Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 72 / No. 8
February 24, 2023

Interim Estimates of 2022–23 Seasonal Influenza Vaccine Effectiveness — Wisconsin, October 2022–February 2023

Huong Q. McLean, PhD[1]; Joshua G. Petrie, PhD[1]; Kayla E. Hanson, MPH[1]; Jennifer K. Meece, PhD[1]; Melissa A. Rolfes, PhD[2]; Gregg C. Sylvester, MD[3]; Gabriele Neumann, PhD[4]; Yoshihiro Kawaoka, DVM, PhD[4]; Edward A. Belongia, MD[1]

In the United States, 2022–23 influenza activity began earlier than usual, increasing in October 2022, and has been associated with high rates of hospitalizations among children* (*1*). Influenza A(H3N2) represented most influenza viruses detected and subtyped during this period, but A(H1N1) pdm09 viruses cocirculated as well. Most viruses characterized were in the same genetic subclade as and antigenically similar to the viruses included in the 2022–23 Northern Hemisphere influenza vaccine (*1*,*2*). Effectiveness of influenza vaccine varies by season, influenza virus subtype, and antigenic match with circulating viruses. This interim report used data from two concurrent studies conducted at Marshfield Clinic Health System (MCHS) in Wisconsin during October 23, 2022–February 10, 2023, to estimate influenza vaccine effectiveness (VE). Overall, VE was 54% against medically attended outpatient acute respiratory illness (ARI) associated with laboratory-confirmed influenza A among patients aged 6 months–64 years. In a community cohort of children and adolescents aged <18 years, VE was 71% against symptomatic laboratory-confirmed influenza A virus infection. These interim analyses indicate that influenza vaccination substantially reduced the risk for medically attended influenza among persons aged <65 years and for symptomatic influenza in children and adolescents. Annual influenza vaccination is the best strategy for preventing influenza and its complications. CDC recommends that health care providers continue to administer annual influenza vaccine to persons aged ≥6 months as long as influenza viruses are circulating (*2*).

VE against medically attended influenza was estimated using a test-negative case-control design. Patients aged 6 months–64 years were actively recruited during or after outpatient medical care for ARI (i.e., telehealth, primary care, urgent care, or emergency department), and before or during appointments for clinical testing for SARS-CoV-2 at selected MCHS facilities. Patients were eligible if they had a cough of ≤7 days' duration and had not taken an influenza antiviral medication. Participants completed a brief survey and provided a respiratory specimen for influenza and SARS-CoV-2 testing. Participants who received a positive real-time reverse transcription–polymerase chain reaction (RT-PCR) test result for SARS-CoV-2 were excluded from VE estimation. Participants

*Routine influenza surveillance in the United States indicated that influenza viruses began to circulate and outpatient visits for influenza-like illness were increased above seasonal baseline levels in epidemiologic week 40 (the week ending October 8, 2022).

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

were considered vaccinated if MCHS health records indicated receipt of seasonal influenza vaccine according to Advisory Committee on Immunization Practices (ACIP) recommendations ≥14 days before illness onset[†] (*2*). VE against influenza A viruses and against influenza A(H3N2) viruses was estimated as 100% x (1 – adjusted odds ratio [aOR]). The aOR is the ratio of the odds of vaccination among those who received a positive influenza test result (case-patients) to the odds of vaccination among those who received negative test results for influenza and SARS-CoV-2 (control-patients). Estimates were adjusted for age, month of illness onset, and self-reported presence of one or more higher-risk condition[§] using logistic regression.

VE against symptomatic influenza in children and adolescents was estimated from an ongoing, prospective, community-cohort study in central Wisconsin (*3*). Each week, participants (or their guardians) reported the absence or presence of specific symptoms during the previous 7 days. An anterior nasal swab was self- or guardian-collected for research testing when participants reported one or more of the following: fever, cough, loss of smell or taste, sore throat, muscle or body aches, shortness of breath, diarrhea, nasal congestion or runny nose, or nausea or vomiting. Influenza infection was defined as a positive result from research testing or a positive result from clinical testing (results extracted from MCHS health records). Unvaccinated person-time was defined as the time from October 23, 2022 (7 days before occurrence of the first influenza case), until receipt of seasonal influenza vaccine. Vaccinated person-time began ≥14 days after receipt of influenza vaccine (based on health records) according to ACIP recommendations. Person-time for the 13 days after receipt of vaccine was excluded from the analysis. Hazard ratios comparing the rate of influenza A virus infection among vaccinated and unvaccinated participants were estimated using Cox proportional hazards models with time-varying influenza vaccination status, age, the presence of one or more higher-risk condition, and COVID-19 vaccination status. VE was estimated as 100% x (1 – adjusted hazard ratio). Influenza and SARS-CoV-2 RT-PCR testing and genetic characterization of influenza-positive specimens for both studies were performed at MCHS research laboratory. Protocols for both studies were reviewed and approved by the Institutional Review Board at

[†] Persons aged ≥6 months are recommended to receive annual influenza vaccination. Certain children aged 6 months–8 years need 2 doses of influenza vaccine, depending on influenza vaccination history. Persons aged ≥9 years are recommended to receive 1 dose of influenza vaccine each year, regardless of influenza vaccination history. For the test-negative case-control design analysis, children aged 6 months–8 years were excluded if they needed 2 doses and, at the time of illness, they had received only 1 dose of influenza vaccine ≥14 days earlier, meaning that they were partially vaccinated. For the cohort study, children aged 6 months–8 years were excluded from the study at the time of the first dose if they needed 2 doses and they had received only 1 dose of influenza vaccine.

[§] Based on self-report of asthma or another chronic lung disease, cancer, diabetes, heart disease including high blood pressure, immunocompromising condition, kidney disease, liver disease, obesity, or pregnancy in the 12 months preceding the test-negative case-control study enrollment and self-report of asthma, immunocompromised state, serious heart condition, or other chronic lung disease for the community cohort study.

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].

MCHS and were conducted consistent with applicable federal law and CDC policy.[¶]

During December 2, 2022–February 10, 2023, a total of 545 children, adolescents, and adults with medically attended ARI were included in the test-negative design case-control study; 116 (21%) received a positive test result for influenza A virus, and none received a positive test result for influenza B virus. Among 115 (99%) influenza A virus subtypes determined, 29 (25%) were A(H1N1)pdm09 viruses, and 86 (75%) were A(H3N2) viruses (Table 1). All of the 43 characterized viruses were genetically similar to vaccine components; 34 A(H3N2) viruses belonged to subclade 2a.2 and nine A(H1N1)pdm09 viruses belonged to subclade 5a.2. The proportion of patients with influenza differed by month of illness onset. Among ARI patients, 186 (34%) had documentation of receipt of 2022–23 influenza vaccine; the percentage vaccinated differed by sex, higher-risk condition, and COVID-19 vaccination status. A

[¶] 45 C.F.R. part 46; 21 C.F.R. part 56.

TABLE 1. Selected characteristics of enrolled patients with medically attended acute respiratory illness and participants of a community cohort, by influenza test result and seasonal influenza vaccination status — Wisconsin, October 2022–February 2023

	Test-negative case-control study*				Community cohort study†		
		No. (%)				No. (%)	
Characteristic	No. of participants	Vaccinated[§]	Positive influenza test result	Negative influenza and SARS-CoV-2 test results	No. of participants	Vaccinated[¶]	Positive influenza test result
Total	**545**	**186 (34)**	**116 (21)**	**429 (79)**	**241**	**94 (39)**	**34 (14)**
Age group**							
6 mos–17 yrs	223	69 (31)	42 (19)	181 (81)	241	94 (39)	34 (14)
18–64 yrs	322	117 (36)	74 (23)	248 (77)	NA	NA	NA
Sex							
Female	318	127 (40)	65 (20)	253 (80)	116	49 (42)	17 (15)
Male	227	59 (26)	51 (22)	176 (78)	125	45 (36)	17 (14)
Race and ethnicity							
Hispanic or Latino	35	12 (34)	6 (17)	29 (83)	2	2 (100)	1 (50)
White, non-Hispanic	482	161 (33)	105 (22)	377 (78)	233	92 (39)	33 (14)
Other races, non-Hispanic[††]	28	13 (46)	5 (18)	23 (82)	6	0 (—)	0 (—)
Higher-risk conditions[§§]							
Yes	154	69 (45)	30 (19)	124 (81)	31	13 (42)	6 (19)
No	391	117 (30)	86 (22)	305 (78)	210	84 (39)	28 (13)
≥2 COVID-19 vaccine doses[¶¶]							
Yes	258	133 (52)	51 (20)	207 (80)	115	61 (53)	20 (17)
No	287	53 (18)	65 (23)	222 (77)	126	33 (26)	14 (11)
Month of illness onset							
Nov–Dec 2022	227	75 (33)	86 (38)	141 (62)	NA	NA	32 (94)
Jan–Feb 2023	318	111 (35)	30 (9)	288 (91)	NA	NA	2 (6)
Influenza test result							
Negative	429	160 (37)	NA	429 (100)	207***	88 (43)	NA
Influenza A–positive	116	26 (22)	116 (100)[†††]	NA	34	6 (18)	34 (100)[†††]
A(H3N2)	86	16 (19)	86 (74)[†††]	NA	29	5 (17)	29 (85)[†††]
A(H1N1)pdm09	29	10 (34)	29 (25)[†††]	NA	1	0 (—)	1 (3)[†††]
A: unknown subtype	1	0 (—)	1 (1)[†††]	NA	4	1 (25)	4 (12)[†††]

Abbreviations: ACIP = Advisory Committee on Immunization Practices; ccIIV4 = cell culture–based vaccine; MCHS = Marshfield Clinic Health System; NA = not applicable.

