 | **12,742 (64.5)** | 3,866 (64.3) | 8,876 (64.6) | 0.89 (0.85–0.93) |
| 55–64 | **20,390** | 5,661 | 14,729 | **14,280 (70.0)** | 3,912 (69.1) | 10,368 (70.4) | 0.96 (0.92–1.01) |
| ≥65 | **10,822** | 2,605 | 8,217 | **7,857 (72.6)** | 1,797 (69.0) | 6,060 (73.7) | Ref |
| **Healthy Places Index quartile§§** | | | | | | | |
| 1 (least healthy) | **21,505** | 5,697 | 15,808 | **12,246 (56.9)** | 3,160 (55.5) | 9,086 (57.5) | 0.97 (0.93–1.00) |
| 2 | **25,127** | 6,655 | 18,472 | **15,809 (62.9)** | 4,056 (60.9) | 11,753 (63.6) | 1.07 (1.04–1.10) |
| 3 | **29,234** | 8,404 | 20,830 | **18,254 (62.4)** | 5,181 (61.6) | 13,073 (62.8) | 1.06 (1.03–1.09) |
| 4 (healthiest) | **40,548** | 14,399 | 26,149 | **23,840 (58.8)** | 8,394 (58.3) | 15,446 (59.1) | Ref |
| Unknown | **2,931** | 707 | 2,224 | **1,168 (39.8)** | 293 (41.4) | 875 (39.3) | NA§§ |

**Abbreviations:** ID = intradermal; NA = not applicable; NH = non-Hispanic; Ref = referent group; SC = subcutaneous.

* Persons who received a second dose by same route of administration as that of the first dose.

† Route of administration was not reported for every first dose.

§ Irrespective of route of administration of first dose.

¶ Within the same column (e.g., comparing persons aged >64 years with other age groups).

** Odds of returning for a second dose, irrespective of route of administration.

†† Data submitted to California Immunization Registry do not include sexual orientation or gender identity information and are generally based on the sex or gender entered at the time of the person's first dose of any vaccine; however, some records have been updated to reflect a person's gender identity as being "other" or "nonbinary."

§§ There are many reasons why demographic variables might be unknown and statistical findings could be biased. Thus, odds ratios were not calculated when demographic variables were unknown.

¶¶ Healthy Places Index quartiles are based on data from 25 identified key drivers of health and life expectancy at birth. Each county and zip code are assigned to a quartile based on these 25 measures, ranked from 1 (least healthy) to 4 (healthiest). https://map.healthyplacesindex.org

persons (64.1%), the odds were lower among those who were non-Hispanic Black or African American (Black) (51.3%), Hispanic or Latino (Hispanic) (56.6%), non-Hispanic Asian (Asian) (60.8%), and non-Hispanic multiracial or other race (58.1%). Similarly, the odds of completing the 2-dose series were lower among those aged 45–54 years (64.5%), 35–44 years (58.9%), 25–34 years (51.7%), and 18–24 years (42.9%), compared with those among aged ≥65 years (72.6%), but were similar among those aged 55–64 years (70.0%). The odds of receiving a second dose, when compared to persons in HPI quartile 4 (58.8%), were similar among persons living in quartile 1 (56.9%), but higher among persons living in quartile 2 (62.9%) and 3 (62.4%).

Overall, among 119,345 first doses administered since August 9, 2022, 83,483 (70.0%) were administered by the ID route and 35,862 (30.0%) by the SC route.¶¶ The proportion of ID doses began to decline in October 2022 (Figure 1). Despite this decline and concerns regarding ID administration, the proportion of persons receiving a second dose after ID administration of the first dose (60.2%) was not lower than the proportion of those who received second dose after SC administration of the first dose (58.8%) (Supplementary Table, https://stacks.cdc.gov/view/cdc/131259). This finding was consistent among Asian, Black, White, Hispanic, and multiracial or other race persons; persons aged 18–64 years; persons in all four HPI quartiles (*5*); and persons assigned male sex at birth. Among persons aged ≥65 years and those assigned female sex assignment at birth, completion of the series was less likely after SC administration of the first dose. Disaggregation of the data by month found that completion rates among persons receiving their first dose during August 9, 2022–August 31, 2022, were 66.3% and 62.0% among those who received the vaccine by SC and ID administration, respectively, compared with 47.1% and 58.9%, respectively, among those who completed the vaccination series during September 1, 2022–March 31, 2023 (Figure 2) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/131001).***

## Discussion

Despite concern that reactogenicity related to ID administration of JYNNEOS vaccine might lead to lower series completion rates, analysis of California Immunization Registry data found comparable series completion rates irrespective of the route of administration of the first dose. Lower overall series completion, irrespective of route of administration, was observed among persons assigned female sex at birth, certain racial and ethnic groups, and younger persons. In no demographic group was series completion more likely when the first dose was administered by the SC route compared with ID although persons with female sex assignment at birth and those aged ≥65 years were more likely to complete the series when the first dose was administered via the ID route.

