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Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2022

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At its November 2021 meeting, the Advisory Committee on Immunization Practices* (ACIP) approved the Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2022. The 2022 adult immunization schedule summarizes ACIP recommendations, including several changes to the cover page, tables, and notes from the 2021 immunization schedule.† In addition, the 2022 adult immunization schedule provides an appendix that lists the contraindications to and precautions for all routinely recommended vaccines in the schedule. This schedule can be found on the CDC immunization schedule website (https://www.cdc.gov/vaccines/schedules). Health care providers are advised to use the cover page, tables, notes, and appendix together. This adult immunization schedule is recommended by ACIP (https://www.cdc.gov/vaccines/acip) and approved by CDC (https://www.cdc.gov), the American College of Physicians (https://www.acponline.org), the American Academy of Family Physicians (https://www.aafp.org), the American College of Obstetricians and Gynecologists (https://www.acog.org), the American College of Nurse-Midwives (https://www.midwife.org), the American Academy of Physician Associates (https://www.aapa.org), and the Society for Healthcare Epidemiology of America (https://www.shea-online.org).

* Recommendations for routine use of vaccines in adults are developed by ACIP, a federal advisory committee chartered to provide expert external advice and guidance to the CDC director on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in adults are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists. ACIP recommendations approved by the CDC director become agency guidelines on the date published in the *Morbidity and Mortality Weekly Report*. Additional information about ACIP is available at https://www.cdc.gov/vaccines/acip.

† Past immunization schedules are available at https://www.cdc.gov/vaccines/schedules/past.html.

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ACIP's recommendations for the use of each vaccine are developed after in-depth reviews of vaccine-related data, including the epidemiology and societal impacts of the vaccine-preventable disease, vaccine efficacy and effectiveness, vaccine safety, quality of evidence, feasibility of program implementation, and economic analyses of immunization policy (*1*). The adult immunization schedule is published annually to consolidate and summarize updates to ACIP recommendations on vaccination of adults and to assist health care providers in implementing current ACIP recommendations. The use of vaccine trade names in this report and in the adult immunization schedule is for identification purposes only and does not imply endorsement by ACIP or CDC.

For further guidance on the use of each vaccine, including any changes that might occur between annual publication of the adult immunization schedule, health care providers are referred to the respective ACIP vaccine recommendations at https://www.cdc.gov/vaccines/hcp/acip-recs.[§] Printable versions of the 2022 adult immunization schedule and ordering instructions are available at https://www.cdc.gov/vaccines/schedules/hcp/adult.html#note. For CDC's interim clinical considerations for the use of COVID-19 vaccines, health care providers are referred to: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html.

[§] CDC encourages organizations to use syndication as a more reliable method for displaying the most current and accurate immunization schedules on an organization's website rather than copying these schedules to their websites. Use of content syndication requires a one-time step that ensures an organization's website displays current schedules as soon as they are published or revised; instructions for the syndication code are available on CDC's website (https://www.cdc.gov/vaccines/schedules/syndicate.html). CDC also offers technical assistance for implementing this form of content syndication (requests can be e-mailed to ncirdwebteam@cdc.gov).

Changes in the 2022 Adult Immunization Schedule

Vaccine-specific changes in the 2022 immunization schedule for adults aged ≥19 years include new or updated ACIP recommendations for hepatitis B vaccine (HepB) (*2*), influenza vaccine (*3*), pneumococcal vaccines (*4*), recombinant zoster vaccine (RZV) (*5*), and COVID-19 vaccine (available at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html). Changes have also been made to the human papillomavirus (HPV); measles, mumps, and rubella (MMR); meningococcal; and varicella (VAR) vaccination sections to improve clarity in the language. In addition, an appendix listing the contraindications to and precautions for each vaccine has been added to the schedule this year.

Cover page

- A step instructing providers to review the newly added appendix has been added to the "How to use the adult immunization schedule" box.
- The Society for Healthcare Epidemiology of America has been added as a partner organization approving the adult schedule.

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- PCV15 (Vaxneuvance) and PCV20 (Prevnar 20) have been added to the table of vaccine abbreviations and trade names.
- PCV13 (Prevnar 13) has been removed from the list of vaccine abbreviations and trade names.
- A QR code has been added at the bottom of the cover page for health care providers to access the online schedule (https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html).

Table 1 (Routine Immunization Schedule)

- **Zoster row**: For adults aged 19–49 years, the color of the row was changed to purple indicating that RZV is now recommended for adults in this age group who have immunocompromising conditions. The text overlay now states, "2 doses for immunocompromising conditions (see notes)."
- **Pneumococcal row**: All recommended pneumococcal vaccines (i.e., PCV15, PCV20, and PPSV23) have been collapsed into one row. Guidance on which vaccines are indicated for certain age groups is displayed by the corresponding colors and overlying text. For adults aged 19–64 years, the row is purple, indicating that pneumococcal vaccination is recommended for adults in this age group only if they have an additional risk factor or another indication. For adults aged ≥65 years, the row is yellow, indicating that pneumococcal vaccination is universally recommended for adults in this age group, if they have never received a pneumococcal conjugate vaccine previously or if their previous pneumococcal vaccination history is unknown. The text overlay now states, "1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)."
- **Hepatitis B row**: For adults aged 19–59 years, the row is yellow, indicating that HepB vaccination is universally recommended for adults in this age group, and purple for adults aged ≥60 years, indicating that HepB vaccination is recommended for adults in this age group if they have an additional risk factor or another indication. The text overlay now states "2, 3, or 4 doses depending on vaccine or condition."

Table 2 (Immunization by Medical Indication Schedule)

- **Header**: For the HIV infection columns, CD4 percentages are displayed along with CD4 counts to harmonize presentation of this information with that in the child/adolescent schedule.
- **Legend**: The description of the color red in the legend has been reworded to "Contraindicated or not recommended."
- **LAIV4 row**: The text overlay in the red box was changed to "Contraindicated" to increase clarity in the language and to align more closely with ACIP recommendations.
- **MMR row**: The text overlay for the red boxes was changed to "Contraindicated" to increase clarity in the language and to align more closely with ACIP recommendations.
- **VAR row**: The text overlay for the red boxes was changed to "Contraindicated" to increase clarity in the language and to align more closely with ACIP recommendations.
- **RZV row:** Under the Immunocompromised and HIV infection columns, the row is yellow indicating that RZV is recommended for these subgroups. In addition, the text overlay under these columns now states, "2 doses at age ≥19 years."
- **HepB row**: The row is now entirely yellow, indicating that hepatitis B vaccination is recommended for all risk-based groups in Table 2. The text overlay states, "3 doses (see notes)" in the pregnancy column, and "2, 3, or 4 doses depending on vaccine or condition," in the remaining columns.

Notes

The notes for each vaccine are presented in alphabetical order. Edits have been made throughout the Notes section to harmonize language between the child/adolescent and the adult immunization schedules to the greatest extent possible.

- **COVID-19**: The hyperlinks to the ACIP recommendations for the use of COVID-19 vaccines and the CDC's Interim Clinical Considerations for the use of COVID-19 vaccines are included in this box.
- **HepB**: The "Routine vaccination" section now states that adults aged 19–59 years are recommended to receive a 2-, 3-, or 4-dose series, with details provided. The "Special situations" section outlines the risk-based recommendations for adults aged ≥60 years. In addition, language has been added stating that "anyone age 60 years or older who does not meet risk-based recommendations may still receive Hepatitis B vaccination."
- **HPV**: A minor edit was made to the "Routine vaccination" section to increase clarity; it now states, "No additional dose recommended when any HPV vaccine series has been completed using the recommended dosing intervals." In addition, minor wording changes were made to the "Special situations" section, under the immunocompromising conditions sub-bullet, which now reads, "3-dose series, even for those who initiate vaccination at age 9 through 14 years." Wording for the pregnancy sub-bullet was rearranged to improve clarity.
- **Influenza**: The language was edited to clarify the age as "19 years or older," to be consistent with the schedule. A hyperlink to the 2021–22 influenza recommendations and a bullet for the 2022–23 influenza recommendations were added. The "Special situations" section was condensed by referring health care providers to the appendix listing the contraindications and precautions for the influenza vaccines.

- **Meningococcal vaccination**: At the end of the section, a note was added that states, "MenB vaccines may be administered simultaneously with MenACWY vaccines if indicated, but at a different anatomic site, when feasible."
- **MMR:** In the "Special situations" section, CD4 percentages in addition to CD4 counts in the HIV infection bullet were added to harmonize language with the child/adolescent schedule.
- **Pneumococcal vaccination:** The section has been updated to reflect ACIP's new recommendations for PCV15 and PCV20 vaccines. The "Routine vaccination" section now states that persons aged ≥65 years "who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive 1 dose of PCV15 or 1 dose of PCV20. If PCV15 is used, this should be followed by a dose of PPSV23." Similarly, the "Special situations" section has changed, and this section states that anyone "aged 19 through 64 years with certain underlying medical conditions or other risk factors who has not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive 1 dose of PCV15 or 1 dose of PCV20. If PCV15 is used, this should be followed by a dose of PPSV23." Guidance for dosing intervals between PCV15 and PPSV23 and for patients who have previously received PCV13 or PPSV23 in the past is also included. A note added at the end lists all the underlying medical conditions or risk factors that would render those aged 19–64 years eligible to receive pneumococcal vaccination.
- **Varicella**: In the "Special situations" section, CD4 percentages in addition to CD4 counts in the HIV infection bullet were added to harmonize language with the child/adolescent schedule.
- **Zoster**: In the "Special situations" section under the pregnancy bullet, the language was revised to increase clarity. This bullet now states, "There is currently no ACIP recommendation for RZV use in pregnancy. Consider delaying RZV until after pregnancy." In addition, the immunocompromising conditions bullet was revised to reflect the new ACIP recommendations for zoster vaccination. This bullet now states, "RZV is recommended for use in persons aged 19 years and older who are or will be immunodeficient or immunosuppressed because of disease or therapy."

Appendix (Contraindications and Precautions)

- The appendix includes all the contraindications to and precautions for each of the vaccines listed in the 2022 adult immunization schedule. The information presented in this appendix is adapted from the 2021–22 influenza vaccine recommendations (*3*) and from ACIP General Best Practice Guidelines for Immunization (*6*).

Additional Information

The Recommended Adult Immunization Schedule, United States, 2022, is available at https://www.cdc.gov/vaccines/schedules/hcp/adult.html and in the *Annals of Internal Medicine* (https://www.acpjournals.org/doi/10.7326/M22-0036). The full ACIP recommendations for each vaccine are also available at https://www.cdc.gov/vaccines/hcp/acip-recs/index.html. All vaccines identified in Tables 1 and 2 (except PCV15, PCV20, and zoster vaccine) also appear in the Recommended Immunization Schedule for Children and Adolescents, United States, 2022 (https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html). The notes and appendices for vaccines that appear in both the adult immunization schedule and the child and adolescent immunization schedule have been harmonized to the greatest extent possible.

Acknowledgments

Rosters of current and past members of the Advisory Committee on Immunization Practices are available at https://www.cdc.gov/vaccines/acip/committee/members-archive.html.

ACIP Combined Immunization Schedule Work Group

Kevin Ault (Chair). Members: Henry Bernstein, Carolyn Bridges, Uzo Chukwuma, Sybil Cineas, Sarah Coles, Sean Dade, Katherine Debiec, Marci Drees, John Epling, Holly Fontenot, Sandra Fryhofer, Kathleen Harriman, Robert Hopkins, Molly Howell, Paul Hunter, Karen Ketner, David Kim, Jane Kim, Marie-Michelle Leger, Susan Lett, Veronica McNally, Sarah McQueen, Amy B. Middleman, Sean O'Leary, Diane Peterson, Chad Rittle, William Schaffner, Ken Schmader, Rhoda Sperling, Patricia Stinchfield, Peter Szilagyi, L.J. Tan, Thomas Weiser. Contributors: Neil Murthy (CDC co-Lead), A. Patricia Wodi (CDC co-Lead). CDC Contributors: Anna Acosta, Tara Anderson, Kathy Byrd, Margaret Cortese, Kathleen Dooling, Amy Parker-Fiebelkorn, Mark Freedman, Paul Gastañaduy, Lisa Grohskopf, Susan Hariri, Aaron Harris, Fiona Havers, Holly Hill, Tara Jatlaoui, Suzanne Johnson-DeLeon, Miwako Kobayashi, Ram Koppaka, Andrew Kroger, Tatiana Lanzieri, Mona Marin, Lauri Markowitz, Sarah Mbaeyi, Lucy McNamara, Elissa Meites, Noele Nelson, Sara Oliver, Gabriela Paz-Bailey, Priti Patel, Tamara Pilishvili, Hilda Razzaghi, Janell Routh, Sarah Schillie, Mark Weng, Akiko Wilson, JoEllen Wolicki.

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References

1. CDC. Charter of the Advisory Committee on Immunization Practices. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://www.cdc.gov/vaccines/acip/committee/acip-charter.pdf
2. CDC: Advisory Committee on Immunization Practices (ACIP). ACIP Recommendations. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. Accessed January 25, 2022. https://www.cdc.gov/vaccines/acip/recommendations.html
3. Grohskopf LA, Alyanak E, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2021–22 influenza season. MMWR Recomm Rep 2021;70(RR-5):1–28. PMID:34448800 https://doi.org/10.15585/mmwr.rr7005a1
4. Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among U.S. adults: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:109–17. PMID:35085226 https://doi.org/10.15585/mmwr.mm7104a1
5. Anderson TC, Masters NB, Guo A, et al. Use of recombinant zoster vaccine in immunocompromised adults aged ≥19 years: recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:80–4. PMID:35051134 https://doi.org/10.15585/mmwr.mm7103a2
6. Kroger A, Bahta L, Hunter P. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Atlanta, GA: Advisory Committee on Immunization Practices: 2021. https://www.cdc.gov/vaccines/hcp/acip-recs/general- recs/downloads/generalrecs.pdf

Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger — United States, 2022

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At its November 2021 meeting, the Advisory Committee on Immunization Practices* (ACIP) approved the Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger—United States, 2022. The 2022 child and adolescent immunization schedule, found on the CDC immunization schedule website (https://www.cdc.gov/vaccines/schedules), summarizes ACIP recommendations, including several changes from the 2021 immunization schedule† on the cover page, tables, and notes. The 2022 child and adolescent schedule also includes a newly created appendix that lists the contraindications and precautions for all vaccine types in the schedule. Health care providers are advised to use the tables, notes, and appendix together. This immunization schedule is recommended by ACIP (https://www.cdc.gov/vaccines/acip) and approved by CDC (https://www.cdc.gov), the American Academy of Pediatrics (https://www.aap.org), the American Academy of Family Physicians (https://www.aafp.org), the American College of Obstetricians and Gynecologists (http://www.acog.org), the American College of Nurse-Midwives (https://www.midwife.org), the American Academy of Physician Associates (https://www.aapa.org), and the National Association of Pediatric Nurse Practitioners (https://www.napnap.org).

ACIP's recommendations for the use of each vaccine are developed after in-depth reviews of vaccine-related data, including the epidemiology and societal impacts of the vaccine-preventable disease, vaccine efficacy and effectiveness, vaccine safety, quality of evidence, feasibility of program implementation, and economic analyses of immunization policy (*1*). The child and adolescent immunization schedule is published annually to consolidate and summarize updates to ACIP recommendations on vaccination of children and adolescents, and to assist health care providers in implementing current ACIP recommendations. The use of vaccine trade names in this report and in the child and adolescent immunization schedule is for identification purposes only and does not imply specific product endorsement by ACIP or CDC.