* A total of 109 participants received a positive test result for SARS-CoV-2 virus infection and were excluded. Participants with uncertain influenza vaccination status (12), with receipt of vaccine ≤13 days before illness (four), or who were aged <9 years and partially vaccinated (seven) were excluded from analysis.

† One child was partially vaccinated according to ACIP recommendations before the analysis period and was excluded.

§ Defined as receipt of any seasonal influenza vaccine according to ACIP recommendations ≥14 days before illness onset based on MCHS vaccination records. Most vaccinated participants (84%) received ccIIV4.

¶ Defined as receipt of seasonal influenza vaccine according to ACIP recommendations ≥14 days before influenza infection or before the end of follow-up based on MCHS vaccination records. Most vaccinated participants (84%) received ccIIV4.

** Age on the date of the clinical encounter for acute respiratory illness for the test-negative case-control study and as of September 1, 2022, for the community cohort study.

†† Includes persons who are American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, and multiracial.

§§ Based on self-report of asthma or another chronic lung disease, cancer, diabetes, heart disease including high blood pressure, immunocompromising condition, kidney disease, liver disease, obesity, or pregnancy during the 12 months preceding the test-negative case-control study enrollment and self-report of asthma, immunocompromised state, serious heart condition, or other chronic lung disease for the community cohort study.

¶¶ Based on self-report for the test-negative case-control study and health records for the community cohort study.

*** Includes cohort participants with acute respiratory illness who received negative influenza test results, those with no reported acute respiratory illness, and three persons with influenza infections occurring within 14 days after vaccination who were excluded from the study at the time of vaccination.

††† Column percentages.

TABLE 2. Estimated 2022–23 influenza vaccine effectiveness* — Wisconsin, October 2022–February 2023

	Test-negative case-control study, persons aged 6 mos–64 yrs					Community cohort study, persons aged 1–17 yrs				
	Positive influenza test result		Negative influenza and SARS-CoV-2 test results			Vaccinated		Not vaccinated		
Influenza type	Total	No. of persons vaccinated (%)	Total	No. of persons vaccinated (%)	Adjusted VE,* % (95% CI)	No. of person-days	No. of positive influenza test results	No. of person-days	No. of positive influenza test results	Adjusted VE,† % (95% CI)
A	**116**	26 (22)	**429**	160 (37)	54 (23–73)	7,292	6	15,678	28	71 (31–90)
A(H3N2)	**86**	16 (19)	**429**	160 (37)	60 (25–79)	NE	NE	NE	NE	NE

Abbreviations: aOR = adjusted odds ratio; NE = not estimated; VE = vaccine effectiveness.

* VE was estimated using the test-negative design as 100% x (1 − aOR) in which aOR represents ratio of odds of being vaccinated among influenza-positive cases to odds of being vaccinated among influenza-negative and SARS-CoV-2–negative controls; odds ratios were estimated using logistic regression with adjustment for age, month of illness onset, and presence of one or more higher-risk condition (self-report of asthma or another chronic lung disease, cancer, diabetes, heart disease including high blood pressure, immunocompromising condition, kidney disease, liver disease, obesity, or pregnancy in the 12 months preceding enrollment). https://www.cdc.gov/flu/vaccines-work/us-flu-ve-network.htm

† VE was estimated from a Cox proportional hazards model with time-varying influenza vaccination status, age, presence of at least one higher-risk condition (self-report of asthma, immunocompromised state, serious heart condition, or other chronic lung disease), and receipt of ≥2 COVID-19 vaccine doses before the analysis period.

large majority of vaccinated participants (84%) received cell culture–based vaccine (ccIIV4). Among the 116 participants who received a positive influenza test result, 26 (22%) received the 2022–23 seasonal influenza vaccine, compared with 160 (37%) of 429 participants who received negative test results for influenza and SARS-CoV-2 (Table 2). The overall adjusted VE against outpatient medically attended ARI associated with influenza A was 54% and 60% against influenza A(H3N2) viruses.

Among 241 community cohort participants aged 1–17 years, 94 (39%) had documented receipt of the 2022–23 influenza vaccine (Table 1); 84% received ccIIV4. Among community cohort participants who received the 2022–23 influenza vaccine, 65% had documentation of receipt of ≥2 COVID-19 vaccine doses. During October 23, 2022–February 10, 2023, 37 (15%) participants received a positive test result for influenza A virus infection; however, three of these occurred ≤14 days after influenza vaccination and were excluded from the study at the time of vaccination. Among the remaining 34 influenza virus infections included in the analysis, 29 were caused by A(H3N2),** one by A(H1N1)pdm09, and four by influenza A viruses with unknown subtype. Six children (18%) with influenza A had received the 2022–23 seasonal influenza vaccine. Among 15,678 unvaccinated person-days, 28 influenza A virus infections occurred (incidence = 1.79 per 1,000 person-days), and among 7,292 vaccinated person-days, six influenza A virus infections occurred (incidence = 0.82 per 1,000 person-days) (Table 2). VE against symptomatic influenza A virus infection was 71%.

Discussion

Influenza activity for the 2022–23 winter season increased earlier than usual, with high rates of influenza-associated hospitalizations among children (*2*). The interim estimates of 2022–23 influenza VE from two concurrent studies in Wisconsin suggest that the current season's influenza vaccines are providing substantial protection against influenza. These findings are consistent with estimates reported in the Southern Hemisphere for the 2022 season and Canada for the current season, where similar viruses predominated (*4*,*5*). However, influenza vaccination coverage in the United States this season has been lower than during pre–COVID-19 pandemic seasons, particularly among children, pregnant women, and in rural areas (*6*). Increased vaccination coverage is needed to realize the full potential of seasonal influenza vaccines.

The interim estimates reported reflect early season VE and might differ from end-of-season VE estimates with additional enrollments, or if a change in circulating viruses would occur later in the season. Through the week ending February 4, 2023, influenza activity was low nationally. However, CDC continues to monitor influenza activity through routine surveillance for any indications that activity might increase again; two waves of influenza activity have occurred during many previous seasons (*7*). Seasonal influenza vaccines protect against influenza A and B viruses, both of which might continue or begin to circulate later in the season, resulting in potentially serious complications.

The findings in this report are subject to at least four limitations. First, the studies were restricted to participants from a single geographic area (central Wisconsin). However, viruses that predominated in the study population were similar to those that predominated across the United States (*1*). Second, older adults aged ≥65 years were excluded from the test-negative study. Age-specific VE estimates against influenza virus infection caused by A(H3N2) viruses are generally lower for older adults (*8*). Third, sample sizes were small for the interim analysis, which limited the precision of VE estimates, and VE against illness associated with A(H1N1)pdm09 virus infections

** Six A(H3N2) viruses from the community cohort study were genetically characterized and belonged to subclade 2a.2.

Summary

What is already known about this topic?

Effectiveness of influenza vaccine varies by season, influenza virus subtype, and antigenic match with circulating viruses.

What is added by this report?

Data from two concurrent studies in Wisconsin found that effectiveness of the 2022–23 influenza vaccine was 54% for preventing medically attended influenza A infection among persons aged <65 years and 71% for preventing symptomatic influenza A illness among children and adolescents aged <18 years.

What are the implications for public health practice?

The 2022–23 influenza vaccine provides substantial protection against circulating influenza A viruses and remains the best way to protect against influenza. Influenza vaccination is recommended as long as influenza viruses are circulating.

and age-specific estimates could not be determined. Finally, confounding and bias are of concern with observational studies; however, estimates were comparable across two study designs, and the test-negative study design yields valid estimates of influenza VE in most scenarios (*9*).

Annual influenza vaccination is the best strategy for preventing influenza and its complications. During the 2022–23 season to date, influenza A viruses that predominated are genetically and antigenically similar to current vaccine components. Interim VE estimates from this report indicate that the current season's influenza vaccine substantially reduces the risk for medical visits among persons aged 6 months–64 years and symptomatic illness associated with influenza A virus infection among children and adolescents aged <18 years. Influenza vaccination is recommended for all persons aged ≥6 months for as long as influenza viruses are circulating in the community.