Noninferiority in immunogenicity between ID and standard administration routes for influenza, rabies, and hepatitis B vaccinations has been demonstrated (*6*). JYNNEOS vaccine effectiveness against medically attended mpox has been reported to be as high as 86% for 2 doses and 75% for 1 dose (*7*). When comparing route of administration, no significant differences in vaccine effectiveness have been demonstrated to date (*7*,*8*). Although ID vaccine recipients have reported differences in period of swelling after vaccination (*9*), a CDC analysis of data from the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink found no significant differences in the prevalence of adverse events reported for ID versus SC administration of JYNNEOS (*10*).

**Summary**

**What is already known about this topic?**

Demographic disparities among persons completing the 2-dose mpox vaccination series have been previously described.

**What is added by this report?**

California residents who received their first dose of mpox vaccine by intradermal or subcutaneous administration had comparable 2-dose series completion rates (60.2% and 58.8%, respectively). Similar series completion rates by route of administration were observed across all race and ethnicity groups, persons aged 18–64 years, community health conditions, and persons assigned male sex at birth.

**What are the implications for public health practice?**

Route of administration of the first dose was not associated with lower overall 2-dose series completion rates. Continued efforts are needed to ensure persons at risk for mpox receive both recommended doses.

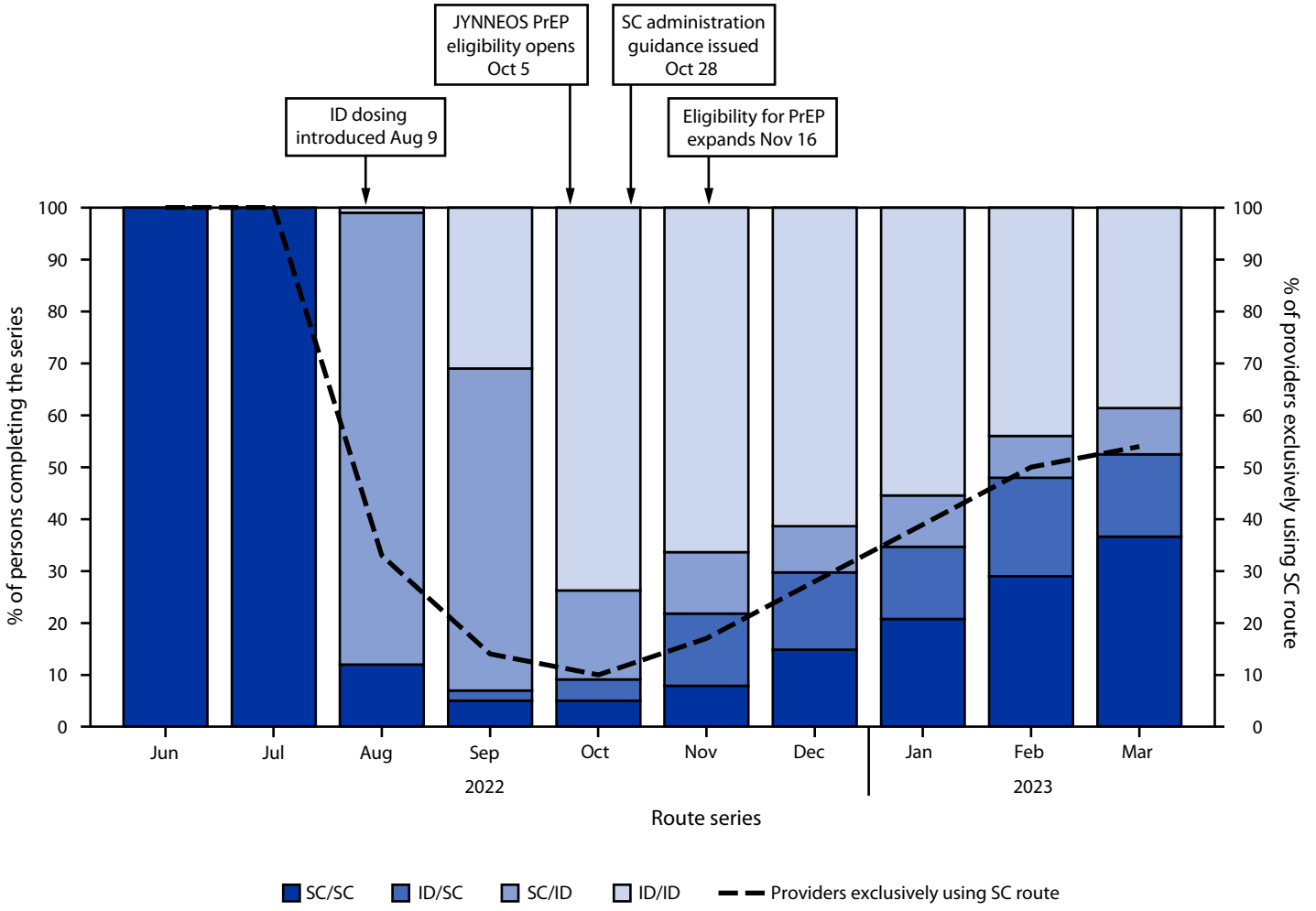
### Limitations

The findings in this report are subject to at least five limitations. First, the California Immunization Registry does not include data on behavioral risk; thus, certain risk factors that might have affected series completion could not be evaluated. Second, ID administration was introduced after many persons (i.e., those vaccinated during May 26–August 8, 2022) had already received their first dose. Among these early vaccine recipients, 75.1% completed the series; whether their series