For further guidance on the use of each vaccine, health care providers are referred to the respective ACIP vaccine recommendations at https://www.cdc.gov/vaccines/hcp/acip-recs. Providers should be aware that changes in recommendations for specific vaccines can occur between these annual updates to the child and adolescent immunization schedule. If errors or omissions are discovered within the schedule, CDC will post revised versions on the CDC immunization schedule website.§ Printable versions of the 2022 child and adolescent immunization schedule and ordering instructions are available on the immunization schedule website. For CDC's interim clinical considerations for the use of COVID-19 vaccines, health care providers are referred to https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html.

Changes in the 2022 Child and Adolescent Immunization Schedule

Vaccine-specific changes in the 2022 child and adolescent immunization schedule for children and adolescents aged ≤18 years include new or updated ACIP recommendations for influenza vaccine (*2*), dengue vaccine (*3*), and COVID-19 vaccine (https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html). Changes also include clarification of the recommendations for *Haemophilus influenzae* type b vaccine (Hib); hepatitis A vaccine (HepA); hepatitis B vaccine (HepB); human papillomavirus vaccine (HPV); measles,

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mumps, and rubella vaccine (MMR); meningococcal serogroups A, C, W, Y vaccine (MenACWY); tetanus, diphtheria, and pertussis vaccine (Tdap); and varicella vaccine (VAR). In addition, a newly created appendix was added that lists the contraindications and precautions for each vaccine type included in the schedule. Following are the changes to the cover page, Tables 1, 2, and 3, the Vaccine Notes, and the Appendix.

Cover Page

- Dengue vaccine (DENGVAXIA) has been added to the table of vaccine abbreviations and trade names.
- Instructions on how to use the child and adolescent immunization schedule have been updated to include a fifth step asking health care providers to review the appendix, which lists the contraindications and precautions for each vaccine type.
- Instructions on how health care providers can contact CDC with questions and comments about the schedule have been added.
- The section on helpful information was updated to include information on accessing Vaccine Information Statements.
- A QR code directing providers to the immunization schedule website has been added.

Table 1 (Routine Immunization Schedule)

- The color of the columns for children aged 4–6 years, children aged 11–12 years, and adolescents aged 16 years has been changed from gray to black to align with the color of the other age range columns. The sentence in the table header stating "School entry and adolescent vaccine age groups are shaded in gray" has been deleted.
- **Tdap row:** The overlying text in the column for children aged 11–12 years has been changed from "Tdap" to "1 dose" to be consistent with the format used for other vaccines in the table.
- **HPV row:** The asterisk that was previously present for children aged 9–10 years and its associated descriptive text in the table legend (i.e., "*can be used in this age group") have been deleted. Instead, the color for children aged 9–10 years has been changed from blue to checked yellow, which is a new color in Table 1. Within the table's legend, a new checked yellow box has been added, which now indicates that "Recommended vaccination can begin in this age group."
- **Dengue row:** A new row has been added with the boxes for children and adolescents aged 9–16 years highlighted in yellow to indicate the recommended age for routine dengue vaccination. The overlying text "Seropositive in endemic areas only (see notes)" has been added to the yellow boxes.

Table 2 (Catch-Up Immunization Schedule)

- **Hib row:** The text for the 4-week minimum interval between doses 2 and 3 has been revised to include recommendations for DTaP-IPV-Hib-HepB (Vaxelis). The text now reads, "if current age is younger than 12 months ***and*** first dose was administered at younger than age 7 months ***and*** at least 1 previous dose was PRP-T (ActHib, Pentacel, Hiberix), Vaxelis, or unknown." In addition, Hib-HepB (Comvax) was deleted from the text for the 8-week minimum interval between doses 2 and 3 because this vaccine product is no longer available.
- **Dengue row:** A new row has been added for the dengue vaccine outlining the minimum age and minimum interval between doses.

Table 3 (Immunization by Medical Indication Schedule)

- The definition of severe immunosuppression because of HIV infection has been revised to be consistent with ACIP's General Best Practice Guidelines for Immunization (*4*) and now reads, "<15% or total CD4 cell count of <200/mm^3."
- **Legend:** The text that defines the red box in the table's legend has been edited for clarity and now reads, "Contraindicated or not recommended—vaccine should not be administered." In addition, the text that defines the checked yellow box in the table's legend has been edited and now reads, "Vaccination is recommended, and additional doses might be necessary based on medical condition or vaccine. See Notes."
- **Dengue:** A new row has been added to outline dengue vaccine recommendations by medical conditions or other indications.

Notes

- **Additional information:** The text for COVID-19 vaccination has been updated to include a hyperlink to the webpage for CDC's interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States.
- **Dengue:** This new section was added to provide details for routine dengue vaccination in areas with endemic dengue. In addition, a hyperlink referring health care providers to the latest guidance on areas with endemic dengue and prevaccination laboratory testing is included.
- **Hib:** The note was updated to include the recommendations for routine and catch-up vaccination when DTaP-IPV-Hib-HepB (Vaxelis) is used.
- **HepA:** The note was revised to clarify that the age for routine vaccination is age 12–23 months.
- **HepB:** In the "Special situations" section, the text has been revised to clarify and emphasize the recommendations for postvaccination serology and revaccination.

- **HPV:** In the "Special situations" section, the text for immunocompromising conditions has been revised to clarify that 3 doses should be administered regardless of age at initial vaccination.
- **Influenza:** The note has been updated to reflect the recommendations for the 2021–22 influenza season. The "Special situations" section was condensed by moving information on contraindications and precautions for influenza vaccines to the newly created appendix.
- **MMR:** The note on routine vaccination was updated to include recommendations for use of measles, mumps, rubella, and varicella vaccine (MMRV).
- **MenACWY:** Language was added to the notes regarding the recommendation for simultaneous administration with meningococcal serogroup B vaccine (MenB). The text reads, "MenACWY vaccines may be administered simultaneously with MenB vaccines if indicated, but at a different anatomic site, when feasible."
- **VAR:** The note has been updated to include recommendations for using MMRV and to clarify that a second dose inadvertently administered after at least a 4-week interval may be counted as a valid dose.

Appendix (Contraindications and Precautions)

A newly created appendix listing the contraindications and precautions for each vaccine type included in the 2022 child and adolescent immunization schedule has been added. The information in the appendix is adapted from ACIP General Best Practice Guidelines for Immunization (*4*) and ACIP recommendations for use of 2021–22 influenza vaccines (*2*).

Additional Information

The Recommended Child and Adolescent Immunization Schedule, United States, 2022 is available at https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. The full ACIP recommendations for each vaccine are also available at https://www.cdc.gov/vaccines/hcp/acip-recs. All vaccines identified in Tables 1, 2, and 3 (except diphtheria, tetanus, and acellular pertussis vaccine [DTaP], rotavirus, poliovirus vaccines, and PCV13 [Prevnar 13]) also appear in the Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2022, available at https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html. The notes and appendix for vaccines that appear in both the child and adolescent immunization schedule and the adult immunization schedule have been harmonized to the greatest extent possible.

Acknowledgments

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References

1. CDC. Charter of the Advisory Committee on Immunization Practices. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://www.cdc.gov/vaccines/acip/committee/acip-charter.pdf
2. Grohskopf LA, Alyanak E, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2021–22 influenza season. MMWR Recomm Rep 2021;70(No. RR-5):1–28. PMID:34448800 https://doi.org/10.15585/mmwr.rr7005a1
3. 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
4. Kroger A, Bahta L, Hunter P. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Atlanta, GA: Advisory Committee on Immunization Practices; 2021. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf

Multistate Outbreak of SARS-CoV-2 B.1.1.529 (Omicron) Variant Infections Among Persons in a Social Network Attending a Convention — New York City, November 18–December 20, 2021

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On December 2, 2021, the Minnesota Department of Health (MDH) notified CDC of a COVID-19 case caused by sequence-confirmed SARS-CoV-2 B.1.1.529 (Omicron) variant in a Minnesota resident (patient A), the first such case identified in the state and one of the earliest identified in the United States. Patient A had attended a large indoor convention in New York, New York with approximately 53,000 attendees from 52 U.S jurisdictions and 30 foreign countries during November 19–21, 2021, and had close contact[†] during 5 days with 29 fellow attendees. The convention required attendees to have received ≥1 COVID-19 vaccine dose and enforced mask-use while indoors. On November 22, these close contact attendees were directly and immediately notified by patient A of their exposure to SARS-CoV-2, and they sought testing over the next few days while quarantined or isolated. As part of the larger investigation into SARS-CoV-2 transmission at the convention, a subinvestigation was conducted during December by CDC, MDH, and respective state and local health departments to characterize the epidemiology of Omicron variant infection among this group of close contacts and determine the extent of secondary household transmission. Among 30 convention attendees that included patient A (the index patient) and the 29 other close contacts, 23 were interviewed, among whom all were fully vaccinated, including 11 (48%) who had received a booster dose; all 23 sought testing, and 16 (70%) received a positive SARS-CoV-2 test result. Fewer attendees who had received a booster dose before the convention received a positive test result (six of 11) compared with those who had not received a booster dose (10 of 12). The 16 attendees with positive test results had a total of 20 household contacts, 18 of whom sought testing after exposure; six received a positive test result for SARS-CoV-2. None of the persons with positive test results was hospitalized or died. There was limited convention-associated transmission identified outside of this cluster; the larger investigation included cases of both SARS-CoV-2 B.1.617.2 (Delta) and Omicron, and all Omicron cases were associated with this group (*1*). Data from this investigation reinforces the importance of COVID-19 booster doses in combination with early notification and other multicomponent prevention measures to limit transmission and prevent severe illness from Omicron and other SARS-CoV-2 variants.

Patient A flew to New York City on November 18 to attend a large convention with approximately 53,000 attendees. While in New York City, patient A stayed in a vacation rental with three other attendees and remained in close contact with 29 attendees during the 5-day visit. Patient A participated in several convention sessions and engaged in an informal schedule of social activities outside the convention that was shared with the 29 attendees, including mostly unmasked visits to restaurants, bars, clubs, and karaoke venues. The convention required proof of receipt of ≥1 COVID-19 vaccine dose, and mask use indoors at the convention was enforced for all attendees. Patient A was fully vaccinated in April 2021 and had received a booster dose on November 4. Patient A reported symptoms starting November 22, the day after the convention ended, upon returning home to Minnesota. The same day, patient A received a message from another attendee in this group who had received a positive at-home antigen test result that day (the first positive test result, but not the first reported symptom onset in the group). Patient A immediately informed all 29 attendees of their exposure so that they could take precautions and seek testing. Patient A sought real-time reverse transcription–polymerase chain reaction (RT-PCR) testing on November 23, which detected SARS-CoV-2 infection. A CDC-led investigation was initiated on December 3, 2021, in collaboration with MDH and the state and local health departments of the 29 other attendees.

Investigation and Findings

Through a case investigation interview with patient A on November 30, contact tracing,[§] and collaboration with various

[*] These authors contributed equally to this report.

[†] Close contact is defined as being <6 feet away from an infected person (laboratory-confirmed or a clinical diagnosis) for a cumulative total of ≥15 minutes over a 24-hour period. https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/appendix.html#contact

[§] https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/contact-tracing.html

state and local health departments, the 29 attendees who had close contact with patient A during the event were identified. A questionnaire was developed to collect demographic, epidemiologic, and clinical information for the index patient and the 29 close contact attendees. In addition, a second questionnaire was developed to collect similar information from household contacts of any of these attendees (including patient A) with confirmed SARS-CoV-2 infection. During November 30–December 20, 2021, investigators conducted interviews with patient A, close contact attendees, and household contacts who did not attend the convention. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[¶]

Among the 30 attendees (patient A and their 29 close contacts), 23 (77%) residing in 13 states[**] were interviewed; 12 (52%) were men, and the median age was 24 years. All 23 attendees had received a primary COVID-19 vaccination series (135–281 days before convention),[††] with 11 (48%) having received a booster dose (six and five received the booster ≥14 days and <14 days, respectively, before the convention); one person reported a history of COVID-19 (Table 1).

Upon notification, all 23 interviewed attendees sought testing (15 within 2 days among 19 with known first test date), and 18 (78%) used one or more at-home antigen tests. Positive SARS-CoV-2 test results were received by 16 persons in 10 states[§§] (attack rate = 70%), including two of three who used at-home antigen tests only, three of five who used laboratory-based tests only, and 11 of 15 who used both at-home antigen and laboratory-based tests. Five attendees' specimens (from five states) were sequenced and were identified as Omicron variant sublineage BA.1 with no discernable difference. In addition, three household members of a single attendee had this same Omicron sequence confirmed, but the convention attendee in this household used an at-home antigen test only, and no sequence confirmation was available. Among 11 (48%) of the 23 interviewed attendees who had received a COVID-19 booster dose before the convention, six received a positive test result. Among 12 (52%) attendees who had not received a booster, 10 received a positive test result. All infected attendees reported at least one symptom (median = five) with symptom onset during November 21–26; seven reported symptom onset within 2 days of the final day of the convention. The median duration of symptoms was 11 days; the most commonly reported symptoms included nasal congestion, fatigue, cough, and sore throat. The median incubation period was 2–5 days (based on earliest and latest exposure). No hospitalizations or deaths were reported.

TABLE 1. Characteristics of members of SARS-CoV-2 Omicron cluster who attended a New York City convention (N = 23) — 13 states,* November 18–December 20, 2021

Characteristic	No. (column %) Total (N = 23)[†]	No. of attendees (row %) SARS-CoV-2 test-positive[§] (n = 16)	No. of attendees (row %) SARS-CoV-2 test-negative[¶] (n = 7)
Median age, yrs (range)	**24 (21–41)**	24 (22–41)	23 (21–31)
Male sex	**12 (52)**	7 (58)	5 (42)
No. days at the convention			
3	**21 (91)**	14 (67)	7 (33)
2	**2 (9)**	2 (100)	0 (—)
Reported mask use at the convention			
Always	**20 (87)**	15 (75)	5 (25)
Sometimes	**3 (13)**	1 (33)	2 (67)
History of previous COVID-19 infection			
Yes	**1 (4)**	1 (100)	0 (—)
No	**22 (96)**	15 (68)	7 (32)
Primary vaccination series product**			
Pfizer-BioNTech	**14 (61)**	10 (71)	4 (29)
Moderna	**6 (26)**	3 (50)	3 (50)
Janssen (Johnson & Johnson)	**3 (13)**	3 (100)	0 (—)
Received booster vaccine[††]			
Yes	**11 (48)**	6 (55)	5 (45)
No	**12 (52)**	10 (83)	2 (17)
Viral testing, self-tests			
≥1 self-test (antigen)	**18 (78)**	13 (72)	5 (28)
≥1 positive result (n = 18)	**12 (67)**	12 (100)	0 (—)
Viral testing, laboratory-based tests			
≥1 laboratory-based test	**20 (87)**	14 (70)	6 (30)
≥1 positive result (n = 20)	**13 (65)**	13 (100)	0 (—)
Location of test (n = 20)			
Clinic	**14 (70)**	10 (71)	4 (29)
Pharmacy	**4 (20)**	2 (50)	2 (50)
Community testing center	**2 (10)**	2 (100)	0 (—)
Type of test (n = 20)			
Antigen test	**2 (10)**	1 (50)	1 (50)
RT-PCR (or other NAAT)	**18 (90)**	13 (72)	5 (28)
Social activities outside of the convention			
Outdoor sightseeing	**5 (22)**	3 (60)	2 (40)
Indoor sightseeing	**1 (4)**	1 (100)	0 (—)
Indoor restaurants	**19 (83)**	13 (68)	6 (32)
Outdoor restaurants	**7 (30)**	5 (71)	2 (29)
Bars	**18 (78)**	12 (67)	6 (33)
Nightclubs	**9 (39)**	6 (67)	3 (33)
Karaoke	**22 (96)**	16 (73)	6 (27)

Abbreviations: NAAT = nucleic acid amplification test; RT-PCR = reverse transcription–polymerase chain reaction.