Acknowledgments

Brooklyn Arbs, Liz Armagost, Saydee Benz, Adam Bissonnette, Riley Bonifer, Bobbi Bradley, Michaela Braun, Brianna Breu, Gina Burbey, Corey-Beth Cielinski, Leila Deering, Christian Delgadillo, Heather Dirkx, Roxy Eibergen, Alex Ermeling, Kelsey Ewert, Kallie Falteisek, Rachel Fernandez, Hope Florence, Sandy Freeman, Wayne Frome, Tammy Gault, Emily Gruenling, Sherri Guzinski, Angela Harless, Mitch Hertel, Garrett Heuer, Lee Jepsen, Julie Karl, Burney Kieke, Jennifer King, Stephanie Kohl, Sarah Kohn, Diane Kohnhorst, Sarah Kopitzke, Tamara Kronenwetter Koepel, Erik Kronholm, Kate Lassa, Thao Le, Alaura Lemieux, Carrie Marcis, Megan Maronde, Dave McClure, Isaac McCready, Andrea McGaver, Karen McGreevey, Nidhi Mehta, Laura Michalik, Vicki Moon, Jennifer Moran, Mike Owens, DeeAnn Polacek, Martha Presson, Nicole Price, Maxine Racanelli, Chris Rayburn, Miriah Rotar, Carla Rottscheit, Jesse Rozmarynowski, Jackie Salzwedel, Juan Saucedo, Kelly Scheffen, Alex Slenczka, Jacob Solis, Elisha Stefanski, Melissa Strupp, Lyndsay Watkins, Marshfield Clinic Health System; providers, managers, and clinical staff members, Marshfield Clinic Lake Hallie Center, Marshfield Clinic Wausau Center, Marshfield Medical Center-Eau Claire, Marshfield Medical Center-Marshfield, and Marshfield Medical Center-Weston; Karita Ambrose, Ashesh Gandhi, Mendel Haag, CSL Seqirus; David Pattinson, University of Wisconsin-Madison; Jessie Chung, Brendan Flannery, CDC.

Corresponding author: Huong Q. McLean, mclean.huong@marshfieldresearch.org.

[1]Marshfield Clinic Research Institute, Marshfield, Wisconsin; [2]Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; [3]CSL Seqirus, Summit, New Jersey; [4]Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Huong Q. McLean, Joshua G. Petrie, Jennifer K. Meece, Edward A. Belongia, and Kayla E. Hanson report institutional support from CSL Seqirus. Gregg C. Sylvester is an employee of CSL Seqirus. Yoshihiro Kawaoka reports institutional funding from Fujifilm Toyama Chemical Company, LTD, Shionogi & Company, LTD, Daiichi Sankyo Pharmaceutical, Otsuka Pharmaceutical, KM Biologics, Kyoritsu Seiyaku, Fuji Rebio, Tauns Laboratories, Inc., and FluGen. Yoshihiro Kawaoka and Gabriele Neumann report status as a cofounder and stockholder of FluGen. No other potential conflicts of interest were disclosed.

References

1. CDC. Influenza (flu): weekly U.S. influenza surveillance report. Atlanta, GA: US Department of Health and Human Services, CDC; 2023. Accessed February 14, 2023. https://www.cdc.gov/flu/weekly/index.htm
2. Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2022–23 influenza season. MMWR Recomm Rep 2022;71(No. RR-1):1–28. PMID:36006864 https://doi.org/10.15585/mmwr.rr7101a1
3. McLean HQ, McClure DL, King JP, et al. mRNA COVID-19 vaccine effectiveness against SARS-CoV-2 infection in a prospective community cohort, rural Wisconsin, November 2020 to December 2021. Influenza Other Respir Viruses 2022;16:607–12. PMID:35178857 https://doi.org/10.1111/irv.12970
4. Olivares Barraza MF, Fasce RA, Nogareda F, et al. Influenza incidence and vaccine effectiveness during the southern hemisphere influenza season—Chile, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1353–8. PMID:36301733 https://doi.org/10.15585/mmwr.mm7143a1
5. Skowronski DM, Chuang ES, Sabaiduc S, et al. Vaccine effectiveness estimates from an early-season influenza A(H3N2) epidemic, including unique genetic diversity with reassortment, Canada, 2022/23. Euro Surveill 2023;28:2300043. PMID:36729117 https://doi.org/10.2807/1560-7917.ES.2023.28.5.2300043
6. CDC. Influenza (flu): weekly flu vaccination dashboard. Atlanta, GA: US Department of Health and Human Services, CDC; 2023. Accessed February 14, 2023. https://www.cdc.gov/flu/fluvaxview/dashboard/vaccination-dashboard.html
7. Merced-Morales A, Daly P, Abd Elal AI, et al. Influenza activity and composition of the 2022–23 influenza vaccine—United States, 2021–22 season. MMWR Morb Mortal Wkly Rep 2022;71:913–9. PMID:35862284 https://doi.org/10.15585/mmwr.mm7129a1
8. Belongia EA, McLean HQ. Influenza vaccine effectiveness: defining the H3N2 problem. Clin Infect Dis 2019;69:1817–23. PMID:31102401 https://doi.org/10.1093/cid/ciz411
9. Haber M, An Q, Foppa IM, Shay DK, Ferdinands JM, Orenstein WA. A probability model for evaluating the bias and precision of influenza vaccine effectiveness estimates from case-control studies. Epidemiol Infect 2015;143:1417–26. PMID:25147970 https://doi.org/10.1017/S0950268814002179

Effect of Predeparture Testing on Postarrival SARS-CoV-2–Positive Test Results Among International Travelers — CDC Traveler-Based Genomic Surveillance Program, Four U.S. Airports, March–September 2022

Stephen M. Bart, PhD[1]; Teresa C. Smith, MPH[1]; Sarah Anne J. Guagliardo, PhD[1]; Allison Taylor Walker, PhD[1]; Benjamin H. Rome, MBA[2]; Siyao Lisa Li[2]; Thomas W. S. Aichele, MBA[2]; Rob Stein[3]; Ezra T. Ernst[3]; Robert C. Morfino, MBA[2]; Martin S. Cetron, MD[1]; Cindy R. Friedman, MD[1]

Beginning December 6, 2021, all international air passengers boarding flights to the United States were required to show either a negative result from a SARS-CoV-2 viral test taken ≤1 day before departure or proof of recovery from COVID-19 within the preceding 90 days (*1*). As of June 12, 2022, predeparture testing was no longer mandatory but remained recommended by CDC (*2*,*3*). Various modeling studies have estimated that predeparture testing the day before or the day of air travel reduces transmission or importation of SARS-CoV-2 by 31%–76% (*4*–*7*). Postarrival SARS-CoV-2 pooled testing data from CDC's Traveler-based Genomic Surveillance program were used to compare SARS-CoV-2 test results among volunteer travelers arriving at four U.S. airports during two 12-week periods: March 20–June 11, 2022, when predeparture testing was required, and June 12–September 3, 2022, when predeparture testing was not required. In a multivariable logistic regression model, pooled nasal swab specimens collected during March 20–June 11 were 52% less likely to be positive for SARS-CoV-2 than were those collected during June 12–September 3, after adjusting for COVID-19 incidence in the flight's country of origin, sample pool size, and collection airport (adjusted odds ratio [aOR] = 0.48, 95% CI = 0.39–0.58) (p<0.001). These findings support predeparture testing as a tool for reducing travel-associated SARS-CoV-2 transmission and provide important real-world evidence that can guide decisions for future outbreaks and pandemics.

The Traveler-based Genomic Surveillance Program conducts surveillance of travelers at international airports for early detection of new and emerging SARS-CoV-2 variants and to fill gaps in international surveillance (*8*). International travelers aged ≥18 years arriving at airports in Newark, New Jersey (Newark Liberty Airport); New York, New York (John F. Kennedy International Airport); Atlanta, Georgia (Hartsfield-Jackson Atlanta International Airport); and San Francisco, California (San Francisco International Airport), who volunteered to participate provided a postarrival lower nasal swab sample in the airport (*8*). After providing signed consent, participants completed a standardized survey that included questions regarding demographic characteristics, flight country of origin, and whether predeparture testing had occurred and, if so, whether an antigen or molecular test had been performed. In the airport, dry nasal swab samples were pooled (5–25 samples per pool) by the flight country of origin. Pooled samples were sent to a laboratory in the Ginkgo Bioworks laboratory network for SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) testing (*8*).

Postarrival RT-PCR testing results during March 20–June 11, when the predeparture test requirement was in effect, were compared with those during June 12–September 3, when predeparture testing was voluntary. To account for worldwide differences in COVID-19 incidence, pooled test results were matched with daily 7-day average country-level COVID-19 incidence (cases per 100,000 population) from the World Health Organization* based on pool collection date and the flight country of origin. To account for reporting differences by country, normalized incidence was estimated by dividing the 7-day average COVID-19 incidence on the date of pool collection for the flight country of origin by the maximum 7-day average daily incidence for that country during March 20–September 3, then multiplying by 100.