¶¶ Before Food and Drug Administration authorization of ID administration of JYNNEOS vaccine on August 9, 2022, an additional 53,892 total doses were administered by the SC route.

*** A decreasing trend in second dose return rate among persons receiving their first dose subcutaneously during June–September 2022 has been observed and might coincide with declining mpox incidence and changing demographic characteristics of vaccine recipients.

**FIGURE 1. Route of JYNNEOS vaccine administration used by persons completing the 2-dose mpox vaccine series, by month of administration of the second dose and proportion of health care providers exclusively offering subcutaneous administration[*,†,§,¶] — California, June 2022–March 2023**




**Abbreviations:** CDPH = California Department of Public Health; FDA = Food and Drug Administration; ID = intradermal; PrEP = preexposure prophylaxis; SC = subcutaneous.

* After FDA's authorization of ID administration on August 9, 2022, CDPH immediately recommended that persons receive mpox vaccine via ID route, with exceptions for persons with history of keloid formation and persons aged <18 years. Previously, only SC administration of JYNNEOS vaccine was authorized.

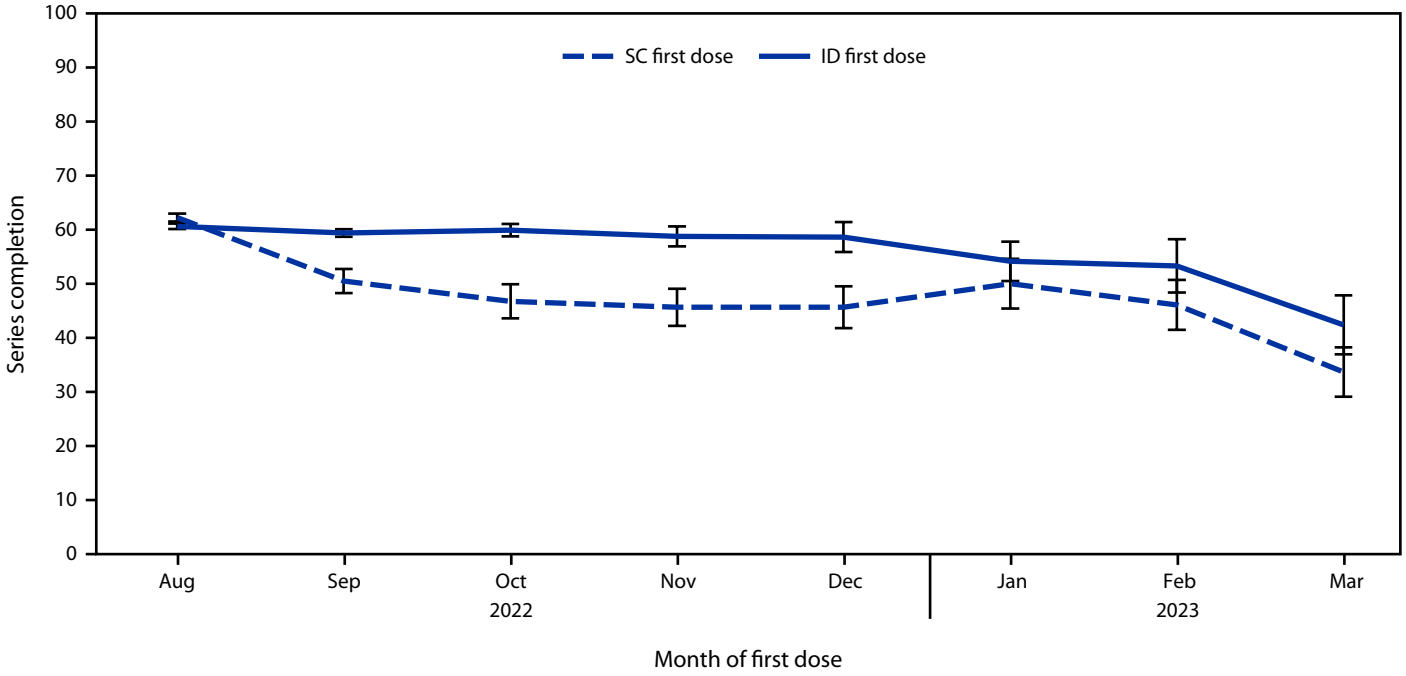
† On October 5, 2022, CDPH released guidance to local health jurisdictions and medical providers offering JYNNEOS vaccine to expand the pool of persons eligible to those at risk of infection (i.e., preexposure prophylaxis). Before this date, CDPH guidance recommended JYNNEOS be used to vaccinate persons exposed to *Monkeypox virus* (i.e., postexposure prophylaxis) or those with the greatest risk of infection, including persons who frequented venues where *Monkeypox virus* had been circulating (i.e., expanded postexposure prophylaxis).