* Arizona, California, Connecticut, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Jersey, New York, North Carolina, Texas, and Virginia.

† Twenty-three of 30 attendees in this cluster were interviewed.

§ Positive result by antigen or NAAT/RT-PCR test.

¶ Negative result based on at least one viral test after exposure.

** https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

†† All booster doses were administered as an mRNA COVID-19 vaccine.

¶ 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.

** Arizona, California, Connecticut, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Jersey, New York, North Carolina, Texas, and Virginia.

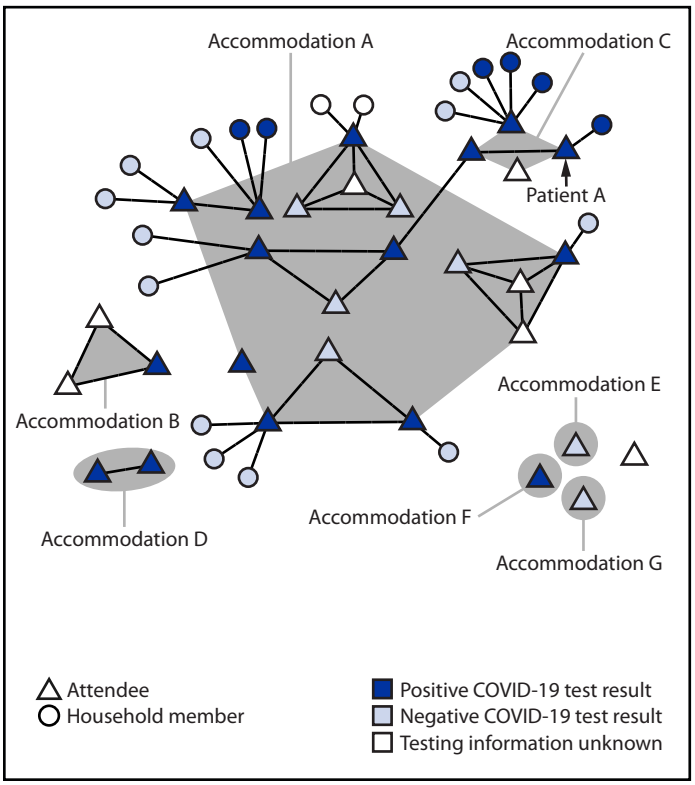
†† https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

§§ Arizona, California, Connecticut, Massachusetts, Minnesota, Missouri, New Jersey, North Carolina, Texas, and Virginia.

Overall, 21 (91%) of 23 interviewed attendees participated in the convention all 3 days. Twenty (87%) attendees reported mask-use "always" and three (13%) reported mask-use "sometimes" while at the convention (mostly removing mask to eat and take pictures). Attendees engaged in activities outside the convention, including karaoke, eating indoors, and visiting bars/clubs (Table 1). Among 14 interviewed attendees who stayed at accommodation A, nine received a positive test result, as did seven of nine who stayed in other accommodations (Figure). No attendee reported international travel before the convention.

Upon return home, the 16 attendees with positive test results exposed 20 household contacts (median age = 55 years) during their infectious period. Among household contacts, 11 (55%) were male, and none reported a previous history of COVID-19 (Table 2). Nineteen (95%) household contacts were fully vaccinated, and 10 (50%) had received a booster dose 2–94 days before exposure to the attendee (median = 27 days). Among 18 household contacts tested following exposure to an attendee with a positive SARS-CoV-2 test result, six (33%) received a positive result, including four who had received a booster dose >14 days before exposure. Symptom onsets ranged from November 26 to December 7 (median symptom duration = 13 days). Four patients reported fewer than five symptoms; the most commonly reported symptoms were nasal congestion, fatigue, cough, runny nose, and change in taste. The median incubation period was 1–5 days (based on earliest and latest exposure). No hospitalizations or deaths were reported.

FIGURE. SARS-CoV-2 infections among a cluster of attendees of a New York City convention, by accommodation while in New York City and forward household transmission — 13 states,* November 18–December 20, 2021†



* Arizona, California, Connecticut, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Jersey, New York, North Carolina, Texas, and Virginia.
† This figure was produced using MicrobeTrace. https://pubmed.ncbi.nlm.nih.gov/34492010/

TABLE 2. Characteristics of household contacts exposed to SARS-CoV-2 Omicron by a household member who acquired infection during trip to a New York City convention (N = 20)* — 10 states,† November 18–December 20, 2021

Characteristic	No. (column %) Total (N = 20)	No. of household contacts (row %) SARS-CoV-2 test-positive§ (n = 6)	SARS-CoV-2 test-negative (n = 12)
Median age, yrs (range)	**55 (10–84)**	58 (20–84)	55 (10–63)
Male sex	**11 (55)**	4 (40)	6 (60)
Relationship to convention attendee			
Spouse or child	**2 (10)**	0 (—)	2 (100)
Parent	**11 (55)**	2 (22)	7 (78)
Grandparent	**2 (10)**	2 (100)	0 (—)
Sibling	**5 (25)**	2 (40)	3 (60)
Primary vaccine series¶			
Pfizer-BioNTech	**14 (70)**	4 (33)	8 (67)
Moderna	**3 (15)**	1 (33)	2 (67)
Janssen (Johnson & Johnson)	**2 (10)**	1 (50)	1 (50)
No vaccine	**1 (5)**	0 (—)	1 (100)
Received booster vaccine before exposure (n = 19)**			
Yes	**10 (53)**	4 (40)	6 (60)
No	**9 (47)**	2 (29)	5 (71)
Viral testing			
Rapid	**7 (35)**	4 (57)	3 (43)
Not rapid	**11 (55)**	2 (18)	9 (82)
Not applicable	**2 (10)**	0 (—)	0 (—)
Exposures to convention attendee			
Spent >15 minutes within 6 ft	**18 (90)**	6 (38)	10 (62)
Had face-to-face contact (within approximately 2 ft)	**14 (70)**	5 (38)	8 (62)
Spent any time within 6 ft while attendee was coughing or sneezing	**1 (5)**	1 (100)	0 (—)
Had direct contact with attendee (e.g., hug or kiss)	**11 (55)**	2 (22)	7 (78)
Slept in same bedroom	**1 (5)**	0 (—)	0 (—)
Shared a bathroom	**5 (25)**	2 (40)	3 (60)
Prepared food or share meal	**15 (75)**	5 (38)	8 (62)
Traveled in same vehicle (e.g., car, bus, or airplane), sitting within 6 ft	**10 (50)**	2 (22)	7 (78)
No. of days exposed to convention attendee			
1–2	**5 (25)**	2 (50)	2 (50)
3–5	**2 (10)**	0 (—)	2 (100)
≥6	**13 (65)**	4 (33)	8 (67)

Abbreviations: NAAT = nucleic acid amplification test; RT-PCR = reverse transcription–polymerase chain reaction.
* Two household members never sought testing.
† Arizona, California, Connecticut, Massachusetts, Minnesota, Missouri, New Jersey, North Carolina, Texas, and Virginia.
§ Positive result by antigen or NAAT/RT-PCR test.
¶ https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html
** All booster doses were administered as an mRNA COVID-19 vaccine.

Public Health Response

On December 2, 2021, MDH notified respective state and local health departments of four convention attendees with close contact to the index patient regarding potential exposure to the SARS-CoV-2 Omicron variant. That same day, CDC issued an Epidemic Information Exchange (Epi-X) to U.S. health departments to identify COVID-19 cases among event attendees. On December 6, CDC requested permission to conduct interviews with the index patient, close contact attendees, and their households; additional state and local health departments were notified as other close contacts were identified.

Discussion

In this group of convention attendees with several days of close contact, SARS-CoV-2 Omicron variant attack rates were high, both among the attendees (70%) and among household contacts of infected attendees (33%). Among 16 cases that occurred within this attendee cluster, all persons had been vaccinated, as were the six household contacts who became infected. The high attack rates among fully vaccinated persons illustrate Omicron variant's partial escape from vaccine-induced immunity (*2*); however, illness was relatively mild among this cohort, consistent with evidence that vaccinated persons with infections are less likely to experience serious illness. Potential contributing factors to the high attack rates include unmasked and prolonged contact in social settings and residential accommodations. This finding among this group contrasts with the observed overall transmission at the convention, which was relatively low; all Omicron cases identified from the larger investigation were associated with this group of close contact attendees. The low overall transmission at the convention is likely because of short interactions among participants in less confined space combined with high vaccination coverage, high prevalence of mask use, and high-efficiency particulate air filtration (*1*).

Among this attendee cluster with close unmasked contact and known booster status, a lower proportion of those who had received a COVID-19 booster dose received a positive test result (six of 11) compared with those who had not received a booster dose (10 of 12). Although this attendee cluster was small, the finding that prevalence was lower among those who had received a booster is consistent with other study findings (*2–4*). Vaccination, including booster doses,[¶¶] reduces risk for infection; persons who have received a booster dose can still become infected, but they are less likely to experience severe illness, hospitalization, or death.

[¶¶] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html

Summary

What is already known about this topic?

The SARS-CoV-2 Omicron variant is highly transmissible; is believed to have partial escape from infection- and vaccine-induced immunity; and is responsible for the recent rapid increase in U.S. cases.

What is added by this report?

Attack rates among a cohort of persons attending a convention were high, but lower among infected attendees' household members. There were fewer infections among vaccinated attendees who had received a COVID-19 vaccine booster dose.

What are the implications for public health practice?

Data from this investigation reinforce the importance of COVID-19 booster doses and early notification in combination with other multicomponent prevention measures to limit transmission and prevent severe illness from Omicron and other SARS-CoV-2 variants.

The findings in this report are subject to at least four limitations. First, testing for statistical significance was not performed because of the small sample size. Second, high use of at-home testing and time between positive test results and this investigation limited the availability of residual samples for sequencing; infections without sequencing data might have been caused by other variants. Third, seven close contact attendees never responded to requests for interview, which could have biased results. Finally, because at-home tests might have lower sensitivity than RT-PCR tests,[***] some infections might have been undetected.

Early notification and testing with at-home antigen tests resulted in immediate quarantine or isolation and early diagnoses for the persons in this cluster, which might have reduced secondary attack rates in these households (*5*). Patient A notified the group after learning that another attendee was infected, 1–4 days after possible exposure, prompting contacts to seek testing, monitor for symptoms, and isolate or quarantine. The high use of at-home antigen tests suggests that persons with access to these tests will use them and share results. Although at-home antigen tests might have lower sensitivity than RT-PCR tests, broad access might result in earlier detection and notification, thus assisting in interrupting transmission. This investigation reinforces the importance of COVID-19 booster doses and early notification in combination with other multicomponent prevention measures to limit transmission and prevent severe illness from Omicron and other SARS-CoV-2 variants.

[***] https://www.cdc.gov/coronavirus/2019-ncov/testing/self-testing.html

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References

1. Sami S, Horter L, Valencia D, et al. Investigation of SARS-CoV-2 transmission associated with a large indoor convention—New York City, November–December 2021. MMWR Morb Mortal Wkly Rep 2022;71:243–8.
2. Nemet I, Kliker L, Lustig Y, et al. Third BNT162b2 vaccination neutralization of SARS-CoV-2 Omicron infection. N Engl J Med 2022;386:492–4. PMID:34965337 https://doi.org/10.1056/NEJMc2119358
3. Bar-On YM, Goldberg Y, Mandel M, et al. Protection against Covid-19 by BNT162b2 booster across age groups. N Engl J Med 2021;385:2421–30. PMID:34879188 https://doi.org/10.1056/NEJMoa2115926
4. Collie S, Champion J, Moultrie H, Bekker LG, Gray G. Effectiveness of BNT162b2 vaccine against Omicron variant in South Africa. N Engl J Med 2022;386:494–6. PMID:34965358 https://doi.org/10.1056/NEJMc2119270
5. Grijalva CG, Rolfes MA, Zhu Y, et al. Transmission of SARS-COV-2 infections in households—Tennessee and Wisconsin, April–September 2020. MMWR Morb Mortal Wkly Rep 2020;69:1631–4. PMID:33151916 https://doi.org/10.15585/mmwr.mm6944e1

Investigation of SARS-CoV-2 Transmission Associated With a Large Indoor Convention — New York City, November–December 2021

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During November 19–21, 2021, an indoor convention (event) in New York City (NYC), was attended by approximately 53,000 persons from 52 U.S. jurisdictions and 30 foreign countries. In-person registration for the event began on November 18, 2021. The venue was equipped with high efficiency particulate air (HEPA) filtration, and attendees were required to wear a mask indoors and have documented receipt of at least 1 dose of a COVID-19 vaccine.* On December 2, 2021, the Minnesota Department of Health reported the first case of community-acquired COVID-19 in the United States caused by the SARS-CoV-2 B.1.1.529 (Omicron) variant in a person who had attended the event (*1*). CDC collaborated with state and local health departments to assess event-associated COVID-19 cases and potential exposures among U.S.-based attendees using data from COVID-19 surveillance systems and an anonymous online attendee survey. Among 34,541 attendees with available contact information, surveillance data identified test results for 4,560, including 119 (2.6%) persons from 16 jurisdictions with positive SARS-CoV-2 test results. Most (4,041 [95.2%]), survey respondents reported always wearing a mask while indoors at the event. Compared with test-negative respondents, test-positive respondents were more likely to report attending bars, karaoke, or nightclubs, and eating or drinking indoors near others for at least 15 minutes. Among 4,560 attendees who received testing, evidence of widespread transmission during the event was not identified. Genomic sequencing of 20 specimens identified the SARS-CoV-2 B.1.617.2 (Delta) variant (AY.25 and AY.103 sublineages) in 15 (75%) cases, and the Omicron variant (BA.1 sublineage) in five (25%) cases. These findings reinforce the importance of implementing multiple, simultaneous prevention measures, such as ensuring up-to-date vaccination, mask use, physical distancing, and improved ventilation in limiting SARS-CoV-2 transmission, during large, indoor events.†

An indoor convention in NYC with approximately 53,000 attendees was held during November 19–21, 2021. The facility was equipped with HEPA filters, and attendees were required to have documented receipt of at least 1 dose of COVID-19 vaccine and to use face masks while indoors. On December 2, 2021, the Minnesota Department of Health identified a case of COVID-19 caused by the Omicron variant in an attendee. State and local health departments collaborated with CDC to determine the extent of transmission during the convention and to make public health recommendations.

Two primary data sources were used in this investigation. The first was a list of attendees residing within the jurisdictions of participating state and local health departments. These attendees were matched with data from COVID-19 surveillance systems using personal identifiers (name and complete or partial address). Health departments identified positive and negative SARS-CoV-2 test results, demographic data, and vaccination histories§ for attendees. An event-associated case was defined as SARS-CoV-2 infection confirmed by reverse transcription–polymerase chain reaction or antigen testing in an event attendee during November 18–December 5, 2021.