To identify factors associated with positive postarrival SARS-CoV-2 pooled test results, bivariate comparisons and univariable logistic regression were performed. Factors with significant univariable associations (p<0.05) were incorporated into a multivariable mixed effects logistic regression model that included collection airport as a random effect. Alternative periods (during the 4–8 weeks preceding June 12 and those on or after that date) were considered in sensitivity analyses. Analyses were conducted in R (version 4.0.2; R Foundation). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†

During March 20–September 3, 2022, a total of 28,056 arriving travelers from 24 countries received testing for SARS-CoV-2, yielding 3,049 pooled samples with a median of eight participant samples per pool (range = 5–25). During March 20–June 11, among 16,668 Traveler-based Genomic Surveillance participants, 13,190 (79.1%) reported having had a predeparture test; during June 12–September 3, this percentage declined by 80% to 1,786 of 11,123 (16.1%) participants reporting having had a predeparture test (Figure 1). Among

* https://covid19.who.int/data

† 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.

14,976 participants who reported the type of predeparture test, 10,349 (69.1%) reported receiving an antigen test.

During the analysis period, 691 (22.7%) of 3,049 sample pools tested positive for SARS-CoV-2 by RT-PCR. The percentage of positive pools increased 56% from 17.9% (291 of 1,622) during March 20–June 11, to 28.0% (400 of 1,427) during June 12–September 3 (p<0.001) (Figure 1) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/124584). The increase in the percentage of positive postarrival test results between March 20–June 11 and June 12–September 3 occurred across countries, collection airports, incidences, and pool sizes and was apparent in both bivariate analyses and univariable logistic regression. Participants during each period were similar in age and gender; however, during the period beginning June 12, fewer participants reported U.S. residency (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/124585).

Multivariable model results showed that pools of samples collected during March 20–June 11 (when predeparture testing was mandatory) were 52% less likely to be positive than were those when predeparture testing was voluntary (aOR = 0.48, 95% CI = 0.39–0.58) (p<0.001), after adjusting for COVID-19 incidence in the flight's country of origin, pool size, and collection airport (Table). COVID-19 incidence in the flight's country of origin and pool size also remained significant predictors of positive pooled test results in the multivariable model.

Sensitivity analyses were conducted by repeating the regression models using 4- and 8-week periods around June 12 and adjusting for the same covariates. Lower odds of positive test results before June 12 remained significant (4-week periods: aOR = 0.65, 95% CI = 0.44–0.96 [p<0.001]; 8-week periods: aOR = 0.48, 95% CI = 0.37–0.63 [p<0.001]) (Figure 2) (Supplementary Table 3, https://stacks.cdc.gov/view/cdc/124586).

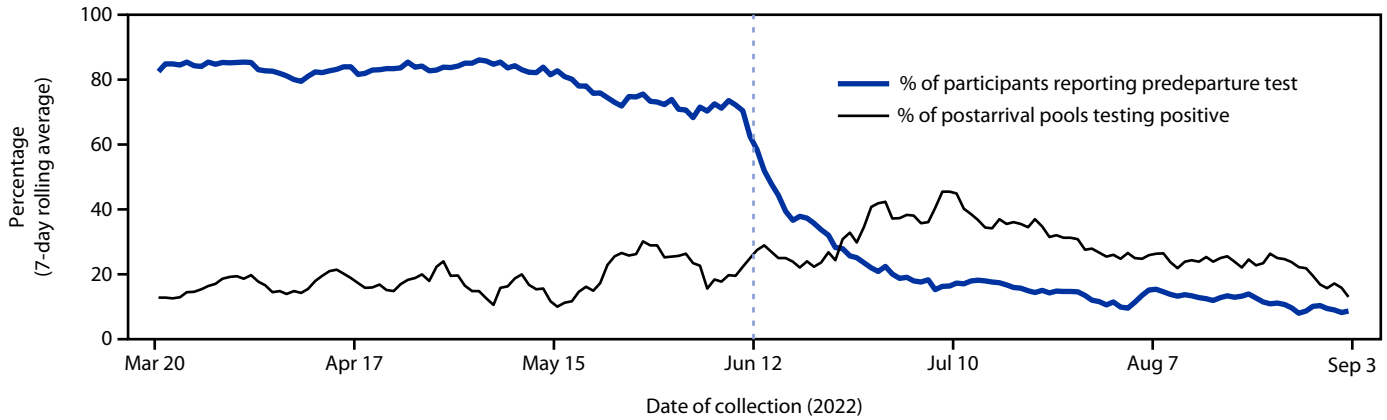
Discussion

Postarrival SARS-CoV-2 test results were 52% less likely to be positive when the predeparture COVID-19 testing requirement was in effect than during the 12-week period after it was discontinued; this finding was true even when controlling for other factors such as incidence in the flight's country of origin and pool size. These findings, based on observed, real-world traveler data, support the value of predeparture testing as a tool for reducing SARS-CoV-2 transmission associated with travel and were consistent with estimates from previous modeling studies (*4*–*7*).

Sensitivity analyses using shorter time frames around removal of the predeparture testing requirement produced similar findings. Although still statistically significant, the magnitude of this effect decreased when 4-week windows were considered, possibly because of smaller sample sizes during the shorter time frame or higher rates of voluntary predeparture testing during the 4 weeks after the removal of the predeparture test requirement on June 12.

The findings in this report are subject to at least five limitations. First, because participation in the Traveler-based Genomic Surveillance Program is voluntary, results might not be representative of all international travelers; however, any participation bias was likely consistent across both periods. Second, because of the pooled sampling and testing strategy employed, trends among individual participants could not be assessed. Third, incidence data were matched with pooled test results based on a flight's country of origin, and it is possible that participants began their itinerary in a different country and later connected to the U.S.-bound flight. Fourth, as testing rates decline globally, reported incidence data might not fully reflect actual COVID-19 risk in a given country (*9*). Finally,

FIGURE 1. Percentages (7-day rolling average) of participants reporting a predeparture SARS-CoV-2 test* and pools† testing positive for SARS-CoV-2§ during postarrival testing — Traveler-based Genomic Surveillance Program, United States, March 20–September 3, 2022



* Molecular or antigen test; a predeparture SARS-CoV-2 test was required for most travelers entering the United States before June 12, 2022.
† In the airport, dry nasal swab samples from participants were pooled (5–25 samples per pool) by the flight country of origin.
§ By reverse transcription–polymerase chain reaction.

TABLE. Unadjusted and adjusted mixed effects logistic regression results for postarrival pooled SARS-CoV-2 test results during 12-week windows before and after June 12, 2022 — Traveler-based Genomic Surveillance Program, four U.S. airports,* March 20–September 3, 2022

Variable (referent group)	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Time window (Jun 12–Sep 3)				
Mar 20–Jun 11	0.56 (0.47–0.67)	<0.001	0.48 (0.39–0.58)	<0.001
Normalized incidence† (0–20)				
20–40	1.4 (1.1–1.8)	0.004	1.3 (1.0–1.6)	0.052
40–60	2.0 (1.5–2.6)	<0.001	1.8 (1.3–2.3)	<0.001
60–80	2.2 (1.6–3.1)	<0.001	2.1 (1.5–3.0)	<0.001
80–100	2.3 (1.8–3.0)	<0.001	2.2 (1.7–2.8)	<0.001
Pool size (5–9 participants)				
10–14	1.4 (1.1–1.6)	0.002	1.5 (1.2–1.9)	<0.001
≥15	1.4 (1.1–1.8)	0.004	2.6 (1.9–3.4)	<0.001

Abbreviation: OR = odds ratio.