§ As incidence of mpox decreased and supply became ample, CDPH issued guidance on October 28, 2022, permitting provider and patient discretion regarding route of administration, allowing for vaccine to be administered either intradermally or subcutaneously.

¶ On November 16, 2022, CDPH again issued guidance to expand vaccine eligibility to all persons who might be at risk for *Monkeypox virus* exposure and persons who request vaccination.

** The proportion of providers across California who were exclusively administering vaccine to patients via SC route began to steadily increase in November 2022. This change coincides with the proportion of persons who were completing the series (i.e., second dose) with a subcutaneously administered vaccine dose. The surveillance data used in this analysis cannot differentiate between persons who requested vaccine to be administered subcutaneously versus those who were seen by providers who offered vaccine exclusively to patients via SC route.

**FIGURE 2. Percentage of persons completing the 2-dose mpox vaccination series, by administration route of the first dose and month of administration of the first dose — California, August 9, 2022–March 31, 2023*,†**




**Abbreviations:** ID = intradermal; SC = subcutaneous.

* The percentage of all persons in any given month who completed the vaccine series ≥24 days after their first dose and received their second dose no later than April 30, 2023, stratified by the route of administration of the first dose. For example, 51% and 59% of persons whose first dose was administered by SC and ID route, respectively, in September 2022 completed the vaccine series no later than April 30, 2023.

† August includes August 9–31, 2022, when both ID and SC administration were authorized. August 1–8, 2022, was excluded.

completion rates would have been similar had their first dose been administered intradermally is not known. Third, declining case rates, starting in August 2022, might have led to reduced interest in mpox vaccination and could have affected self-perceived risk and the need for a second dose in certain populations. Fourth, these data only determine odds of completing the vaccination series and do not consider persons who chose not to initiate the series. Finally, California-specific data might not be generalizable to other jurisdictions.

### Implications for Public Health Practice

JYNNEOS vaccination series completion in California was not affected by route of first dose administration. Issues including access to vaccination, assessment of patient risk, and communication to disaffected populations by trusted messengers might be considered for future studies on disparities in vaccine acceptance. It remains important that health care providers discuss the benefits and risks associated with different administration routes with patients and ensure that patients understand the importance of completing the 2-dose JYNNEOS vaccination series. Similarly, contacting patients overdue for their second dose, particularly in groups with the lowest odds of series completion (e.g., persons aged 18–24 years), might help improve vaccination rates. Focused outreach, culturally sensitive messaging, and direct engagement by trusted messengers to groups disproportionately represented in mpox cases (e.g., Black and Hispanic persons) remain essential to ensuring that patients receive the benefit of a complete 2-dose series, and ultimately, to preventing future outbreaks.

## Acknowledgments

Jessica Byers, Saharai Caldera, Jennifer Capello, Gil Chavez, Jennie Chen, Cora Hoover, Lily Horng, Caterina Liu, Robert Snyder, Eric Tang, California Department of Public Health Mpox Response Team; Shua Chai, Seema Jain, Maria Volk, James Watt, California Department of Public Health.

Corresponding author: Tarek Salih, tarek.salih@cdph.ca.gov.