* https://www1.nyc.gov/assets/home/downloads/pdf/executive-orders/2021/eeo-225.pdf

† https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/index.html

§ Persons who had received a primary vaccination series had completed all recommended doses of a Food and Drug Administration–authorized COVID-19 vaccine (2 doses of BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna], or 1 dose of Ad.26.COV2.S (Janssen [Johnson & Johnson]) ≥14 days before specimen collection and had documentation in their state immunization information system or self-report of vaccination details (including vaccine product and dates of receipt). Persons who had received a booster dose had completed a primary vaccination series and received another dose of vaccination regardless of the time frame. Persons who had received only 1 dose of a 2-dose vaccination series or had completed vaccination <14 days before specimen collection were considered partially vaccinated.

Sequencing of available specimens was conducted by state public health laboratories using multiple platforms[¶]; variant identification results were shared with CDC.

The second data source, an online anonymous survey, was administered via text message (29,766 text messages sent) and email (28,893 emails delivered) to approximately 35,000 attendees from 52 jurisdictions with available contact information, during December 11–19, 2021. Respondents were asked to report SARS-CoV-2 testing history and results, COVID-19 vaccination status, symptom history,[**] and exposure data during the event, and close contacts during and after the event. Available surveillance information and survey responses from U.S. resident attendees who received positive and negative test results were compared. Wilcoxon rank-sum tests were used for continuous data, and Pearson's chi-square or Fisher's exact tests were used for categorical data; statistical significance was defined as p<0.05.[††] This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§§]

Using COVID-19 surveillance systems, 48 public health jurisdictions reviewed data for 34,072 registered attendees; 39 jurisdictions reported a positive or negative result for 4,560 (13.4%) attendees, including 13 (<1%) self-tests[¶¶] (from two states) (Table 1). Among 3,845 (84.3%) attendees with test and vaccination data, 3,248 (84.5%) had received a primary vaccination series, an additional 467 (12.1%) had received a booster dose,[***] and 130 (3.4%) were partially vaccinated.

Among the 4,560 attendees with test result data, 119 (2.6%) event-associated cases were identified by January 6, 2022, from 16 jurisdictions (Figure). Among event-associated cases the median age was 26.5 years (IQR = 23.0–36.6 years), 65 (54.6%) were New York residents, and among 116 with gender data available, 54 (46.6%) were male (Table 1). Vaccination information was available for 88 persons with event-associated cases, 85 (96.6%) completed vaccination, including five who had received a booster dose. Among event-associated cases, the median interval from completing primary vaccination series to positive test result was 210 days (IQR = 193–232 days), and from booster dose to positive test result was 14 days (IQR = 12–20 days). Among the 3,630 (80%) test-negative attendees who completed primary vaccination or received booster dose, the median interval from completion of primary vaccination series to test date was 207 days (IQR = 187–225 days) and from receipt of booster dose to test date was 34 days (IQR = 22–66 days). One attendee with event-associated COVID-19 was hospitalized; no deaths were reported.

Genomic sequencing of 20 specimens identified the Delta variant (AY.25 and AY.103 sublineages) in 15 (75%) cases, and the Omicron variant (BA.1 sublineage) in five (25%). All attendees with Omicron cases were part of a known epidemiologic and phylogenetic cluster (*2*); no Delta variant cases were part of a cluster.[†††]

[†††] The closely linked Omicron cases involved lineage BA.1 SARS-CoV-2 with no discernable difference in the genomic regions with reliable sequence, consistent with the epidemiologic links.

TABLE 1. Demographic characteristics and vaccination history of persons who attended a large, indoor convention in New York City and had a SARS-CoV-2 test result during November 18–December 5 reported by health department COVID-19 surveillance systems, by test result — 39 U.S. jurisdictions, November–December 2021

	No. (%)			
Characteristic	Total (N = 4,560)	Positive test (n = 119)	Negative test (n = 4,441)	p-value*
Demographic				
Sex				
Known no.†	**4,485 (98.4)**	116 (97.5)	4,369 (98.4)	NA
Male	**2,364 (52.7)**	54 (46.6)	2,310 (52.9)	0.18
Female	**2,121 (47.3)**	62 (53.4)	2,059 (47.1)	
Median age, yrs, (IQR)	**26.1 (22.2–31.4)**	26.5 (23.0–36.6)	26.1 (22.2–31.4)	0.18
State of residence				
New York	**3,967 (87.0)**	65 (54.6)	3,902 (87.9)	<0.01
Outside of New York	**593 (13.0)**	54 (45.4)	539 (12.1)	
Vaccination history				
Vaccination status				
Known no.†	**3,845 (84.3)**	88 (73.9)	3,757 (84.6)	NA
Primary vaccination series received	**3,248 (84.5)**	80 (90.9)	3,168 (84.3)	0.17
Booster dose received	**467 (12.1)**	5 (5.7)	462 (12.3)	
Partially vaccinated	**130 (3.4)**	3 (3.4)	127 (3.4)	
Days from booster dose to test date§				
Known no.†	**467 (100)**	5 (100)	462 (100)	NA
Median	**34**	14	34	<0.01
IQR	**22–66**	12–20	22–66	NA
Days from primary vaccination series to test date¶				
Known no.†	**3,248 (100)**	80 (100)	3,168 (100)	NA
Median	**207**	210	207	0.34
IQR	**188–225**	193–232	187–225	NA

Abbreviation: NA = not applicable.

* Testing for statistical significance was conducted using nonparametric tests (i.e., Wilcoxon rank-sum) to compare continuous data and Pearson's chi-square or Fisher's exact test to compare categorical data. Statistical significance was defined as p<0.05.

† "Known no." is defined as number of persons for individual variables that did not have missing data.

§ Percentage among those who received a booster dose.

¶ Percentage among those who received a primary vaccination series.

[¶] Sequencing platforms included Nanopore (Oxford Nanopore Technologies); NextSeq (Illumina); NovaSeq 6000 (Illumina); Miseq System (Illumina); PacBio Sequel II Systems (PacBio); and GridION (Oxford Nanopore Technologies).

[**] COVID-19–like symptoms were based on the Council of State and Territorial Epidemiologists surveillance case definition for COVID-19. https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2020-08-05/

[††] Respondents who did not confirm attending the convention or who resided outside the United States were excluded from the analysis.

[§§] 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.

[¶¶] https://www.cdc.gov/coronavirus/2019-ncov/testing/self-testing.html

[***] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html

Among 7,259 respondents from the online survey (approximately 21% response rate) across 48 jurisdictions, 4,259 attendees reported receiving a COVID-19 test during November 18–December 5, 2021 (Table 2). Among these, 48 (1.1%) respondents from 10 jurisdictions reported SARS-CoV-2 infections during the investigation date range (including six from self-tests). The median age among test-positive attendees was 28 years (IQR = 23.0–35.0 years), 13 (27.7%) of 47 with reported gender were male, 15 (32.6%) of 46 with reported race/ethnicity were non-Hispanic White, and 19 (42.2%) of 45 reporting residency were New York residents. Among 47 test-positive survey respondents reporting vaccination information, 37 (78.7%) completed a primary vaccination series, six (12.8%) received a booster dose, and four (8.5%) were partially vaccinated. Among 4,157 test-negative respondents, 2,274 (54.7%) completed primary vaccination, 1,511 (36.3%) received a booster dose, and 372 (8.9%) were partially vaccinated. The median interval from booster dose receipt to a SARS-CoV-2–positive specimen was 12 days (IQR = 10–21 days) and to a negative specimen was 20 days (IQR = 10–35 days).

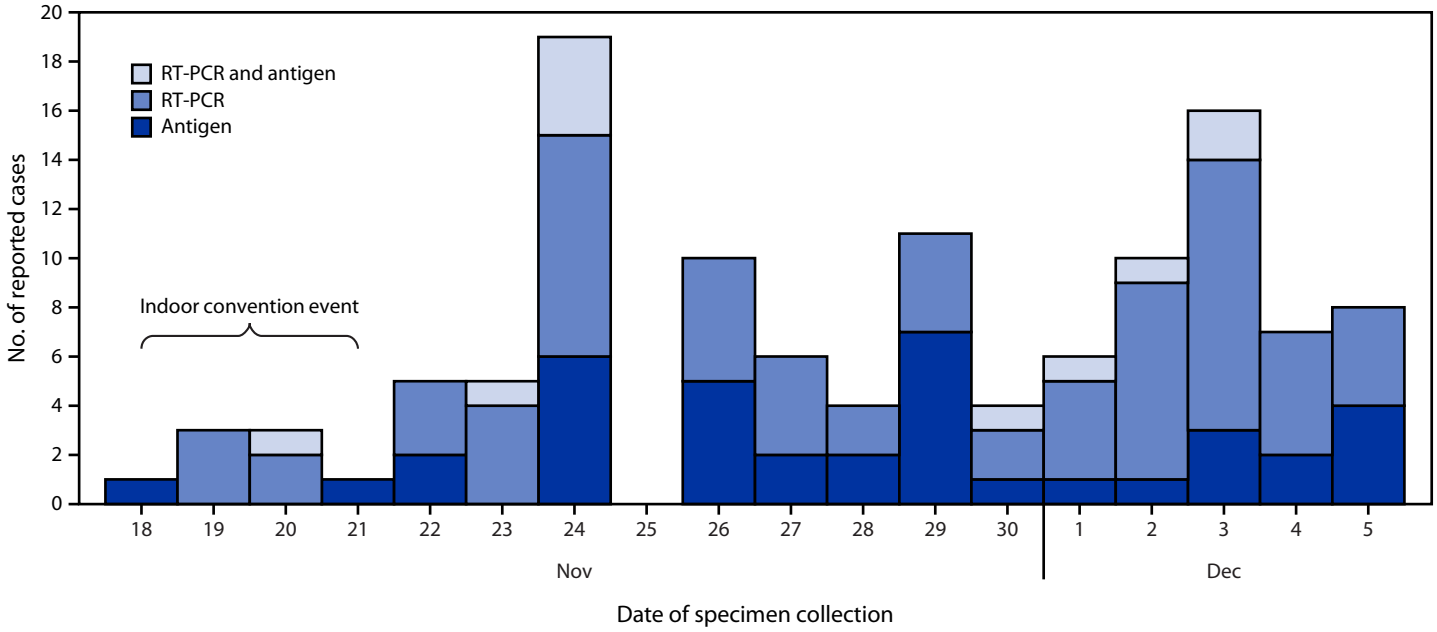
Among the 48 test-positive respondents, 34 (70.8%) reported COVID-19 compatible symptoms, compared with 312 (7.4%) of 4,203 test-negative respondents. Nasal congestion or runny nose (91.2%) and fatigue (88.2%) were common symptoms reported among test-positive respondents; among test-negative respondents, nasal congestion or runny nose (223 of 310; 71.9%) and sore throat (191 of 305; 62.6%) were most commonly reported. No hospitalizations were reported.

Test-positive survey respondents reported engaging in certain activities more frequently than did test-negative respondents, including attending bars (16.7% versus 6.9%), karaoke (18.8% versus 2.4%), or nightclubs (10.4% versus 3.0%) outside of the convention, and eating or drinking indoors near others for at least 15 minutes at the convention (62.5% versus 43.7%) (all $p<0.05$). Differences were also found in reporting close contact with someone with a positive COVID-19 test result within 10 days of symptom onset or test result (44.1% versus 6.0%) ($p<0.05$). Most (4,041 [95.2%]) attendees, reported always wearing a mask over their nose and mouth while indoors; no difference was found in type of mask used by test result. Among 4,245 survey respondents, 87 (2.0%) reported knowing at least one person (mean = 2.4) whom they met, interacted with, or worked with during the event who received a positive SARS-CoV-2 test result since attending the event.

On December 2, 2021, after identification of the first Omicron case, CDC issued an Epidemic Information Exchange (Epi-X) notification to U.S. health departments to identify COVID-19 cases among event attendees. On December 3, 2021, the NYC Test and Trace program[§§§]

[§§§] https://www.nychealthandhospitals.org/test-and-trace/

FIGURE. Event-associated cases* of SARS-CoV-2 infection (n = 119)[†] among attendees of a large indoor convention in New York City, by date of specimen collection and test type[§] — 16 jurisdictions, November–December 2021



Abbreviation: RT-PCR = reverse transcription–polymerase chain reaction.
* Reported by health department COVID-19 surveillance systems.
[†] Among 4,560 attendees with test result data, 119 (2.6%) event-associated cases were identified by January 6, 2022, from 16 jurisdictions.
[§] Antigen, RT-PCR, and RT-PCR and antigen are mutually exclusive groups.

TABLE 2. Demographic characteristics, potential exposures, and close contacts of New York City convention attendees who participated in an anonymous online survey and self-reported SARS-CoV-2 test results during November 18–December 5, by test result — 48 U.S. jurisdictions, November–December 2021