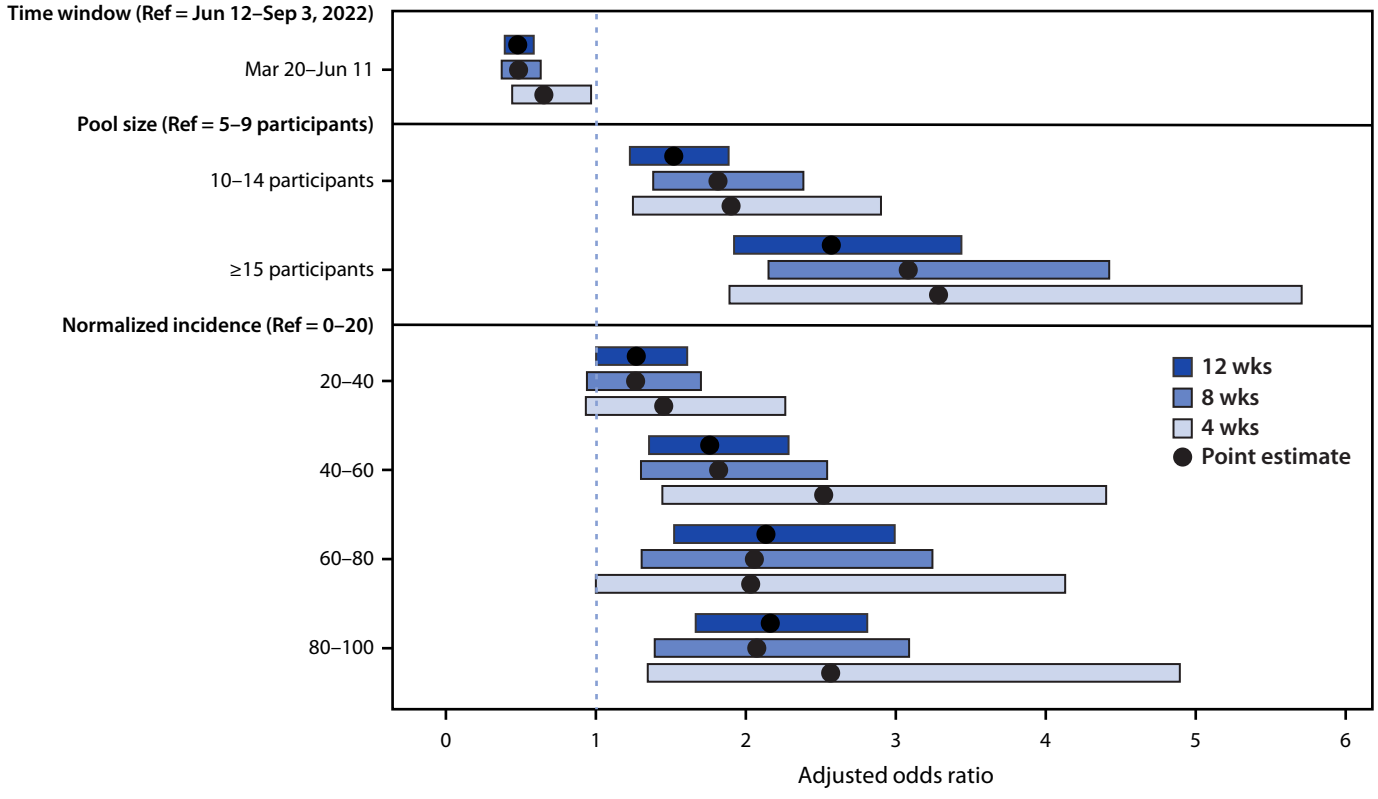
* John F. Kennedy International Airport, New York, New York; Newark Liberty International Airport, Newark, New Jersey; Hartsfield-Jackson Atlanta International Airport, Atlanta, Georgia; and San Francisco International Airport, San Francisco, California.

† Incidence was normalized by dividing the 7-day average COVID-19 incidence (cases per 100,000 population) for the flight origin country on the date of collection by the maximum 7-day average daily incidence for that country during the analysis period and multiplying by 100.

not all travelers during March 20–June 11 had a predeparture test, such as those who recently had COVID-19 (*1*), and some travelers during June 12–September 3 voluntarily chose to test, potentially diminishing this estimate of the effect of predeparture testing.

Reducing the number of persons traveling while infected with SARS-CoV-2 through predeparture testing could reduce air travel–associated transmission in airports, aircraft, and destination communities. CDC continues to recommend testing before and after international travel (*3*). Along with other strategies, including isolation of persons with confirmed or suspected COVID-19 and masking, testing before international travel is an important element of a multipronged COVID-19 prevention strategy. In December 2022, results from this analysis were used alongside other evidence to support a predeparture test requirement for travelers boarding flights to the United States from China to slow importation of SARS-CoV-2 during a surge in COVID-19 cases there (*10*). These findings provide important real-world evidence supporting the effectiveness of predeparture testing that can guide decisions for future outbreaks and pandemics.

FIGURE 2. Comparison of mixed effects models*,† for pooled SARS-CoV-2 test results across different time windows before and after June 12, 2022 — Traveler-based Genomic Surveillance Program, United States, March 20–September 3, 2022



Abbreviation: Ref = referent group.

* Adjusted odds ratio point estimates are relative to each Ref with 95% CIs.

† Incidence was normalized by dividing the 7-day average COVID-19 incidence (cases per 100,000 population) for the flight origin country on the date of collection by the maximum 7-day average daily incidence for that country during the analysis period and multiplying by 100.

Summary

What is already known about this topic?

During December 6, 2021–June 11, 2022, SARS-CoV-2 testing ≤1 day before departure or proof of recent COVID-19 recovery were required for passengers boarding U.S.-bound flights. Mathematical models have estimated predeparture testing effectiveness in preventing travel-associated transmission.

What is added by this report?

CDC's Traveler-based Genomic Surveillance Program collects postarrival nasal swabs for SARS-CoV-2 testing from volunteering international air travelers. Among 3,049 pooled (28,056 individual) samples collected during March 20–September 3, 2022, the predeparture testing requirement was associated with 52% lower postarrival SARS-CoV-2 positivity.

What are the implications for public health practice?

Predeparture testing can reduce SARS-CoV-2 transmission risk during or after travel by reducing the number of infectious travelers. These results can help guide decisions for future outbreaks.

Acknowledgments

Traveler-based Genomic Surveillance Program participants; Olubunmi Akinkugbe, Nicole Cohen, Susan Dwyer, Jonathan Georges, Samantha Loh, Mary Luc, Duncan MacCannell, Sarah Meehan, Ian Ruskey, Erica Sison, Quarantine and Border Health Services Branch, CDC; Andrew Rothstein, Cherish Weiler, Ginkgo Bioworks; XpresCheck; airport management and staff members.

Corresponding author: Stephen M. Bart, sbart@cdc.gov.

[1]Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [2]Ginkgo Bioworks, Inc., Boston, Massachusetts; [3]XpresCheck, XWELL, New York, New York.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Benjamin H. Rome, Siyao Lisa Li, Thomas W.S. Aichele, and Robert C. Morfino are employed by Ginkgo Bioworks and own Ginkgo Bioworks employee stocks or restricted stock units (RSU) grants. Ezra T. Ernst is employed by XWELL and owns XWELL employee stocks or RSU grants. No other potential conflicts of interest were disclosed.

References

1. CDC. Requirements for negative pre-departure COVID-19 test result or documentation of recovery from COVID-19 for all airline or other aircraft passengers arriving into the United States from any foreign country. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. https://www.govinfo.gov/content/pkg/FR-2021-12-07/pdf/2021-26603.pdf
2. CDC. Rescinding requirement for negative pre-departure COVID-19 test result or documentation of recovery from COVID-19 for all airline or other aircraft passengers arriving into the United States from any foreign country. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.govinfo.gov/content/pkg/FR-2022-06-15/pdf/2022-13022.pdf
3. CDC. International travel to and from the United States. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel-during-covid19.html
4. Kiang MV, Chin ET, Huynh BQ, et al. Routine asymptomatic testing strategies for airline travel during the COVID-19 pandemic: a simulation study. Lancet Infect Dis 2021;21:929–38.
5. Johansson MA, Wolford H, Paul P, et al. Reducing travel-related SARS-CoV-2 transmission with layered mitigation measures: symptom monitoring, quarantine, and testing. BMC Med 2021;19:94.
6. Clifford S, Quilty BJ, Russell TW, et al.; Centre for Mathematical Modelling of Infectious Diseases (CMMID) COVID-19 Working Group. Strategies to reduce the risk of SARS-CoV-2 importation from international travellers: modelling estimations for the United Kingdom, July 2020. Euro Surveill 2021;26:2001440.
7. Wells CR, Gokcebel S, Pandey A, Galvani AP, Townsend JP. Testing for COVID-19 is much more effective when performed immediately prior to social mixing. Int J Public Health 2022;67:1604659.
8. Wegrzyn RD, Appiah GD, Morfino R, et al. Early detection of SARS-CoV-2 variants using traveler-based genomic surveillance at four U.S. airports, September 2021–January 2022. Clin Infect Dis 2022;76:e540–3.
9. World Health Organization. WHO ACT-Accelerator Facilitation Council Working Group report on diagnostics and therapeutics. Geneva, Switzerland: World Health Organization; 2022. Accessed November 4, 2022. https://www.who.int/docs/default-source/coronaviruse/act-accelerator/council-working-group-on-diagnostics-and-therapeutics-v4.pdf?sfvrsn=920f4bf9_2&download=true
10. CDC. Requirements for negative pre-departure COVID-19 test results or documentation of recovery from COVID-19 for aircraft passengers traveling to the United States from the People's Republic of China. Atlanta, GA: US Department of Health and Human Services, CDC; 2023. https://www.govinfo.gov/content/pkg/FR-2023-01-05/pdf/2023-00080.pdf

Notes from the Field

Aircraft Wastewater Surveillance for Early Detection of SARS-CoV-2 Variants — John F. Kennedy International Airport, New York City, August–September 2022

Robert C. Morfino, MBA[1,*]; Stephen M. Bart, PhD[2,*]; Andrew Franklin, MBA[1]; Benjamin H. Rome, MBA[1]; Andrew P. Rothstein, PhD[1]; Thomas W. S. Aichele, MBA[1]; Siyao Lisa Li[1]; Aaron Bivins, PhD[3]; Ezra T. Ernst[4]; Cindy R. Friedman, MD[2]

As SARS-CoV-2 testing declines worldwide, surveillance of international travelers for SARS-CoV-2 enables detection of emerging variants and fills gaps in global genomic surveillance (*1*). Because SARS-CoV-2 can be detected in feces and urine of some infected persons (*2*), wastewater surveillance in airports and on aircraft has been proposed by the global public health community† as a low-cost mechanism to monitor SARS-CoV-2 variants entering the United States. Sampling wastewater directly from aircraft can be used to link SARS-CoV-2 lineage data with flight origin countries without active engagement of travelers (*3*).