[1]California Department of Public Health; [2]Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

## References


1. Administration for Strategic Preparedness and Response. JYNNEOS vaccine distribution by jurisdiction: mpox national vaccine strategy. Washington, DC: US Department of Health and Human Services, Administration for Strategic Preparedness and Response; 2022. https://aspr.hhs.gov/SNS/Pages/JYNNEOS-Distribution.aspx
2. CDC. Mpox: technical report 4, United States, 2022. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/poxvirus/mpox/cases-data/technical-report/report-4.html
3. Food and Drug Administration. Monkeypox update: FDA authorizes emergency use of JYNNEOS vaccine to increase vaccine supply [Press release]. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2022. https://www.fda.gov/news-events/press-announcements/monkeypox-update-fda-authorizes-emergency-use-jynneos-vaccine-increase-vaccine-supply
4. Coop CA, Schaefer SM, England RW. Extensive keloid formation and progression after each vaccination. Hum Vaccin 2007;3:127–9. PMID:17643066 https://doi.org/10.4161/hv.3.4.4140
5. Maizlish N, Delaney T, Dowling H, et al. California Healthy Places Index: frames matter. Public Health Rep 2019;134:354–62. PMID:31095451 https://doi.org/10.1177/0033354919849882
6. Schnyder JL, De Pijper CA, Garcia Garrido HM, et al. Fractional dose of intradermal compared to intramuscular and subcutaneous vaccination—a systematic review and meta-analysis. Travel Med Infect Dis 2020;37:101868. PMID:32898704 https://doi.org/10.1016/j.tmaid.2020.101868
7. Dalton AF, Diallo AO, Chard AN, et al.; CDC Multijurisdictional Mpox Case Control Study Group. Estimated effectiveness of JYNNEOS vaccine in preventing mpox: a multijurisdictional case-control study—United States, August 19, 2022–March 31, 2023. MMWR Morb Mortal Wkly Rep 2023;72:553–8. PMID:37200229 https://doi.org/10.15585/mmwr.mm7220a3
8. Payne AB, Ray LC, Cole MM, et al. Reduced risk for mpox after receipt of 1 or 2 doses of JYNNEOS vaccine compared with risk among unvaccinated persons—43 U.S. jurisdictions, July 31–October 1, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1560–4. PMID:36480479 https://doi.org/10.15585/mmwr.mm7149a5
9. Frey SE, Goll JB, Beigel JH. Erythema and induration after mpox (JYNNEOS) vaccination revisited. N Engl J Med 2023;388:1432–5. PMID:36947462 https://doi.org/10.1056/NEJMc2215846
10. Duffy J, Marquez P, Moro P, et al. Safety monitoring of JYNNEOS vaccine during the 2022 mpox outbreak—United States, May 22–October 21, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1555–9. PMID:36480476 https://doi.org/10.15585/mmwr.mm7149a4

# Notes from the Field

## Cruise Ship Norovirus Outbreak Associated with Person-to-Person Transmission — United States Jurisdiction, January 2023

Carolyn A. Crisp, PhD[1,2]; Keisha A. Jenkins, DrPH[2]; Ian Dunn, MPH[3]; Andrew Kupper, MPH[2]; Jona Johnson, PhD[2]; Stefanie White, MPH[2]; Erin D. Moritz, PhD[2]; Luis O. Rodriguez, MS[2]

CDC's Vessel Sanitation Program (VSP) monitors cases of acute gastroenteritis (AGE) on board cruise ships traveling to a U.S. port (*1*). Persons who have ≥3 loose stools (or more than normal for that person) within a 24-hour period or vomiting plus one other sign or symptom (e.g., fever, diarrhea, bloody stool, myalgia, abdominal cramps, or headache) meet the case definition for reportable AGE (*2*). When the percentage of passengers or crew members with AGE is ≥2% and the ship is due to arrive at a U.S. port within 15 days, the Maritime Illness Disease Reporting System alerts VSP and activates an investigation (*1*). During the first week of January 2023, VSP was notified of cases of AGE affecting >2% of passengers on board a ship that had completed three voyages in Europe and was within 15 days of arriving at a U.S. port (voyage 4)* (Figure). Ship medical crew members submitted stool samples from ill travelers for testing. All samples tested positive for norovirus genotype II. While the ship was sailing to a U.S. port, VSP monitored AGE cases on board and reviewed case data. By mid-January, passenger AGE prevalence reached 3.4%.