Characteristic	No. (%) of respondents: Total receiving test* (N = 4,259)	Positive test (n = 48)	Negative test (n = 4,211)	p-value†
Demographic				
Gender				
Known no.§	**4,204 (98.7)**	47 (97.9)	4,157 (98.7)	NA
Female	**2,107 (50.1)**	31 (66.0)	2,076 (49.9)	0.13
Male	**1,834 (43.6)**	13 (27.7)	1,821 (43.8)	
Transgender	**144 (3.4)**	1 (2.1)	143 (3.4)	
Other¶	**119 (2.8)**	2 (4.3)	117 (2.8)	
Median age, yrs, (IQR)	**26 (22.0–31.0)**	28 (23.0–35.0)	26 (22.0–31.0)	0.26
Race/Ethnicity				
Known no.§	**4,175 (98.0)**	46 (95.8)	4,129 (98.1)	NA
Asian, non-Hispanic	**1,127 (27.0)**	12 (26.1)	1,115 (27.0)	0.54
Black, non-Hispanic	**421 (10.1)**	3 (6.5)	418 (10.1)	
Hispanic, any race	**1,097 (26.3)**	10 (21.7)	1,087 (26.3)	
Other, non-Hispanic	**311 (7.4)**	6 (13.0)	305 (7.4)	
White, non-Hispanic	**1,219 (29.2)**	15 (32.6)	1,204 (29.2)	
State of residence				
Known no.§	**4,111 (96.5)**	45 (93.8)	4,066 (96.6)	NA
New York	**2,540 (61.8)**	19 (42.2)	2,521 (62.0)	<0.01
Outside of New York	**1,571 (38.2)**	26 (57.8)	1,545 (38.0)	
Vaccination history				
Vaccination status				
Known no.§	**4,204 (98.7)**	47 (97.9)	4,157 (98.7)	NA
Primary vaccination series received	**2,311 (55.0)**	37 (78.7)	2,274 (54.7)	<0.01
Booster dose received	**1,517 (36.1)**	6 (12.8)	1,511 (36.3)	
Partially vaccinated	**376 (8.9)**	4 (8.5)	372 (8.9)	
Days from booster dose to test date				
Known no.§ (% of those who received booster)	**838 (55.2)**	6 (100)	832 (55.1)	NA
Median	**20**	12	20	0.58
IQR	**10–34**	10–21	10–35	NA
Prevention measures and exposures				
Mask use over nose and mouth while indoors				
Known no.§	**4,246 (99.7)**	48 (100)	4,198 (99.7)	NA
Always	**4,041 (95.2)**	46 (95.8)	3,995 (95.2)	0.07
Sometimes	**184 (4.3)**	1 (2.1)	183 (4.4)	
Never	**11 (0.3)**	1 (2.1)	10 (0.2)	
Rarely	**10 (0.2)**	0 (—)	10 (0.2)	
Type of mask used				
Known no.§	**4,230 (99.3)**	47 (97.9)	4,183 (99.3)	NA
Surgical	**1,872 (44.3)**	21 (44.7)	1,851 (44.3)	0.89
Cloth	**1,812 (42.8)**	21 (44.7)	1,791 (42.8)	
N94/N95	**546 (12.9)**	5 (10.6)	541 (12.9)	
Outside activities during convention attendance				
Known no.§	**4,259 (100)**	48 (100)	4,211 (100)	NA
Outdoor sightseeing	**798 (18.7)**	10 (20.8)	788 (18.7)	0.71
Indoor sightseeing	**544 (12.8)**	9 (18.8)	535 (12.7)	0.20
Bars	**297 (7.0)**	8 (16.7)	289 (6.9)	0.02
Nightclubs	**130 (3.1)**	5 (10.4)	125 (3.0)	0.01
Karaoke	**112 (2.6)**	9 (18.8)	103 (2.4)	<0.01
Ate or drank indoors in close proximity to others for at least15 minutes				
Known no.§	**4,237 (99.5)**	48 (100)	4,189 (99.5)	NA
Yes	**1,859 (43.9)**	30 (62.5)	1,829 (43.7)	0.01
Shared a room with another person during convention attendance				
Known no.	**4,171 (97.9)**	45 (93.8)	4,126 (98.0)	NA
Yes	**1,440 (34.5)**	21 (46.7)	1,419 (34.4)	0.11
Travel to other states in the 14 days before or after travel to NYC (non-New York residents)				
Known no.§	**4,200 (98.6)**	47 (97.9)	4,153 (98.6)	NA
Yes	**679 (16.2)**	10 (21.3)	669 (16.1)	0.32
Travel outside of the United States in the 14 days before or after travel to NYC (non-New York residents)				
Known no.§	**4,189 (98.4)**	47 (97.9)	4,142 (98.4)	NA
Yes	**45 (1.1)**	0 (—)	45 (1.1)	1.00
Contact with anyone who traveled outside the United States (14 days before positive test or symptoms)				
Known no.§	**3,977 (93.4)**	47 (97.9)	3,930 (93.3)	NA
Yes	**25 (0.6)**	1 (2.1)	24 (0.6)	0.26
Exposure notification and close contacts				
Used the COVID Alert NYC app during the event**				
Known no.§	**4,249 (99.8)**	47 (97.9)	4,202 (99.8)	NA
Yes	**271 (6.4)**	4 (8.5)	267 (6.4)	0.54
New York resident	**209 (80.1)**	1 (33.3)	208 (80.6)	0.10
Non-New York resident	**52 (19.9)**	2 (66.7)	50 (19.4)	
No	**3,978 (93.6)**	43 (91.5)	3,935 (93.6)	
Received exposure notification via COVID Alert NYC app during or after the event				
Known no.§ (% among those who used app)	**270 (99.6)**	4 (100)	266 (99.6)	NA
Yes	**75 (27.8)**	1 (25)	74 (27.8)	1.0
No	**195 (72.2)**	3 (75)	192 (72.2)	
Had a close contact report a positive COVID-19 test result within 10 days of respondent's symptom onset or test result				
Known no.§	**335 (7.9)**	34 (70.8)	301 (7.1)	NA
Yes	**33 (9.9)**	15 (44.1)	18 (6.0)	<0.01
Met, interacted, or worked with at least one person during the convention who reported a positive SARS-CoV-2 test result since attending the convention				
Known no.§	**4,245 (99.7)**	48 (100)	4,197 (99.7)	NA
Yes	**87 (2.0)**	7 (14.6)	80 (1.9)	<0.01

Abbreviations: NA = not applicable; NYC = New York City.

* Self-reported SARS-CoV-2 test results from an online, anonymous survey.

† Testing for statistical significance was conducted using nonparametric tests (i.e., Wilcoxon rank-sum) to compare continuous data and Pearson's chi-square or Fisher's exact test to compare categorical data. Statistical significance was defined as p<0.05.

§ Known no. is defined as number of persons for individual variables that did not have missing data.

¶ Other is defined in the survey as "none of these."

** COVID Alert NYC app is a voluntary, anonymous, exposure-notification smartphone application that provides an alert if a person was in close contact with someone who receives a positive SARS-CoV-2 test result. The period for exposure notification was November 18–December 5, 2021.

Summary

What is already known about this topic?

The SARS-CoV-2 Delta (B.1.617.2) and Omicron (B.1.1.529) variants are highly transmissible. Outbreaks have been reported among vaccinated populations in indoor settings where mask use was limited.

What is added by this report?

Despite multiple introductions as evidenced by detection of at least three sublineages of SARS-CoV-2, this investigation did not find evidence of widespread transmission among a highly vaccinated population at a large event in an indoor setting where mask use was required and monitored.

What are the implications for public health practice?

Implementing multiple prevention measures (vaccinations and boosters, consistent mask wearing, enhanced indoor ventilation, and testing after text notification) can limit the transmission of SARS-CoV-2 at large events, including highly transmissible variants.

alerted registered attendees via text and email messages to get tested immediately, wear a face mask, and maintain physical distance from others.

Discussion

This investigation identified 119 event-associated COVID-19 cases, including one hospitalization. A parallel epidemiologic investigation describing a cluster of attendees with social links (*2*) revealed that at least seven U.S.-based persons potentially attended the event during their infectious period.¶¶¶ Despite these potential exposures and multiple introductions as evidenced by genomic identification of at least three different SARS-CoV-2 variants and sublineages, findings from surveillance and survey data from a portion of attendees suggest that this large event did not lead to widespread transmission; 7-day average percentage of positive test results in NYC on December 5, 2021, (3.0%) was similar to that in this investigation (2.6%) *(3)*. Omicron variant accounted for <5% of sequenced cases in NYC by December 4, 2021; transmission could have been higher had the convention occurred after Omicron became the dominant variant *(4)*.

Reported prevention measures (vaccination requirements, enforcement of mask use, and avoidance of unmasked indoor settings), and a venue with HEPA filtration likely accounted for the limited number of event-associated cases. Indoor gatherings in which prevention measures do not occur have been shown to increase the spread of COVID-19 (*5*–*8*). In addition, transmission to household contacts, including to vaccinated or previously infected persons, was documented in the related cluster investigation and a previous Omicron investigation (*2*,*9*).

The findings in this report are subject to at least six limitations. First, case finding and survey distribution were limited to a registration list of 35,613 ticket purchasers, but the event organizer reported that approximately 53,000 persons had attended. Second, matching attendees with case surveillance data was conducted by jurisdictions using only name and address, which potentially limited the number of cases and vaccination records identified or misidentified attendees. In addition, self-testing results were not included by most jurisdictions. Third, few specimens were available for sequencing (17% of event-associated cases). Fourth, the limited reach (14% of reported attendees) and low response rate of the survey (approximately 21%) can increase potential biases if respondents differ systematically from nonrespondents. Fifth, responses were subject to self-reporting bias; attendees who sought testing might be more likely to respond or respond according to social desirability bias. Finally, the definition of event-association case could have included cases from transmission unrelated to the event.

Findings from this survey and a related cluster investigation (*2*) of a portion of attendees suggest transmission occurred primarily among social circles and during indoor unmasked activities during the event rather than at official event activities. These findings reinforce the importance of implementing multiple, simultaneous prevention measures, such as ensuring up-to-date vaccination, mask use, physical distancing, and improved ventilation in limiting SARS-CoV-2 transmission, including highly transmissible Delta and Omicron variants, during large indoor events.

¶¶¶ Infectious period for the cluster investigations was defined as 2 days before and 10 days after their symptom onset date.

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References

1. Minnesota Department of Health. Lab testing confirms state's first COVID-19 case involving Omicron variant [Press release]. Saint Paul, MN: Minnesota Department of Health; 2021. https://www.health.state.mn.us/news/pressrel/2021/covid120221.html
2. Smith-Jeffcoat SE, Pomeroy MA, Sleweon S, et al. Multistate outbreak of SARS-CoV-2 B.1.1.529 (Omicron) variant infections among persons in a social network attending a convention—New York City, November 18–December 20, 2021. MMWR Morb Mortal Wkly Rep 2022;238-42.
3. NYC Health. COVID-19: data. New York, NY: NYC Health; 2022. Accessed January 13, 2022. https://www1.nyc.gov/site/doh/covid/covid-19-data.page#testing
4. NYC Health. Coronavirus data: variants. New York, NY: NYC Health; 2022. Accessed January 13, 2022. https://github.com/nychealth/coronavirus-data/blob/master/variants/now-variant-epi-data.csv
5. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2
6. Hamner L, Dubbel P, Capron I, et al. High SARS-CoV-2 attack rate following exposure at a choir practice—Skagit County, Washington, March 2020. MMWR Morb Mortal Wkly Rep 2020;69:606–10. PMID:32407303 https://doi.org/10.15585/mmwr.mm6919e6
7. Sami S, Turbyfill CR, Daniel-Wayman S, et al. Community transmission of SARS-CoV-2 associated with a local bar opening event—Illinois, February 2021. MMWR Morb Mortal Wkly Rep 2021;70:528–32. PMID:33830981 https://doi.org/10.15585/mmwr.mm7014e3
8. Muller N, Kunze M, Steitz F, et al. Severe acute respiratory syndrome coronavirus 2 outbreak related to a nightclub, Germany, 2020. Emerg Infect Dis 2020;27:645–8. PMID:33263514 https://doi.org/10.3201/eid2702.204443
9. Jansen L, Tegomoh B, Lange K, et al. Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) variant cluster — Nebraska, November–December 2021. MMWR Morb Mortal Wkly Rep 2021;70:1782–4. PMID:34968376 https://doi.org/10.15585/mmwr.mm705152e3

Safety Monitoring of COVID-19 Vaccine Booster Doses Among Adults — United States, September 22, 2021–February 6, 2022

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During September 22, 2021–February 6, 2022, approximately 82.6 million U.S. residents aged ≥18 years received a COVID-19 vaccine booster dose.* The Food and Drug Administration (FDA) has authorized a booster dose of either the same product administered for the primary series (homologous) or a booster dose that differs from the product administered for the primary series (heterologous). These booster authorizations apply to all three COVID-19 vaccines used in the United States (*1*–*3*).† The Advisory Committee on Immunization Practices (ACIP) recommended preferential use of an mRNA COVID-19 vaccine (mRNA-1273 [Moderna] or BNT162b2 [Pfizer-BioNTech]) for a booster, even for persons who received the Ad26.COV2.S (Janssen [Johnson & Johnson]) COVID-19 vaccine for their single-dose primary series.§ To characterize the safety of COVID-19 vaccine boosters among persons aged ≥18 years during September 22, 2021–February 6, 2022, CDC reviewed adverse events and health impact assessments following receipt of a booster that were reported to v-safe, a voluntary smartphone-based safety surveillance system for adverse events after COVID-19 vaccination, and adverse events reported to the Vaccine Adverse Event Reporting System (VAERS), a passive vaccine safety surveillance system managed by CDC and FDA. Among 721,562 v-safe registrants aged ≥18 years who reported receiving a booster, 88.8% received homologous COVID-19 mRNA vaccination. Among registrants who reported a homologous COVID-19 mRNA booster dose, systemic reactions were less frequent following the booster (58.4% [Pfizer-BioNTech] and 64.4% [Moderna], respectively) than were those following dose 2 (66.7% and 78.4%, respectively). The adjusted odds of reporting a systemic reaction were higher following a Moderna COVID-19 vaccine booster, irrespective of the vaccine received for the primary series. VAERS has received 39,286 reports of adverse events after a COVID-19 mRNA booster vaccination for adults aged ≥18 years, including 36,282 (92.4%) nonserious and 3,004 (7.6%) serious events. Vaccination providers should educate patients that local and systemic reactions are expected following a homologous COVID-19 mRNA vaccine booster; however, these reactions appear less common than those following dose 2 of an mRNA-based vaccine. CDC and FDA will continue to monitor vaccine safety and provide data to guide vaccine recommendations and protect public health.

V-safe (https://vsafe.cdc.gov/en/) is a voluntary, smartphone-based U.S. safety surveillance system established to monitor adverse events after COVID-19 vaccination. The platform allows existing registrants to report receiving a COVID-19 booster dose and new registrants to enter information about all COVID-19 vaccine doses received. Health surveys are sent daily during the first week after receipt of each dose and include questions about local injection site and systemic reactions and health impacts.¶ CDC's v-safe call center contacts registrants who indicate that medical care was sought after vaccination and encourages completion of a VAERS report, if indicated.

VAERS is a U.S. national passive vaccine safety surveillance system managed by CDC and FDA that monitors adverse events after vaccination (*4*). VAERS accepts reports from health care providers, vaccine manufacturers, and members of the public.** VAERS reports are classified as serious if there are any reports of hospitalization, prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death.†† VAERS staff members

* https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic

† The FDA has authorized a booster dose of either the same product administered for the primary series (homologous) or a booster dose that differs from the product administered for the primary series (heterologous). These booster authorizations apply to all three COVID-19 vaccines used in the United States: 1) Pfizer-BioNTech COVID-19 vaccine ≥5 months after dose 2 for persons aged ≥12 years, 2) Moderna COVID-19 vaccine ≥5 months after dose 2 for persons aged ≥18 years, and 3) Janssen COVID-19 vaccine ≥2 months after a single dose for persons aged ≥18 years.

§ https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

¶ Health surveys are sent for the most recent dose entered via text messages that link to web-based surveys on days 0–7 after receipt of vaccine dose; then weekly through 6 weeks after vaccination; and then at 3, 6, and 12 months after vaccination. Local injection site reactions include itching, pain, redness, and swelling. Systemic reactions include abdominal pain, myalgia, chills, diarrhea, fatigue, fever, headache, joint pain, nausea, rash, and vomiting. Health impacts include inability to perform normal daily activities, inability to work or attend school, and receipt of medical care.