During August 1–September 9, 2022, the biotech company Ginkgo Bioworks, in collaboration with CDC, evaluated the feasibility of SARS-CoV-2 variant detection in aircraft wastewater from incoming international flights. Aircraft wastewater samples were collected from selected flights from the United Kingdom, Netherlands, and France arriving at John F. Kennedy International Airport in New York City. Wastewater (approximately 0.25 gal [1 L]) was collected from each plane during normal maintenance using a device that attaches to the lavatory service panel port and the lavatory service truck hose.

After concentration with affinity-capture magnetic nanoparticles (*4*), wastewater samples were tested for SARS-CoV-2 by reverse transcription–polymerase chain reaction (RT-PCR).§ Samples with cycle thresholds <40 underwent whole genome sequencing using ARTIC (version 4.1; ARTIC Network) primers.¶ Multiple lineages within samples were identified using Freyja, a tool for deconvolution of complex samples.** Sequences meeting quality control criteria (e.g., >70% genome coverage)†† were assigned to sublineages using Pangolin (version 4.1.3)§§ and reported to the airline, public SARS-CoV-2 genomic data repositories, and the CDC National Wastewater Surveillance System. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶¶

During August 1–September 9, 2022, one sample was collected from each of 88 flights (Figure). Sample collection added approximately 3 minutes to normal aircraft maintenance times. Eighty samples were tested for SARS-CoV-2.*** Overall, 65 samples (81%) were positive; the percentage that were positive was similar among the three flight origin countries sampled (Netherlands: 81% [22 of 27]; France: 81% [22 of 27]; and United Kingdom: 81% [21 of 26]). Twenty-seven SARS-CoV-2 genomes were detected in 25 wastewater samples; sequencing quality control criteria were not met for the remaining 40 positive samples. All identified genomes were Omicron sublineages (United Kingdom: 12 BA.5 and one BA.4.6; France: eight BA.5; and Netherlands: five BA.5 and one BA.2.75). In each of 23 samples, single SARS-CoV-2 genomes were identified and assigned to the BA.5 (21), BA.4.6 (one), and BA.2.75 (one) sublineages. In each of two additional samples, two distinct SARS-CoV-2 genomes were identified and assigned to different BA.5 sublineages (Figure). The SARS-CoV-2 genomes identified in aircraft lavatory wastewater were consistent with Western European sequences uploaded to the Global Initiative on Sharing Avian Influenza Data (GISAID) at the time (approximately 90% BA.5).†††

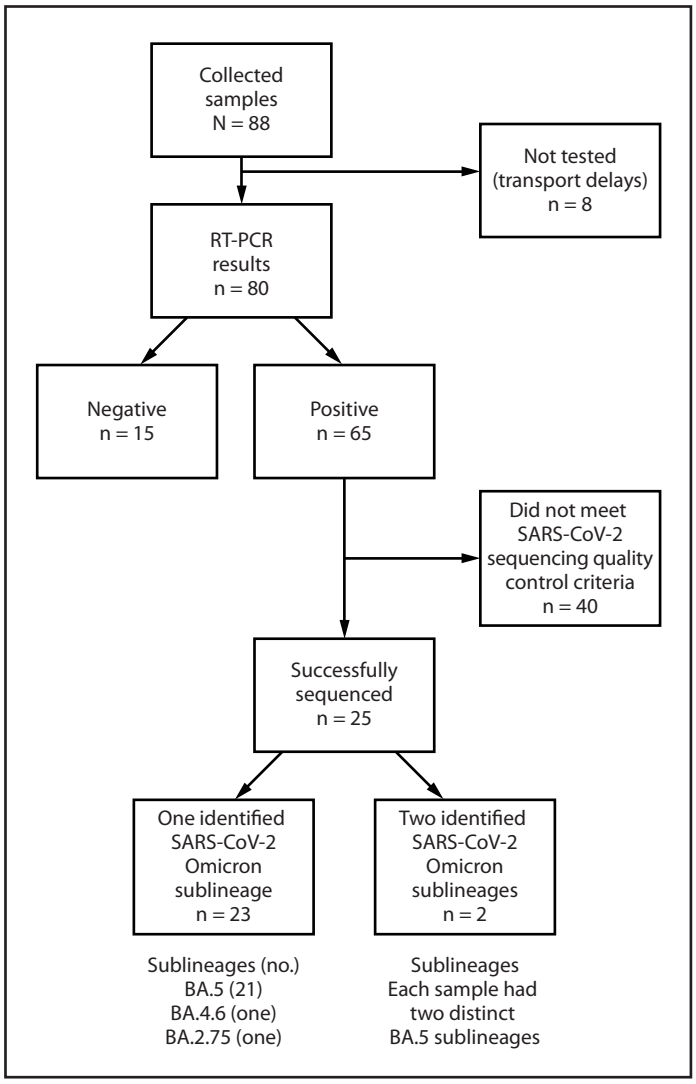
This investigation demonstrated the feasibility of aircraft wastewater surveillance as a low-resource approach compared with individual testing to monitor SARS-CoV-2 variants without direct traveler involvement or disruption to airport operations. Limitations include dependence on lavatory use during the flight, which correlates with flight duration (*5*); inability to distinguish travelers with connecting flight itineraries, which lessens precision when ascertaining variant origin; and potential carryover of residual SARS-CoV-2 RNA between flights yielding viral detections unrelated to travelers on the flight. Stringent genome coverage thresholds might reduce the likelihood of carryover variant identification on subsequent flights.

In addition to routinely monitoring variants entering the United States, this modality can be surged based on global

* These authors contributed equally to this report.
† https://wastewater-observatory.jrc.ec.europa.eu/static/pdf/Sampling%20Aircrafts_FINAL_Version%209%20Jan%202023.pdf
§ Preliminary studies indicated no inhibition of RT-PCR reagents by lavatory fluid.
¶ https://github.com/artic-network/artic-ncov2019/tree/master/primer_schemes/nCoV-2019
** https://github.com/andersen-lab/Freyja
†† Coverage determines whether variant assignment can be made with a certain degree of confidence. The coverage percentage is the proportion of the reference genome aligning with the consensus genome generated during sequencing.
§§ https://cov-lineages.org/resources/pangolin.html
¶¶ 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.
*** Eight samples were not tested because of transport delays.
††† https://covariants.org/

public health needs (e.g., outbreaks or mass gatherings in settings with limited SARS-CoV-2 variant surveillance). In combination with traveler-based surveillance (*1*), aircraft wastewater monitoring can provide a complementary early warning system for the detection of SARS-CoV-2 variants and other pathogens of public health concern.

FIGURE. Collection, testing for SARS-CoV-2, and genomic sequencing of aircraft wastewater samples from selected flights from the United Kingdom, Netherlands, and France — John F. Kennedy International Airport, New York City, August–September 2022



Abbreviation: RT-PCR = reverse transcription–polymerase chain reaction.

Acknowledgments

James Kissmer, participating airline staff members, John F. Kennedy International Airport; Andrew Deagon, Aakash Desai, Alix Hamilton, Cassandra Philipson, Lauren Reining, Birgitte Simen, Sativa Turner, Ginkgo Bioworks; Trevor Lamb, Rob Stein, Henry Streich, Josephine Thorn, Miguel Yapor, XpresCheck; Ben Lepene, Ceres Nanosciences; Martin Cetron, Nicole Cohen, Sarah Guagliardo, Sarah Meehan, Matthew Palo, Ian Ruskey, Teresa Smith, Allison Taylor Walker, Quarantine and Border Health Services Branch, CDC.

Corresponding author: Robert C. Morfino, rmorfino@ginkgobioworks.com.

[1]Ginkgo Bioworks, Boston, Massachusetts; [2]Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [3]Department of Civil & Environmental Engineering, Louisiana State University, Baton Rouge, Louisiana; [4]XpressCheck, XWELL, New York, New York.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Robert C. Morfino, Benjamin H. Rome, Andrew P. Rothstein, Siyao Lisa Li, and Thomas W. S. Aichele report Ginkgo Bioworks employee stocks or restricted stock units (RSU) grants. Aaron Bivins reports grants from the U.S. Environmental Protection Agency, Louisiana Water Resources Research Institute, and Louisiana State University, payments from BioRad Laboratories, and equipment or materials from Ceres Nanosciences. Ezra T. Ernst reports XWELL employee stocks or RSU grants. No other potential conflicts of interest were disclosed.