### Investigation and Outcomes

During mid-January 2023, VSP's outbreak team boarded the ship to conduct an epidemiological and environmental investigation. The investigation focused on exposure sources and routes of transmission. Occupational and social behaviors of crew members were evaluated because the epidemic curve (Figure) suggested that the index case occurred in a crew member during voyage 1 who developed symptoms after embarking, likely leading to transmission among other crew members (voyage 2), and then to passengers (voyage 3). After the investigation, VSP continued to monitor the ship (voyage 5) until it left U.S. jurisdiction. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†

Among 410 reported cases during November 2022–January 2023 (voyages 1–5), 356 (87%) occurred in passengers and 54 (13%) in crew members. The index case likely occurred in a food and beverage crew member sailing on a crew-only voyage (voyage 1). In general, crew members with AGE reported to onboard medical personnel in a timely manner and were isolated until 48 hours after symptoms subsided. Crew member transmission was followed by passenger transmission on voyages 3, 4, and 5. Vomiting and diarrhea were the predominant symptoms among cases. Approximately 70% of crew members with AGE interacted with passengers (i.e., housekeeping and food and beverage services). VSP partnered with the United States Agency for Toxic Substances and Disease Registry's Geospatial Research, Analysis, and Services Program to create four-dimensional visual models of the ship. These models helped visualize continued norovirus transmission and sources of potential exposure (e.g., contaminated surfaces in cabins of persons with AGE and high-touch surfaces in common areas).

### Preliminary Conclusions and Actions

During this investigation, VSP used surveillance data and environmental and spatial analyses to improve field responses and quickly identify sources of norovirus exposure and transmission. Public health response to maritime AGE outbreaks involves robust and timely monitoring of AGE cases and collaborations with cruise companies. To prevent illness transmission across voyages, cruise ship personnel and travelers should always maintain proper hand hygiene and sanitation practices, and passengers and crew members should immediately isolate and report illness symptoms to the ship medical center (*3*). Cruise companies are encouraged to conduct frequent norovirus trainings for crew members, especially those with limited experience working with the cruise company (e.g., those who have served fewer than three contract terms).

#### Acknowledgments

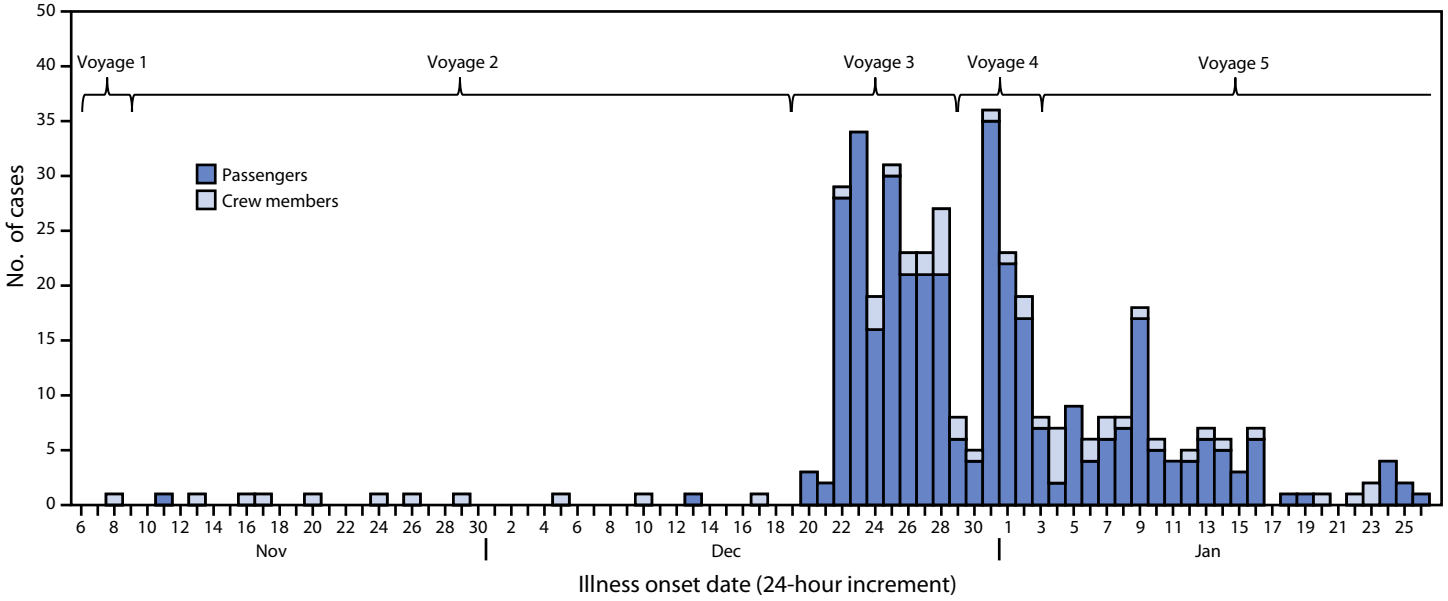
Crew members and representatives of the cruise line; CDC's National Calicivirus Laboratory; the Agency for Toxic Substances and Disease Registry's Geospatial Research, Analysis, and Services Program; Vessel Sanitation Program members; Water, Food, and Environmental Health Services Branch, National Center for Environmental Health, CDC.