** CDC and FDA encourage all health care providers to report adverse events to VAERS and are required by COVID-19 vaccine Emergency Use Authorizations to report certain adverse events after vaccination to VAERS, including death. https://vaers.hhs.gov/faq.html

†† VAERS reports are classified as serious based on the Code of Federal Regulations Title 21 (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr). Reports of serious adverse events receive follow-up by VAERS staff members to obtain additional information, including medical records and, for reports of death, death certificates and autopsy reports, if available.

assign Medical Dictionary for Regulatory Activities (MedDRA) preferred terms to the signs, symptoms, and diagnostic findings in VAERS reports.[§§] Previous reports of myocarditis and pericarditis following receipt of COVID-19 vaccine were identified by a search for selected MedDRA preferred terms (*5*); CDC staff members attempted to collect information from health care providers about clinical course and determined whether the case definition for myocarditis or pericarditis was met.[¶¶]

Local and systemic reactions and health impacts reported during the week following booster vaccination were described for v-safe registrants aged ≥18 years who received a COVID-19 booster (≥2 months after a single dose of Janssen COVID-19 vaccine or ≥5 months after the second dose of a COVID-19 mRNA vaccine) during September 22, 2021–February 6, 2022, and completed at least one v-safe health check-in survey in the week after each vaccination. Registrants who reported receiving a COVID-19 mRNA primary vaccination series followed by a Janssen booster (476) were excluded from the analysis because of small numbers. VAERS reports for persons aged ≥18 years who received a COVID-19 mRNA vaccine booster during September 22, 2021–February 6, 2022, were described by severity (serious versus nonserious), demographic characteristics (i.e., age, sex, race, and ethnicity), and MedDRA preferred terms. Reporting rates for myocarditis reports meeting the case definition after a booster were stratified by sex and age group. Multivariable analyses were conducted to estimate the adjusted odds of reporting an adverse event or health impact by comparing 1) dose 2 and booster for registrants who received homologous COVID-19 mRNA vaccination, and 2) homologous and heterologous booster vaccination. SAS software (version 9.4; SAS Institute) was used to conduct all analyses.[***] These surveillance activities were reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[†††]

Review of v-safe Data

During September 22, 2021–February 6, 2022, a total of 721,562 unique v-safe registrants aged ≥18 years reported having received a COVID-19 vaccine booster; 640,586 (88.8%) reported homologous COVID-19 mRNA vaccination. Among 307,998 registrants who reported a homologous Moderna booster, local and systemic reactions were less frequently reported during the week following booster (71.8% and 64.4%, respectively) than following dose 2 (81.4% and 78.4%, respectively) (p<0.001) (Figure). Among 332,588 registrants who reported a homologous Pfizer-BioNTech booster, local and systemic reactions were also reported less frequently following the booster (64.3% and 58.4%, respectively) than following dose 2 (68.1% and 66.7%, respectively) (p<0.001). Health impacts, including inability to perform daily activities and inability to work, were also reported less frequently following dose 2. Among homologous Moderna booster recipients, receipt of medical care was reported more frequently following the booster (0.8%) than dose 2 (0.7%); however, the difference was not significant (p = 0.06). Among homologous Pfizer-BioNTech booster recipients, receipt of medical care was reported significantly (p<0.001) more frequently following the booster (0.9%) than following dose 2 (0.6%). All registrants who indicated that medical care was sought after vaccination were contacted and encouraged to complete a VAERS report.

Among primary Moderna, Pfizer-BioNTech, and Janssen series v-safe registrants, 94.1%, 95.1%, and 17.2%, respectively, received a homologous booster. Among primary mRNA series vaccine v-safe registrants, 5.9% of Moderna and 4.8% of Pfizer-BioNTech registrants received a heterologous mRNA vaccine booster. Among primary Janssen v-safe registrants, 52.3% received a Moderna booster, and 30.5% received a Pfizer-BioNTech booster (Table 1). Among registrants who received a Moderna COVID-19 vaccine primary series, the

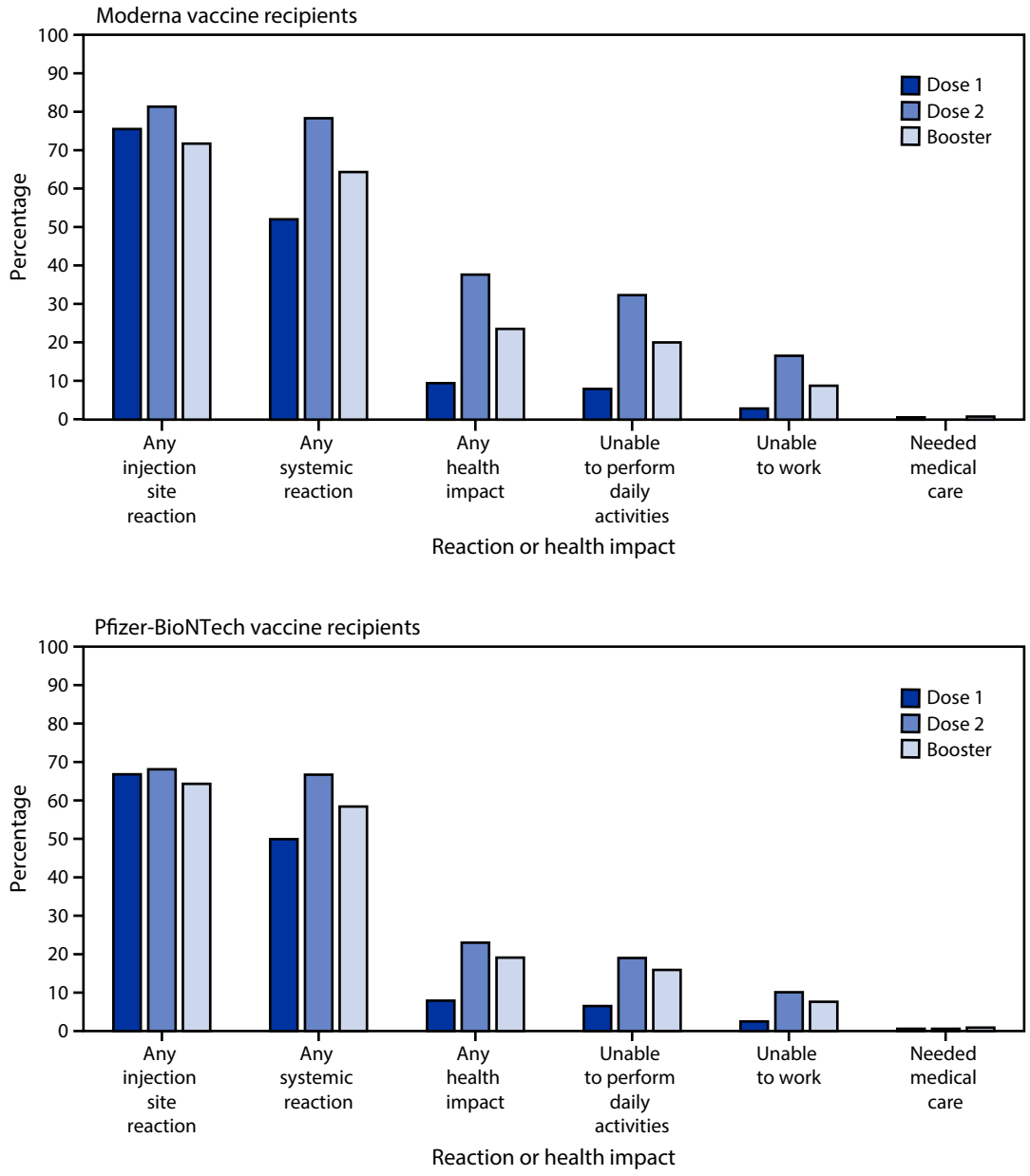
[§§] Each VAERS report might be assigned more than one MedDRA preferred term. A MedDRA coded event does not indicate a medically confirmed diagnosis. https://www.meddra.org/how-to-use/basics/hierarchy

[¶¶] Acute myocarditis was defined as presence of signs and symptoms new onset or worsening of one or more of the following signs or symptoms: chest pain, pressure, discomfort, dyspnea, shortness of breath, pain with breathing, palpitations, or syncope; or two or more of the following signs or symptoms in children aged ≤11 years: irritability, vomiting, poor feeding, tachypnea, or lethargy); and one or more new finding of elevated troponin, electrocardiogram findings consistent with myocarditis, abnormal cardiac function or wall motion on echocardiogram, cardiac magnetic resonance imaging findings consistent with myocarditis, or histopathologic findings consistent with myocarditis; and no other identifiable cause for these findings.

[***] The odds of reporting an adverse event or health impact following dose 2 and booster were compared for registrants who received homologous COVID-19 mRNA vaccination using a multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables (i.e., age, sex, race, and ethnicity). The odds of reporting an event following homologous and heterologous booster vaccination were compared using a logistic regression model that adjusted for demographic variables of registrants; p<0.01 was considered significant. Odds ratios were not adjusted for persons who reported a primary Janssen series because of small numbers. The model did not converge for the 476 registrants who reported COVID-19 mRNA vaccination primary dose followed by a Janssen booster, and these registrants were excluded from the analysis.

[†††] 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. Adverse reactions and health impacts* reported by adults aged ≥18 years who received a homologous Moderna (N = 307,998), or Pfizer-BioNTech (N = 332,588) COVID-19 vaccine booster and completed at least one v-safe health check-in survey on days 0–7 after each vaccine dose, by dose — United States, September 22, 2021–February 6, 2022



* Local injection site reactions include itching, pain, redness, and swelling. Systemic reactions include abdominal pain, myalgia, chills, diarrhea, fatigue, fever, headache, joint pain, nausea, rash, and vomiting. Health impacts include inability to perform normal daily activities, inability to work or attend school, and receipt of medical care. The odds of reporting any local injection site or systemic reaction or health impact following dose 2 and booster dose were compared using a multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables; $p<0.01$ was considered statistically significant. All dose 2 and booster dose comparisons were statistically significant, except receipt of medical care among homologous Moderna COVID-19 vaccine recipients.

odds of reporting a systemic reaction (calculated using a logistic regression model that adjusted for demographic variables) were lower among those who reported a heterologous Pfizer-BioNTech vaccine booster than among those who reported a homologous Moderna COVID-19 vaccine booster (adjusted odds ratio [aOR] = 0.85; 95% CI = 0.82–0.88). Among v-safe registrants who received a Pfizer-BioNTech or Janssen primary series, the odds of reporting a systemic reaction were higher among those who received a heterologous Moderna vaccine booster than among those who received a homologous

TABLE 1. Adjusted odds ratios* and 95% CI for reactions and health impacts following homologous or heterologous COVID-19 vaccine booster dose among adults aged ≥18 years, by primary vaccination series and booster vaccine product received (N = 721,562) — United States, September 22, 2021–February 6, 2022

Primary series/Booster vaccine (no.)	No. of booster doses (%)	Reaction† (%)		
		Any injection site reaction	Any systemic reaction	Any health impact
Moderna§ (n = 327,464)				
Moderna	307,998 (94.1)	71.8	64.4	23.6
Pfizer-BioNTech	19,222 (5.9)	70.7	66.7	23.4
aOR (95% CI)	—	0.70 (0.68–0.73)¶	0.85 (0.82–0.88)¶	0.81 (0.78–0.84)¶
Pfizer-BioNTech§ (n = 349,545)				
Pfizer-BioNTech	332,588 (95.1)	64.3	58.4	19.1
Moderna	16,725 (4.8)	87.7	82.9	39.5
aOR (95% CI)	—	2.41 (2.30–2.53)¶	2.24 (2.14–2.33)¶	2.06 (1.99–2.13)¶
Janssen (n = 44,553)**				
Janssen	7,656 (17.2)	52.3	56.2	16.6
Moderna	23,310 (52.3)	65.9	58.2	19.0
OR (95% CI)	—	1.76 (1.67–1.86)¶	1.08 (1.03–1.14)¶	1.18 (1.10–1.26)¶
Pfizer-BioNTech	13,587 (30.5)	62.0	56.6	16.8
OR (95% CI)	—	1.49 (1.41–1.57)¶	1.01 (0.96–1.07)	1.01 (0.94–1.09)

Abbreviations: aOR = adjusted odds ratio; OR = odds ratio.

* Includes persons who completed at least one v-safe health check-in survey on days 0–7 after receipt of each vaccine dose. The odds of reporting an event following homologous (referent group) and heterologous booster vaccination were compared using a logistic regression model that adjusted for demographic variables (i.e., age, sex, race, and ethnicity) of registrants. Odds ratios were not adjusted for persons who reported a primary Janssen series because of small numbers.

† Local injection site reactions include itching, pain, redness, and swelling. Systemic reactions include abdominal pain, myalgia, chills, diarrhea, fatigue, fever, headache, joint pain, nausea, rash, and vomiting. Health impacts include inability to perform normal daily activities, inability to work or attend school, and receipt of medical care.

§ The model did not converge for the 476 registrants who reported COVID-19 mRNA vaccination primary dose followed by a Janssen booster, and they were excluded from the analysis.

¶ P<0.01 was considered statistically significant.

** Includes persons who received a primary Janssen single-dose and one additional dose of vaccine from the listed manufacturers.

COVID-19 vaccine booster (aOR = 2.24; 95% CI = 2.14–2.33 [Pfizer-BioNTech primary series recipients] and OR = 1.08; 95% CI = 1.03–1.14 [Janssen primary series recipients]).

Review of VAERS Data

During September 22, 2021–February 6, 2022, VAERS received and processed 39,286 reports of adverse events following receipt of a COVID-19 mRNA vaccine booster for persons aged ≥18 years; the median age was 54 years, and 25,966 (66.1%) reports were in women. Most VAERS reports were for nonserious events (36,282; 92.4%); the most commonly reported conditions were headache (5,237; 13.3%), fever (5,194; 13.2%), and pain (4,931; 12.6%). Among 37 reports of myocarditis that met the case definition, 26 (70.3%) were in men, and the median patient age was 32 years. The reporting rate for myocarditis (Table 2) was highest among men aged 18–24 years following Moderna COVID-19 vaccine booster (8.7 per 1 million doses administered). One person with myocarditis reported to VAERS after COVID-19 vaccination died; investigation of this death is ongoing and to date has not eliminated other potential contributory factors.

Discussion

Among 721,562 v-safe registrants aged ≥18 years who reported receiving a COVID-19 vaccine booster, most received homologous COVID-19 mRNA vaccination. Similar to findings from Moderna and Pfizer-BioNTech clinical trials (*6*,*7*), observational v-safe data demonstrated that local and systemic reactions were reported less frequently following a homologous booster dose than after receipt of the second COVID-19 mRNA vaccine dose. Medical care was rarely sought; however, registrants reported care significantly more frequently following administration of Pfizer-BioNTech COVID-19 booster vaccination than after Pfizer-BioNTech COVID-19 dose 2. V-safe does not capture diagnoses associated with hospitalization; however, registrants can include supplemental text for each health check-in. Whether hospitalization was the result of vaccination could not be determined from v-safe data; however, all registrants who reported hospitalization were contacted and encouraged to complete a VAERS report.

A recently published study evaluating the immunogenicity and safety of heterologous booster vaccinations for all COVID-19 vaccines authorized in the United States found that reports of adverse events were similar, regardless of the type of booster received; however, the sample size was not large enough to compare small differences in risk.§§§ In v-safe, heterologous boosters were infrequently reported; however, the odds of reporting a systemic reaction were higher following a Moderna COVID-19 vaccine booster, irrespective of the primary series received. This finding is consistent with reactions reported

§§§ https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2

TABLE 2. Cases and rates* of myocarditis reported to the Vaccine Adverse Event Reporting System† following receipt of an mRNA COVID-19 booster dose among adults aged ≥18 years (N = 37), by age, sex, and vaccine product received — United States, September 22, 2021–February 6, 2022

	No. of cases (rates)*,§			
	Pfizer-BioNTech (n = 18)		Moderna (n = 18)	
Age group, yrs	Men (n = 16)	Women (n<5)	Men (n = 10)	Women (n = 8)
18–24	5 (4.1)	<5 (<1.0)	6 (8.7)	<5 (1.1)
25–29	<5 (1.1)	0 (—)	<5 (3.2)	<5 (1.2)
30–39	<5 (1.7)	<5 (<1.0)	<5 (<1.0)	<5 (1.5)
40–49	0 (—)	0 (—)	0 (—)	<5 (<1.0)
50–64	<5 (<1.0)	0 (—)	0 (—)	<5 (<1.0)
≥65¶	5 (<1.0)	0 (—)	<5 (<1.0)	0 (—)

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; VAERS = Vaccine Adverse Event Reporting System.
* Cases per 1 million doses administered.
† VAERS reports of myocarditis were identified using a combination of MedDRA preferred terms, with symptom onset during day of vaccination through day 6 after vaccination and verified to meet case definition by clinician interview with a health care provider, or clinician review of the medical record. The analysis includes persons receiving both homologous and heterologous booster doses.
§ Cells with fewer than two persons were suppressed and indicated as "<5" for confidentiality.
¶ Includes one report with sex of patient not reported.

to v-safe following Moderna primary series vaccination (*8*). The adjusted odds ratios appear to differ qualitatively from the raw frequencies, possibly because of the strong relationship between age and vaccine received; participants reporting a heterologous booster dose are younger than participants reporting a homologous booster and might therefore be more likely to report reactions following vaccination (*8*).