References

1. Wegrzyn RD, Appiah GD, Morfino R, et al. Early detection of SARS-CoV-2 variants using traveler-based genomic surveillance at four US airports, September 2021–January 2022. Clin Infect Dis 2022;76:e540–3. PMID:35686436 https://doi.org/10.1093/cid/ciac461
2. Jones DL, Baluja MQ, Graham DW, et al. Shedding of SARS-CoV-2 in feces and urine and its potential role in person-to-person transmission and the environment-based spread of COVID-19. Sci Total Environ 2020;749:141364. PMID:32836117 https://doi.org/10.1016/j.scitotenv.2020.141364
3. Ahmed W, Bivins A, Simpson SL, et al. Wastewater surveillance demonstrates high predictive value for COVID-19 infection on board repatriation flights to Australia. Environ Int 2022;158:106938. PMID:34735954 https://doi.org/10.1016/j.envint.2021.106938
4. Karthikeyan S, Ronquillo N, Belda-Ferre P, et al. High-throughput wastewater SARS-CoV-2 detection enables forecasting of community infection dynamics in San Diego County. mSystems 2021;6:e00045–21. PMID:33653938 https://doi.org/10.1128/mSystems.00045-21
5. Jones DL, Rhymes JM, Wade MJ, et al. Suitability of aircraft wastewater for pathogen detection and public health surveillance. Sci Total Environ 2023;856:159162. PMID:36202356 https://doi.org/10.1016/j.scitotenv.2022.159162

Notes from the Field

Epidemiologic Characteristics of SARS-CoV-2 Recombinant Variant XBB.1.5 — New York City, November 1, 2022–January 4, 2023

Elizabeth Luoma, MPH[1]; Rebecca Rohrer, MPH[1]; Hilary Parton, MPH[1]; Scott Hughes, PhD[1]; Enoma Omoregie, PhD[1]; Faten Taki, PhD[1]; Jade C. Wang, MS[1]; Saymon Akther, PhD[1]; Helly Amin[1]; Carolyn Chang, MPH[1]; Iris Cheng, MS[1]; Steve Di Lonardo, MSc[1]; Meredith Eddy, MPH[1]; Lauren Firestein, MPH[1]; Wenhui Li, PhD[1]; Michelle Su, PhD[1]; Ellen H. Lee, MD[1]

The SARS-CoV-2 Omicron XBB.1.5 variant, a recombinant variant of Omicron BA.2.75 and BA.2.10, was first detected in New York City (NYC) in October 2022. As of January 7, 2023, XBB.1.5 was the predominant variant in NYC, accounting for 81% of sequenced specimens; at that time, only 26% of sequenced specimens nationwide were XBB.1.5 (*1*). In addition, in December 2022, only 5% of sequenced genomes in the rest of New York were XBB.1.5, suggesting that NYC was likely the epicenter of XBB.1.5's emergence in the United States (*2*). The World Health Organization has noted that XBB.1.5 does not carry any mutation known to be associated with a potential change in severity, such as the Delta spike mutation P681R; however, there are currently limited data available about disease severity in human populations (*3*). Because NYC witnessed the emergence of XBB.1.5 before much of the United States, and the NYC Department of Health and Mental Hygiene (DOHMH) routinely links whole genome sequencing and epidemiologic data, DOHMH is uniquely positioned to characterize this subvariant. Although a higher percentage of patients infected with XBB.1.5, compared with those infected with a co-circulating variant, were younger, identified as racial and ethnic minorities, and lived in high-poverty neighborhoods, and a lower percentage had completed a primary COVID-19 vaccination series with ≥1 dose of monovalent vaccine booster, there was no evidence of a difference in disease severity.

SARS-CoV-2 specimens collected from NYC residents at five DOHMH COVID-19 Express laboratories, 190 outpatient clinics, and 11 emergency departments across all boroughs within the NYC municipal hospital system were sequenced at DOHMH's Public Health Laboratory or the Pandemic Response Laboratory, which has operated in Manhattan since September 2020. Sequenced isolates were matched to the DOHMH COVID-19 surveillance database (Maven, version 5.5.1; Consilience Software), Citywide Immunization Registry, health information exchanges, and e-Vitals Death Registry to identify demographic characteristics and previous SARS-CoV-2–positive test results, monovalent immunization history,* hospitalization status, and vital status, respectively. Persons infected with XBB.1.5 (3,019) were compared with persons infected with BQ.1† (6,067) during November 1, 2022–January 4, 2023, because both variants were co-circulating in NYC starting in November 2022, and BQ.1 was the predominant variant in NYC when XBB.1.5 emerged. Comparisons across categorical characteristics were made using Pearson chi-square or Fisher's exact test; continuous variables were compared using the Kruskal-Wallis test. Analyses were performed using SAS statistical software (SAS Enterprise Guide; version 7.1; SAS Institute) This activity was reviewed by the NYC DOHMH Institutional Review Board and was determined to be public health surveillance and therefore not subject to human subjects review.

During November–December 2022, the percentage of sequenced SARS-CoV-2 isolates in NYC identified as XBB.1.5 increased eightfold, from 8% to 72%. Compared with patients infected with BQ.1 ($p<0.001$), those with XBB.1.5 infections tended to be younger (median age = 41 years [XBB.1.5] versus 44 years [BQ.1]), Hispanic or Latino or non-Hispanic Black or African American (Black) (68.1% versus 61.5%), and residents of the Bronx, Brooklyn, or Queens (82.6% versus 76.1%); a higher percentage lived in high- or very high–poverty neighborhoods (43.2% versus 41.9%) (Table). The percentage who had received a primary COVID-19 vaccination series and ≥1 dose of monovalent vaccine booster was lower among patients with XBB.1.5 infections (41.1%) than among those with BQ.1 infections (46.0%). The percentages of XBB.1.5 and BQ.1 patients whose specimen was collected ≥90 days after a previous collection of a specimen with a SARS-CoV-2–positive test result, which could suggest possible reinfection, were similar (25.2% [XBB.1.5]; 25.4% [BQ.1]). No difference in the proportion of patients hospitalized or those who died was observed, suggesting no significant difference in disease severity.

Limitations of these data are that patients with sequencing results accounted for 4%–12% of laboratory-confirmed SARS-CoV-2 cases diagnosed in NYC in November and December 2022 (*4*); therefore, characteristics of persons with and without sequencing results might differ. Although a higher percentage of patients with sequencing results, compared with those without sequencing results, were aged 18–64 years (74% versus 68%), resided in high- or very high–poverty neighborhoods (42% versus 37%) and in Brooklyn (35%

* Bivalent booster vaccination data were not available at the time of this analysis because they had not yet been matched to DOHMH's COVID-19 surveillance database.
† BQ.1 included all descendant lineages of BQ.1 (e.g., BQ.1.1 and BQ.1.x).

TABLE. Characteristics of persons infected with SARS-CoV-2 XBB.1.5 and BQ.1* variants† — New York City, November 1, 2022–January 4, 2023

Characteristic	SARS-CoV-2 Omicron variant no. (column %) XBB.1.5 (n = 3,019)	BQ.1 (n = 6,067)	p-value§ (XBB.1.5 versus BQ.1)
Median age, yrs (IQR)	41 (27–57)	44 (30–59)	<0.001
Age group, yrs¶			
0–17	340 (11.3)	497 (8.2)	<0.001
18–44	1,362 (45.1)	2,593 (42.7)	
45–64	897 (29.7)	1,903 (31.4)	
65–74	252 (8.4)	678 (11.2)	
≥75	166 (5.5)	396 (6.5)	
Sex¶			
Female	1,767 (58.5)	3,573 (58.9)	0.72
Male	1,252 (41.5)	2,491 (41.1)	
Race and ethnicity¶,**			
Asian or Pacific Islander	302 (11.4)	715 (13.4)	<0.001
Black or African American	791 (29.9)	1,479 (27.7)	
Hispanic or Latino	1,012 (38.2)	1,802 (33.8)	
White	519 (19.6)	1,277 (24.0)	
Other	23 (0.9)	57 (1.1)	
Borough of residence¶			
The Bronx	562 (18.7)	993 (16.4)	<0.001
Brooklyn	1,103 (36.7)	2,097 (34.7)	
Manhattan	454 (15.1)	1,188 (19.6)	
Queens	819 (27.2)	1,511 (25.0)	
Staten Island	71 (2.3)	257 (4.3)	
Neighborhood poverty level,¶,†† (% of persons)			
Low (<10)	329 (11.5)	767 (13.3)	<0.001
Medium (10–19.9)	1,300 (45.3)	2,591 (44.8)	
High (20–29.9)	745 (26.0)	1,604 (27.7)	
Very high (≥30)	495 (17.2)	824 (14.2)	
Monovalent vaccination history§§			
No recorded dose	746 (24.7)	1,386 (22.9)	<0.001
Partially immunized	159 (5.3)	287 (4.7)	
Primary series only	873 (28.9)	1,602 (26.4)	
Primary series and monovalent booster vaccine dose	1,241 (41.1)	2,792 (46.0)	
Outcomes			
Repeat positive test result¶¶			
Yes	762 (25.2)	1,543 (25.4)	0.84
No	2,257 (74.8)	4,524 (74.6)	
COVID-19 hospitalization***			
Yes	219 (7.3)	389 (6.4)	0.13
No	2,800 (92.7)	5,678 (93.6)	
COVID-19 death†††			
Yes	24 (0.8)	38 (0.6)	0.36
No	2,995 (99.2)	6,029 (99.4)	