Corresponding author: Carolyn A. Crisp, tqy2@cdc.gov.

* Voyage 1 (early November 2022), voyage 2 (early November–mid-December 2022), voyage 3 (mid-to-late December 2022), voyage 4 (late December 2022–early January 2023), and voyage 5 (began in early January and lasted ≥30 days); the ship made port in the United States during mid-January 2023.

† 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

**FIGURE. Cases of acute gastroenteritis (N = 410),* by illness onset date† — Cruise ship A, five voyages, November 2022–January 2023§**




* Cases occurred among 356 passengers and 54 crew members.
† Index case likely occurred on November 8, 2022.
§ Voyage 5 was a world voyage that lasted ≥30 days.

[1]Epidemic Intelligence Service, CDC; [2]Division of Environmental Health Science and Practice, National Center for Environmental Health, CDC; [3]Geospatial Research, Analysis, and Services Program, Agency for Toxic Substances and Disease Registry, Atlanta, Georgia.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

## References

1. Jenkins KA, Vaughan GH Jr, Rodriguez LO, Freeland A. Acute gastroenteritis on cruise ships—Maritime Illness Database and Reporting System, United States, 2006–2019. MMWR Surveill Summ 2021;70(No. SS-6):1–19. PMID:34555008 https://doi.org/10.15585/mmwr.ss7006a1
2. Freeland AL, Vaughan GH Jr, Banerjee SN. Acute gastroenteritis on cruise ships—United States, 2008–2014. MMWR Morb Mortal Wkly Rep 2016;65:1–5. PMID:26766396 https://doi.org/10.15585/mmwr.mm6501a1
3. CDC. Vessel sanitation program: illness prevention resources. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/nceh/vsp/healthy.htm

# Retraction and Republication

## Timing of Introduction of Complementary Foods — United States, 2016–2018

On November 27, 2020, *MMWR* published "Timing of Introduction of Complementary Foods — United States, 2016–2018" (*1*), which was based on data from the National Survey of Children's Health. On April 4, 2023, the National Survey of Children's Health released a technical document describing a processing error that occurred for data released between 2016 and 2021 (*2*). This processing error caused the reported time in months for breastfeeding, age of first formula, and introduction of solid foods to be incorrectly rounded down by 1 in most cases. Updated data files were released in conjunction with the technical document. *MMWR* was notified about this processing error on May 25, 2023. After discussion with the authors on June 16, *MMWR* published an Expression of Concern on June 30 (*3*), per International Committee of Medical Journal Editors and National Library of Medicine best practices (*4*,*5*).

The authors reanalyzed the updated data files and found that the results and interpretations changed from the original report. Therefore, the original report is retracted. In accordance with December 2017 guidance from the International Committee of Medical Journal Editors (*4*), *MMWR* is republishing the report (*6*). The republished report includes the original, retracted report with clearly marked corrections as supplementary materials.