Myocarditis is a rare adverse event associated with receipt of COVID-19 mRNA vaccines; the overall reporting rates of myocarditis following COVID-19 mRNA vaccination were highest among males aged <18 years (*5*). To date, 37 reports to VAERS of myocarditis among adults aged ≥18 years have met the case definition following administration of 81.2 million COVID-19 mRNA booster doses in the United States. One death was reported; investigation is ongoing, and other contributory factors for myocarditis are being evaluated. Among adults, the VAERS reporting rate for myocarditis following COVID-19 mRNA booster was highest (8.7 per 1 million doses administered) among men aged 18–24 years following Moderna COVID-19 booster vaccination; however, this reporting rate is lower than that following dose 2 Moderna COVID-19 vaccine for men aged 18–24 years (56.3 per 1 million doses administered) (*5*).

The findings in this report are subject to at least four limitations. First, v-safe is a voluntary program; therefore, v-safe registrants might not be representative of the entire vaccinated population (<1% of total booster recipients registered in v-safe). Second, VAERS is a passive surveillance system and subject to reporting biases and underreporting, especially of nonserious events (*4*). Third, data were insufficient to analyze COVID-19 mRNA primary series followed by a Janssen booster. Finally, assessment of myocarditis reports to VAERS received during the study period is ongoing, and counts are subject to change.

ACIP recommends that all persons aged ≥12 years receive a COVID-19 booster dose at least 5 months after receipt of dose 2 of an mRNA vaccine for the prevention of COVID-19 (*9*). Preliminary safety findings for booster vaccination from real-world settings are similar to those described in clinical trials (*6*,*7*). Vaccination providers should educate patients that local and systemic reactions are expected following a homologous COVID-19 mRNA vaccine booster. These reactions are less common than those following the second dose in the primary series. CDC and FDA will continue to monitor vaccine safety and will provide updates as needed to guide COVID-19 vaccination recommendations.

Summary

What is already known about this topic?

In preauthorization trials, adverse reactions were reported less frequently following a homologous COVID-19 mRNA vaccine booster dose than after receipt of the second primary dose.

What is added by this report?

Review of surveillance data found that local and systemic reactions were less frequent after a homologous COVID-19 mRNA vaccine booster dose than after the second primary vaccine dose. Myocarditis was rarely reported following an mRNA vaccine booster dose.

What are the implications for public health practice?

All persons aged ≥12 years should receive a COVID-19 booster dose. Vaccination providers should educate patients that local and systemic reactions are expected following a homologous COVID-19 mRNA vaccine booster; however, these reactions are less common than those following the second primary series dose.

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References

1. Food and Drug Administration. Pfizer-BioNTech COVID-19 vaccine letter of authorization. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/media/150386/download
2. Food and Drug Administration. Moderna COVID-19 vaccine decision memorandum. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/media/154405/download
3. Food and Drug Administration. Janssen COVID-19 vaccine decision memorandum. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/media/154359/download
4. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine 2015;33:4398–405. PMID:26209838 https://doi.org/10.1016/j.vaccine.2015.07.035
5. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination, United States, December 2020–August 2021. JAMA 2022;327:331–40. https://doi.org/10.1001/jama.2021.24110
6. Gruber WC. BNT162b2 [COMIRNATY (COVID-19 vaccine, mRNA)] booster (third) dose. Advisory Committee on Immunization Practices meeting; September 22, 2021; Atlanta, Georgia. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-09-22/02-COVID-Gruber-508.pdf
7. Miller J. Safety and immunogenicity of a 50 μg booster dose of Moderna COVID-19 vaccine. Advisory Committee on Immunization Practices meeting; October 21, 2021; Atlanta, Georgia. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/02-COVID-Miller-508.pdf
8. Chapin-Bardales J, Gee J, Myers T. Reactogenicity following receipt of mRNA-based COVID-19 vaccines. JAMA 2021;325:2201–2. PMID:33818592 https://doi.org/10.1001/jama.2021.5374
9. Mbaeyi S, Oliver SE, Collins JP, et al. The Advisory Committee on Immunization Practices' Interim recommendations for additional primary and booster doses of COVID-19 vaccines—United States, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1545–52. PMID:34735422 https://doi.org/10.15585/mmwr.mm7044e2

Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022

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CDC recommends that all persons aged ≥12 years receive a booster dose of COVID-19 mRNA vaccine ≥5 months after completion of a primary mRNA vaccination series and that immunocompromised persons receive a third primary dose.* Waning of vaccine protection after 2 doses of mRNA vaccine has been observed during the period of the SARS-CoV-2 B.1.617.2 (Delta) variant predominance† (*1–5*), but little is known about durability of protection after 3 doses during periods of Delta or SARS-CoV-2 B.1.1.529 (Omicron) variant predominance. A test-negative case-control study design using data from eight VISION Network sites§ examined vaccine effectiveness (VE) against COVID-19 emergency department/urgent care (ED/UC) visits and hospitalizations among U.S. adults aged ≥18 years at various time points after receipt of a second or third vaccine dose during two periods: Delta variant predominance and Omicron variant predominance (i.e., periods when each variant accounted for ≥50% of sequenced isolates).¶ Persons categorized as having received 3 doses included those who received a third dose in a primary series or a booster dose after a 2 dose primary series (including the reduced-dosage Moderna booster). The VISION Network analyzed 241,204 ED/UC encounters** and 93,408 hospitalizations across 10 states during August 26, 2021–January 22, 2022. VE after receipt of both 2 and 3 doses was lower during the Omicron-predominant than during the Delta-predominant period at all time points evaluated. During both periods, VE after receipt of a third dose was higher than that after a second dose; however, VE waned with increasing time since vaccination. During the Omicron period, VE against ED/UC visits was 87% during the first 2 months after a third dose and decreased to 66% among those vaccinated 4–5 months earlier; VE against hospitalizations was 91% during the first 2 months following a third dose and decreased to 78% ≥4 months after a third dose. For both Delta- and Omicron-predominant periods, VE was generally higher for protection against hospitalizations than against ED/UC visits. All eligible persons should remain up to date with recommended COVID-19 vaccinations to best protect against COVID-19–associated hospitalizations and ED/UC visits.

* On November 29, 2021, CDC initially recommended a third dose of mRNA vaccine for all adults 6 months after receipt of the second primary series mRNA COVID-19 vaccine dose. The third dose of the BNT162b2 (Pfizer-BioNTech) vaccine was the same dosage as the primary series; however, the third dose of the mRNA-1273 (Moderna) vaccine was a reduced dosage compared with the primary series for all but immunocompromised persons; the third dose was either a 100-μg or 50-μg dose of Moderna vaccine or a 30-μg dose of the Pfizer-BioNTech vaccine. On January 4, 2022, CDC amended the interval to 5 months after receipt of the second dose for recipients of the Pfizer-BioNTech vaccine. On January 7, 2022, CDC amended the interval to 5 months for recipients of the Moderna vaccine. CDC recommends the Pfizer-BioNTech booster at 5 months, and an additional primary dose for certain immunocompromised children (https://www.cdc.gov/media/releases/2022/s0104-Pfizer-Booster.html). CDC recommends the Moderna booster at 5 months after completion of the primary series. (https://www.cdc.gov/media/releases/2022/s0107-moderna-booster.html). CDC recommends additional primary doses for some immunocompromised persons (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html).

† https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3961378

§ Funded by CDC, the VISION Network includes Baylor Scott & White Health (Texas), Columbia University Irving Medical Center (New York), HealthPartners (Minnesota and Wisconsin), Intermountain Healthcare (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), Regenstrief Institute (Indiana), and University of Colorado (Colorado).

¶ Partners contributing data on medical events (and estimated dates of Omicron predominance) were as follows: California (December 21), Colorado (December 19), Indiana (December 26), Minnesota and Wisconsin (December 25), New York (December 18), Oregon (December 24), Texas (December 16), Utah (December 24), and Washington (December 24). The study period began in September 2021 for partners located in Texas.

** ED data at Columbia University Irving Medical Center and HealthPartners exclude encounters that were transferred to an inpatient setting.

VISION Network methods have been previously published (*6*). Eligible medical encounters were defined as those among adults aged ≥18 years with a COVID-19–like illness diagnosis[††] who had received molecular testing (primarily reverse transcription–polymerase chain reaction assay) for SARS-CoV-2, the virus that causes COVID-19, during the 14 days before through 72 hours after the medical encounter. The study period began on August 26, 2021, 14 days after the first U.S. recommendation for a third mRNA COVID-19 vaccine dose.[§§] The date when the Omicron variant accounted for ≥50% of sequenced isolates was determined for each study site based on state and national surveillance data. Recipients of Ad.26.COV2.S (Janssen [Johnson & Johnson]) vaccine, 1 or >3 doses of an mRNA vaccine, and those for whom <14 days had elapsed since receipt of any dose were excluded.

VE was estimated using a test-negative design, comparing the odds of a positive SARS-CoV-2 test result between vaccinated and unvaccinated patients using logistic regression models conditioned on calendar week and geographic area and adjusting for age, local virus circulation, immunocompromised status, additional patient comorbidities, and other patient and facility characteristics.[¶¶] Immunocompromised status was identified by previously published diagnosis codes.[***] Vaccination status was categorized based on the number of vaccine doses received and number of days between receipt of the most recent vaccine dose and the index medical encounter date (referred to as time since vaccination).[†††] Patients with no record of mRNA vaccination before the index date were considered unvaccinated. Persons categorized as having received 3 doses included those who received a third dose in a primary series or a booster dose after a 2 dose primary series (including the reduced-dosage Moderna booster).

A standardized mean or proportion difference ≥0.2 indicated a nonnegligible difference in distributions of vaccination or infection status. The most remote category of time since vaccination was either ≥4 months or ≥5 months, depending on data availability (no hospitalizations were observed ≥5 months after receipt of a third dose during either period). To test for a trend in waning, time since vaccination categories were specified as an ordinal variable (<2 months = 0; 2–3 months = 1; 4 months = 2; ≥5 months = 3), with statistically significant waning indicated by a p-value <0.05 for the resulting regression coefficient. SAS (version 9.4, SAS Institute) and R software (version 4.1.2, R Foundation) were used to prepare data and perform statistical analysis.

For illustration purposes, the earliest and latest VE estimates for the trend are described. The overall trend can be statistically significant even though the precision of each estimate might be low, with the 95% CIs of estimates including zero. Analyses were stratified by two periods: Delta variant predominance and Omicron variant predominance. This study was reviewed and approved by the institutional review boards at participating sites and under a reliance agreement with the Westat, Inc. Institutional Review Board.[§§§]

Among 241,204 eligible ED/UC encounters, 185,652 (77%) and 55,552 (23%) occurred during the Delta- and Omicron-predominant periods, respectively (Table 1). Among persons with COVID-19–like illness seeking care at ED/UC facilities, 46% were unvaccinated, 44% had received 2 doses of vaccine, and 10% had received 3 doses. The median interval since receipt of the most recent dose before the ED/UC encounter was 214 days (IQR = 164–259 days) among those who had received 2 doses and 49 days (IQR = 30–73) among those who had received 3 doses (CDC, unpublished data, 2022).

During the Delta-predominant period, VE against laboratory-confirmed COVID-19–associated ED/UC encounters was higher after receipt of a third dose than after a second dose; however, VE declined with increasing time since vaccination (Table 2). Among recipients of 3 doses, VE was 97% within 2 months of vaccination and declined to 89% among those vaccinated ≥4 months earlier (p<0.001 for test of trend in waning VE).

[††] COVID-19–like illness diagnoses included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using diagnosis codes from the *International Classification of Diseases, Ninth Revision* and *International Classification of Diseases, Tenth Revision*.

[§§] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised

[¶¶] VE was calculated as [1 − odds ratio] x 100%, estimated using a test-negative design, which can be considered a case-control design in which case-patients were those whose outcome was confirmed COVID-19 and control patients were those with COVID-19–like illness and negative SARS-CoV-2 test results. All VE models were conditioned on calendar week and geographic area and adjusted for age, local virus circulation (percentage of SARS-CoV-2–positive results from testing within the counties surrounding the facility on the date of the encounter), propensity to be vaccinated (calculated separately for each VE estimate), and other patient and facility characteristics. Generalized boostered regression tree methods were used to estimate the propensity to be vaccinated based on sociodemographic characteristics, underlying medical conditions, and facility characteristics.

[***] Immunocompromising conditions were derived from lists used in previous studies of large hospital-based or administrative databases and included the following conditions: 1) solid malignancies, 2) hematologic malignancies, 3) rheumatologic or inflammatory disorders, 4) other intrinsic immune conditions or immunodeficiencies, and 5) organ or stem cell transplants. https://www.cdc.gov/mmwr/volumes/70/wr/mm7044e3.htm?s_cid=mm7044e3_w

[†††] The index date for each medical visit was defined as either the date of collection of a respiratory specimen associated with the most recent positive or negative SARS-CoV-2 test result before the medical visit or the date of the medical visit (if testing occurred only after the admission or visit date).