* BQ.1 included all descendant lineages of BQ.1 (e.g., BQ.1.1 and BQ.1.x).
† Classified by Pangolin identification of lineage. https://pangolin.cog-uk.io/
§ p-values from Pearson chi-square test, Fisher's exact test, or Kruskal-Wallis test as indicated, comparing persons with XBB.1.5 sequences and BQ.1 sequences.
¶ Denominators represent persons with known age, sex, race and ethnicity, borough of residence, and neighborhood poverty level; age was missing for two persons infected with XBB.1.5 variant; sex was missing for three persons infected with BQ.1 variant; race and ethnicity was missing for 1,109 persons, including 372 infected with XBB.1.5 variant and 737 infected with BQ.1 variant; borough of residence was missing for 31 persons, including 10 infected with XBB.1.5 variant and 21 infected with BQ.1 variant; and neighborhood poverty level was missing for 431 persons, including 150 infected with XBB.1.5 variant and 281 infected with BQ.1 variant.
** All persons who identified as Hispanic or Latino (Hispanic), regardless of race, are classified as Hispanic; all other race and ethnicity categories are non-Hispanic.
†† Neighborhood poverty level was defined as the percentage of residents in a zip code tabulation area with household incomes of <100% of the federal poverty level, per the American Community Survey 2014–2018.
§§ Monovalent vaccination history was categorized into four groups of monovalent vaccine doses received ≥14 days before diagnosis: 1) no recorded dose (zero doses), 2) partially immunized (≥1 dose of an mRNA vaccine), 3) primary series only (≥2 doses of an mRNA vaccine or 1 dose of a viral vector vaccine), and 4) primary series plus ≥1 dose of an mRNA or viral vector monovalent vaccine booster. Bivalent vaccine booster data had not been matched to the New York City Department of Health and Mental Hygiene's COVID-19 surveillance database at the time of this analysis.
¶¶ A repeat positive test result was defined as a sequenced SARS-CoV-2 isolate collected ≥90 days after collection of a specimen with a SARS-CoV-2–positive antigen or nucleic acid amplification test result. At-home tests were not recorded in surveillance activities.
*** A COVID-19 hospitalization was defined as 1) a confirmed or probable COVID-19 diagnosis 14 days before through 3 days after date of hospital admission, 2) a COVID-19–related hospitalization reported on the death certificate, or 3) a COVID-19–related hospitalization reported from a case investigator.
††† A COVID-19 death was defined as 1) a SARS-CoV-2–positive test result within 30 days of death or 2) a diagnosis of COVID-19 listed on the death certificate as a primary or contributing cause of death.

versus 29%), identified as Black (28% versus 20%), and had a COVID-19 hospitalization (7% versus 6%), the percentage with COVID-19 deaths was the same (1%) among all patients with laboratory-confirmed cases, irrespective of sequencing status.

XBB.1.5 emerged rapidly in NYC during November–December 2022 and earlier than in the rest of the United States. Preliminary findings from a sample of sequenced isolates in NYC do not suggest more severe disease among patients infected with XBB.1.5 compared with patients infected with BQ.1; however, these findings might change as more data on these outcomes accumulate. Although a small proportion of laboratory-confirmed SARS-CoV-2 cases in NYC are sequenced, linked epidemiologic and genomic data provide a means to evaluate characteristics of emerging variants, including disease severity, that are important for rapid risk assessment (*3*). Routine linkage of epidemiologic and sequencing data allows tracking of emerging variants and ongoing assessment of reinfection, infection after vaccination, and disease severity.

Acknowledgments

Shama Ahuja, Jennifer Baumgartner, Mustapha Mustapha, Celia Quinn, New York City Department of Health and Mental Hygiene; New York City Public Health Laboratory Whole Genome Sequencing Unit; Pandemic Response Laboratory; Celia Quinn, CDC.

Corresponding author: Elizabeth Luoma, eluoma@health.nyc.gov.

[1]New York City Department of Health and Mental Hygiene, Long Island City, New York.

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.

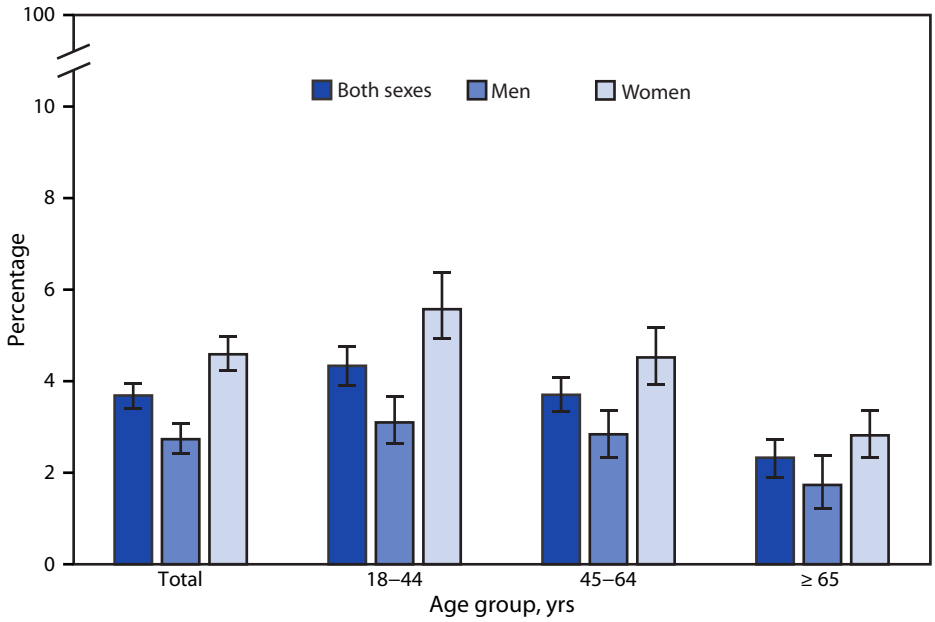
References

1. CDC. CDC COVID data tracker: variant proportions. Atlanta, GA: US Department of Health and Human Services, CDC; 2023. Accessed January 31, 2023. https://covid.cdc.gov/covid-data-tracker/#variant-proportions
2. New York State Department of Health. COVID-19 data in New York: COVID-19 variant data. Albany, NY: New York State Department of Health; 2023. https://coronavirus.health.ny.gov/covid-19-variant-data
3. World Health Organization. XBB.1.5 rapid risk assessment, 11 January 2023. Geneva, Switzerland: World Health Organization; 2023. https://www.who.int/docs/default-source/coronaviruse/11jan2023_xbb15_rapid_risk_assessment.pdf
4. New York City Department of Health and Mental Hygiene. COVID-19: data: variants. New York, NY: New York City Department of Health and Mental Hygiene; 2023. https://www.nyc.gov/site/doh/covid/covid-19-data-variants.page

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years with Serious Psychological Distress in the Past 30 Days,† by Sex and Age Group — National Health Interview Survey,§ United States, 2021



* With 95% CIs indicated by error bars.
† Serious psychological distress is based on responses to six questions, "During the past 30 days, how often did you feel 1) so sad that nothing could cheer you up, 2) nervous, 3) restless or fidgety, 4) hopeless, 5) that everything was an effort, or 6) worthless?" The response options "none of the time," "a little of the time," "some of the time," "most of the time," and "all of the time" were each scored from 0–4 points, respectively, and then summed for a total score ranging from 0–24 points. A value of ≥13 was used to define serious psychological distress. Only respondents who answered all six questions were included in the analysis.
§ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2021, 3.7% of adults aged ≥18 years had serious psychological distress in the past 30 days with percentages higher among women (4.6%) than among men (2.7%). The higher percentages among women were seen across all age groups: 5.6% versus 3.1% in adults aged 18–44 years, 4.5% versus 2.8% in those aged 45–64 years, and 2.8% versus 1.7% in those aged ≥65 years. The percentage of women who had serious psychological distress in the past 30 days decreased with age; the percentage of men who had serious psychological distress in the past 30 days was higher among those aged 18–44 and 45–64 years than among those aged ≥65 years.

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

Reported by: Nazik Elgaddal, MS, nelgaddal@cdc.gov; Laryssa Mykyta, PhD; Cynthia Reuben, MA.

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)