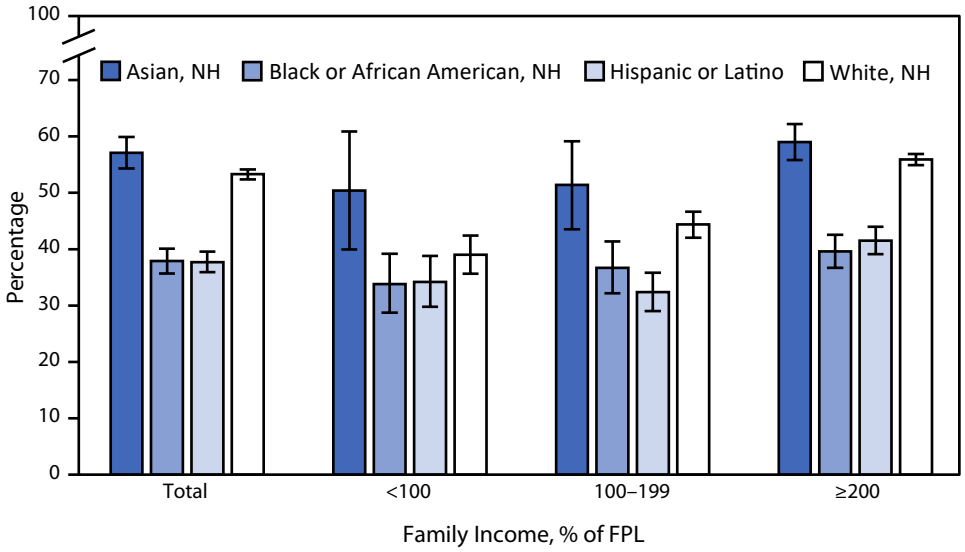
### References


1. Chiang KV, Hamner HC, Li R, Perrine CG. Timing of introduction of complementary foods—United States, 2016–2018. MMWR Morb Mortal Wkly Rep 2020;69:1787–91. PMID:33237894 https://doi.org/10.15585/mmwr.mm6947a4
2. US Census Bureau. National Survey of Children's Health: data revision for breastfeeding, formula and solid foods variables. Suitland, MD: US Department of Commerce, US Census Bureau; 2023. https://www2.census.gov/programs-surveys/nsch/technical-documentation/Data_Correction_for_BREASTFEDEND_FRSTFORMULA_and_FRSTSOLIDS.pdf
3. Expression of concern: timing of introduction of complementary foods—United States, 2016–2018. MMWR Morb Mortal Wkly Rep 2023;72:736. PMID:37384568 https://doi.org/10.15585/mmwr.mm7226a8
4. International Committee of Medical Journal Editors. Corrections, retractions, republications and version control. Vancouver, Canada: International Committee of Medical Journal Editors; 2017. https://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/corrections-and-version-control.html
5. National Library of Medicine. Errata, retractions, and other linked citations in PubMed. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Library of Medicine; 2018. https://www.nlm.nih.gov/bsd/policy/errata.html
6. Chiang KV, Hamner HC, Li R, Perrine CG. Timing of introduction of complementary foods—United States, 2016–2018. MMWR Morb Mortal Wkly Rep 2023;69:1969–74. https://www.cdc.gov/mmwr/volumes/69/wr/mm6953a1.htm?s_cid=mm6953a1_w. Corrected and republished from: MMWR Morb Mortal Wkly Rep 2020;69:1787–91. https://www.cdc.gov/mmwr/volumes/69/wr/mm6947a4.htm?s_cid=mm6947a4_w https://doi.org/10.15585/mmwr.mm6947a4

# QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage* of Adults Aged ≥18 Years who Received an Influenza Vaccination in the Past 12 Months,† by Race and Ethnicity§ and Family Income¶ — National Health Interview Survey, United States, 2021




**Abbreviations:** NH = non-Hispanic; FPL = federal poverty level.
* With 95% CIs indicated by error bars.
† Estimates are based on a sample of the civilian, noninstitutionalized U.S. population and are derived from a response to the question, "There are two types of flu vaccinations. One is a shot and the other is a spray, mist or drop in the nose. During the past 12 months, have you had a flu vaccination?"
§ Adults categorized as non-Hispanic White, non-Hispanic Asian, and non-Hispanic Black or African American indicated one race only; respondents had the option to select more than one racial group. Hispanic or Latino respondents might be of any race or combination of races; all racial groups are non-Hispanic.
¶ As a percentage of the FPL, which is based on family income and family size, using the U.S. Census Bureau's poverty thresholds. Family income was imputed when missing.

In 2021, non-Hispanic Asian (Asian) adults aged ≥18 years were the most likely to receive an influenza vaccination in the past 12 months (57.1%) followed by non-Hispanic White (White) (53.3%) adults; Hispanic or Latino (Hispanic) and non-Hispanic Black or African American (Black) adults were the least likely to receive an influenza vaccination (37.7% and 37.9%, respectively). Among adults with family incomes 100%–199% and ≥200% of FPL, Hispanic and Black adults were significantly less likely than Asian and White adults were to receive an influenza vaccination. Among adults with family incomes <100% of FPL, the differences among Hispanic, Black, and White adults were not statistically significant, but the percentage who had received an influenza vaccination in each of these groups was lower than the percentage among Asian adults. Vaccination coverage increased significantly with each increasing level of family income for White adults only.

**Source:** National Center for Health Statistics, National Health Interview Survey, 2021 data. https://www.cdc.gov/nchs/nhis.htm

**Reported by:** Michael E. Martinez, MPH, MHSA, memartinez@cdc.gov; Emily P. Terlizzi, MPH; Stephen J. Blumberg, PhD.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR* at *https://www.cdc.gov/mmwr/index.html*.

Readers who have difficulty accessing this PDF file may access the HTML file at https://www.cdc.gov/mmwr/index2023.html. Address all inquiries about the *MMWR* Series to Editor-in-Chief, *MMWR* Series, Mailstop V25-5, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to mmwrq@cdc.gov.



ISSN: 0149-2195 (Print)