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

TABLE 1. Characteristics of emergency department and urgent care encounters among adults with COVID-19–like illness,* by mRNA COVID-19 vaccination status† and SARS-CoV-2 test result — 10 states,§ August 2021–January 2022¶

Characteristic	Total no. (column %)	mRNA COVID-19 vaccination status no. (row %)			SMD††	SARS-CoV-2 test result no. (row %)		SMD††
		Unvaccinated	Vaccinated (2 doses)	Vaccinated (3 doses)**		Negative	Positive	
All ED/UC encounters	**241,204 (100)**	110,873 (46)	105,193 (44)	25,138 (10)	—	179,378 (74)	61,826 (26)	—
Variant predominance period								
B.1.617.2 (Delta)	**185,652 (77)**	86,074 (46)	85,371 (46)	14,207 (8)	0.27	148,106 (80)	37,546 (20)	0.50
B.1.1.529 (Omicron)	**55,552 (23)**	24,799 (45)	19,822 (36)	10,931 (20)		31,272 (56)	24,280 (44)	
Site								
Baylor Scott & White Health	**40,621 (17)**	23,827 (59)	14,438 (36)	2,356 (6)	0.70	28,701 (71)	11,920 (29)	0.40
Columbia University§§	**5,681 (2)**	3,039 (53)	2,388 (42)	254 (4)		4,025 (71)	1,656 (29)	
HealthPartners§§	**4,893 (2)**	1,352 (28)	3,270 (67)	271 (6)		4,109 (84)	784 (16)	
Intermountain Healthcare	**61,333 (25)**	25,072 (41)	29,407 (48)	6,854 (11)		50,637 (83)	10,696 (17)	
Kaiser Permanente Northern California	**45,753 (19)**	11,165 (24)	25,335 (55)	9,253 (20)		34,715 (76)	11,038 (24)	
Kaiser Permanente Northwest	**16,625 (7)**	5,895 (35)	8,620 (52)	2,110 (13)		13,561 (82)	3,064 (18)	
Regenstrief Institute	**41,694 (17)**	26,799 (64)	12,541 (30)	2,354 (6)		25,420 (61)	16,274 (39)	
University of Colorado	**24,604 (10)**	13,724 (56)	9,194 (37)	1,686 (7)		18,210 (74)	6,394 (26)	
Age group, yrs								
18–44	**110,203 (46)**	65,073 (59)	40,936 (37)	4,194 (4)	0.81	80,085 (73)	30,118 (27)	0.23
45–64	**64,583 (27)**	28,479 (44)	30,272 (47)	5,832 (9)		45,710 (71)	18,873 (29)	
65–74	**31,172 (13)**	9,390 (30)	15,289 (49)	6,493 (21)		24,304 (78)	6,868 (22)	
75–84	**23,242 (10)**	5,360 (23)	12,160 (52)	5,722 (25)		19,155 (82)	4,087 (18)	
≥85	**12,004 (5)**	2,571 (21)	6,536 (54)	2,897 (24)		10,124 (84)	1,880 (16)	
Sex								
Male¶¶	**97,859 (41)**	47,368 (48)	40,062 (41)	10,429 (11)	0.06	70,430 (72)	27,429 (28)	0.10
Female	**143,345 (59)**	63,505 (44)	65,131 (45)	14,709 (10)		108,948 (76)	34,397 (24)	
Race/Ethnicity								
White, non-Hispanic	**150,419 (62)**	65,355 (43)	67,433 (45)	17,631 (12)	0.30	116,134 (77)	34,285 (23)	0.22
Hispanic	**37,043 (15)**	18,238 (49)	16,054 (43)	2,751 (7)		26,148 (71)	10,895 (29)	
Black, non-Hispanic	**24,702 (10)**	14,633 (59)	8,653 (35)	1,416 (6)		16,534 (67)	8,168 (33)	
Other, non-Hispanic***	**17,683 (7)**	6,153 (35)	9,009 (51)	2,521 (14)		13,360 (76)	4,323 (24)	
Unknown	**11,357 (5)**	6,494 (57)	4,044 (36)	819 (7)		7,202 (63)	4,155 (37)	
Chronic respiratory condition†††								
Yes¶¶	**42,531 (18)**	17,884 (42)	19,359 (46)	5,288 (12)	0.09	35,264 (83)	7,267 (17)	0.22
No	**198,673 (82)**	92,989 (47)	85,834 (43)	19,850 (10)		144,114 (73)	54,559 (27)	
Chronic nonrespiratory condition§§§								
Yes¶¶	**62,192 (26)**	24,884 (40)	29,202 (47)	8,106 (13)	0.17	50,304 (81)	11,888 (19)	0.21
No	**179,012 (74)**	85,989 (48)	75,991 (42)	17,032 (10)		129,074 (72)	49,938 (28)	
Immunocompromised status¶¶¶								
Yes¶¶	**9,546 (4)**	3,348 (35)	4,462 (47)	1,736 (18)	0.12	8,222 (86)	1,324 (14)	0.14
No	**231,658 (96)**	107,525 (46)	100,731 (43)	23,402 (10)		171,156 (74)	60,502 (26)	
Total vaccinated	**130,331 (54)**	—	105,193 (81)	25,138 (19)		111,559 (86)	18,772 (14)	

See table footnotes on the next page.

During the Omicron-predominant period, VE against COVID-19–associated ED/UC encounters was lower overall compared with that during the Delta-predominant period and waned after the second dose, from 69% within 2 months of vaccination to 37% at ≥5 months after vaccination (p<0.001). Protection increased after a third dose, with VE of 87% among those vaccinated within the past 2 months; however, VE after 3 doses declined to 66% among those vaccinated 4–5 months earlier and 31% among those vaccinated ≥5 months earlier, although the latter estimate is imprecise because few data were available on persons vaccinated for ≥5 months after a third dose. The decreasing trend of VE with increasing time since vaccination was significant (p<0.001).

Among 93,408 eligible hospitalizations, 83,045 (89%) and 10,363 (11%) occurred during the Delta- and Omicron-predominant periods, respectively (Table 3). Among persons hospitalized with COVID-19–like illness, 43% were unvaccinated, 45% had received 2 vaccine doses, and 12% had received 3 doses. The median interval since receipt of the most recent dose before hospitalization was 216 days (IQR = 175–257 days) among those who had received 2 doses and 46 days (IQR = 29–67 days) among those who had received 3 doses, (CDC, unpublished data, 2022).

TABLE 1. (*Continued*) Characteristics of emergency department and urgent care encounters among adults with COVID-19–like illness,* by mRNA COVID-19 vaccination status† and SARS-CoV-2 test result — 10 states,§ August 2021–January 2022¶

Characteristic	Total no. (column %)	mRNA COVID-19 vaccination status no. (row %)			SMD††	SARS-CoV-2 test result no. (row %)		SMD††
		Unvaccinated	Vaccinated (2 doses)	Vaccinated (3 doses)**		Negative	Positive	
Vaccine product								
Pfizer-BioNTech	**79,806 (61)**	—	63,912 (80)	15,894 (20)	—	67,179 (84)	12,627 (16)	0.15
Moderna	**48,990 (38)**	—	41,046 (84)	7,944 (16)		42,980 (88)	6,010 (12)	
Combination of mRNA products	**1,535 (1)**	—	235 (15)	1,300 (85)		1,400 (91)	135 (9)	
No. of doses received (interval from receipt of most recent dose to ED/UC encounter)								
2 (<2 mos)	**4,808 (4)**	—	4,808 (100)	—	—	4,507 (94)	301 (6)	0.38
2 (2–3 mos)	**10,644 (8)**	—	10,644 (100)	—		9,332 (88)	1,312 (12)	
2 (4 mos)	**10,175 (8)**	—	10,175 (100)	—		8,945 (88)	1,230 (12)	
2 (≥5 mos)	**79,566 (61)**	—	79,566 (100)	—		65,922 (83)	13,644 (17)	
3 (<2 mos)	**15,614 (12)**	—	—	15,614 (100)		14,694 (94)	920 (6)	
3 (2–3 mos)	**8,759 (7)**	—	—	8,759 (100)		7,639 (87)	1,120 (13)	
3 (4 mos)	**736 (1)**	—	—	736 (100)		509 (69)	227 (31)	
3 (≥5 mos)	**29 (0)**	—	—	29 (100)		11 (38)	18 (62)	

Abbreviations: ED = emergency department; ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision;* SMD = standardized mean or proportion difference; UC = urgent care.

* Medical events with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after admission were included. Recipients of Janssen vaccine, 1 or >3 doses of an mRNA vaccine, and those for whom 1–13 days had elapsed since receipt of any dose were excluded.

† Vaccination was defined as having received the listed number of doses of an mRNA-based COVID-19 vaccine ≥14 days before the medical event index date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before medical event or the admission date if testing only occurred after the admission.

§ California, Colorado, Indiana, Minnesota, New York, Oregon, Texas, Utah, Washington, and Wisconsin.

¶ Partners contributing data on medical events and estimated date of Omicron predominance were in California (December 21), Colorado (December 19), Indiana (December 26), Minnesota and Wisconsin (December 25), New York (December 18), Oregon (December 24), Texas (December 16), Utah (December 24), and Washington (December 24). The study period began in September 2021 for partners located in Texas.

** The "Vaccinated (3 doses)" category includes persons who have received a third dose in their primary series or have received a booster dose following their 2-dose primary series; the third dose could have been either a 100-μg or 50-μg dose of Moderna vaccine or a 30-μg dose of the Pfizer-BioNTech vaccine.

†† An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between medical events for vaccinated versus unvaccinated patients. When calculating SMDs for differences in characteristics across mRNA COVID-19 vaccination status, the SMD was calculated as the average of the absolute value of the SMD for unvaccinated versus vaccinated with 2 doses and the absolute value of the SMD for unvaccinated versus vaccinated with 3 doses. All SMDs are reported as the absolute SMD.

§§ ED data at Columbia University Irving Medical Center and HealthPartners exclude encounters that were transferred to an inpatient setting.

¶¶ Referent group used for SMD calculations for dichotomous variables.

*** Other race includes Asian, Native Hawaiian or other Pacific islander, American Indian or Alaska Native, Other not listed, and multiple races.

††† Chronic respiratory condition was defined using ICD-9 and ICD-10 as the presence of discharge codes for asthma, chronic obstructive pulmonary disease, or other lung disease.

§§§ Chronic nonrespiratory condition was defined using ICD-9 and ICD-10 as the presence of discharge codes for heart failure, ischemic heart disease, hypertension, other heart disease, stroke, other cerebrovascular disease, diabetes type I or II, other diabetes, metabolic disease, clinical obesity, clinically underweight, renal disease, liver disease, blood disorder, immunosuppression, organ transplant, cancer, dementia, neurologic disorder, musculoskeletal disorder, or Down syndrome.

¶¶¶ Immunocompromised status was defined using ICD-9 and ICD-10 as the presence of discharge codes for solid malignancy, hematologic malignancy, rheumatologic or inflammatory disorder, other intrinsic immune condition or immunodeficiency, or organ or stem cell transplant.

During the Delta-predominant period, 2-dose VE against laboratory-confirmed COVID-19–associated hospitalizations declined with increasing time since vaccination and increased after a third dose (Table 2). Among recipients of 3 doses during the Delta-predominant period, VE against COVID-19–associated hospitalizations declined from 96% within 2 months of vaccination to 76% among those vaccinated ≥4 months earlier although the latter estimate is imprecise because few data were available on persons vaccinated for ≥4 months after a third dose during the Delta-predominant period (p<0.001 for test of trend in waning VE).

During the period of Omicron predominance, VE against COVID-19–associated hospitalizations was lower overall and waned with time since vaccination: VE after a second dose declined from 71% within 2 months of vaccination to 54% among those vaccinated ≥5 months earlier (p = 0.01). Among recipients of 3 doses, VE against COVID-19–associated hospitalizations declined from 91% among those vaccinated within the past 2 months to 78% among those vaccinated ≥4 months earlier (p<0.001).

TABLE 2. mRNA COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated† emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years, by number and timing of vaccine doses§ — VISION Network, 10 states,¶ August 2021–January 2022**

Characteristic	Total	SARS-CoV-2 positive test result no. (%)	VE fully adjusted % (95% CI)*	Waning trend p value††
ED/UC encounters				
Overall				
Unvaccinated (Ref)	**110,873**	43,054 (39)	—	—
Any mRNA vaccine, 2 doses	**105,193**	16,487 (16)	72 (72–73)	<0.001
<2 mos	**4,808**	301 (6)	88 (87–90)	
2–3 mos	**10,644**	1,312 (12)	80 (78–81)	
4 mos	**10,175**	1,230 (12)	79 (77–80)	
≥5 mos	**79,566**	13,644 (17)	69 (68–70)	
Any mRNA vaccine, 3 doses	**25,138**	2,285 (9)	89 (89–90)	<0.001
<2 mos	**15,614**	920 (6)	92 (91–93)	
2–3 mos	**8,759**	1,120 (13)	86 (85–87)	
4 mos	**736**	227 (31)	75 (70–79)	
≥5 mos	**29**	18 (62)	50 (-7–77)	
Delta-predominant period				
Unvaccinated (Ref)	**86,074**	29,063 (34)	—	—
Any mRNA vaccine, 2 doses	**85,371**	8,136 (10)	80 (79–81)	<0.001
<2 mos	**4,253**	144 (3)	92 (91–94)	
2–3 mos	**8,662**	527 (6)	88 (86–89)	
4 mos	**8,941**	721 (8)	85 (83–86)	
≥5 mos	**63,515**	6,744 (11)	77 (76–78)	
Any mRNA vaccine, 3 doses	**14,207**	347 (2)	96 (95–96)	<0.001
<2 mos	**10,621**	210 (2)	97 (96–97)	
2–3 mos	**3,542**	134 (4)	93 (92–94)	
≥4 mos	**44**	3 (7)	89 (64–97)	
Omicron-predominant period				
Unvaccinated (Ref)	**24,799**	13,991 (56)	—	—
Any mRNA vaccine, 2 doses	**19,822**	8,351 (42)	41 (38–43)	<0.001
<2 mos	**555**	157 (28)	69 (62–75)	
2–3 mos	**1,982**	785 (40)	50 (45–55)	
4 mos	**1,234**	509 (41)	48 (41–54)	
≥5 mos	**16,051**	6,900 (43)	37 (34–40)	
Any mRNA vaccine, 3 doses	**10,931**	1,938 (18)	83 (82–84)	<0.001
<2 mos	**4,993**	710 (14)	87 (85–88)	
2–3 mos	**5,217**	986 (19)	81 (79–82)	
4 mos	**692**	224 (32)	66 (59–71)	
≥5 mos	**29**	18 (62)	31 (–50–68)	
Hospitalizations				
Overall				
Unvaccinated (Ref)	**40,125**	16,335 (41)	—	—
Any mRNA vaccine, 2 doses	**42,326**	4,294 (10)	82 (81–83)	<0.001
<2 mos	**1,662**	71 (4)	93 (91–94)	
2–3 mos	**3,084**	223 (7)	88 (86–90)	
4 mos	**3,279**	234 (7)	89 (87–90)	
≥5 mos	**34,301**	3,766 (11)	80 (79–81)	

See table footnotes on the next page.

Discussion

In a multistate analysis of 241,204 ED/UC encounters and 93,408 hospitalizations among adults with COVID-19–like illness during August 26, 2021–January 22, 2022, estimates of VE against laboratory-confirmed COVID-19 were lower during the Omicron-predominant than during the Delta-predominant period, after accounting for both number of vaccine doses received and time since vaccination. During both periods, VE after receipt of a third dose was always higher than VE following a second dose; however, VE waned with increasing time since vaccination. During the Omicron-predominant period, mRNA vaccination was highly effective against both COVID-19–associated ED/UC encounters (VE = 87%) and COVID-19 hospitalizations (VE = 91%) within 2 months after a third dose, but effectiveness waned, declining to 66% for prevention of COVID-19–associated ED/UC encounters by the fourth month after receipt of a third dose and to 78% for hospitalizations by the fourth month after receipt of a

TABLE 2. (*Continued*) mRNA COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated† emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years, by number and timing of vaccine doses§ — VISION Network, 10 states,¶ August 2021–January 2022**

Characteristic	Total	SARS-CoV-2 positive test result no. (%)	VE fully adjusted % (95% CI)*	Waning trend p value††
Any mRNA vaccine, 3 doses	**10,957**	471 (4)	93 (92–94)	<0.001
<2 mos	**7,332**	221 (3)	95 (94–95)	
2–3 mos	**3,413**	211 (6)	91 (89–92)	
≥4 mos	**212**	39 (18)	81 (72–87)	
Delta-predominant period				
Unvaccinated (Ref)	**36,214**	14,445 (40)	—	—
Any mRNA vaccine, 2 doses	**38,707**	3,315 (9)	85 (84–85)	<0.001
<2 mos	**1,574**	49 (3)	94 (92–96)	
2–3 mos	**2,790**	154 (6)	91 (89–92)	
4 mos	**3,129**	192 (6)	90 (89–92)	
≥5 mos	**31,214**	2,920 (9)	82 (82–83)	
Any mRNA vaccine, 3 doses	**8,124**	195 (2)	95 (95–96)	<0.001
<2 mos	**6,071**	118 (2)	96 (95–97)	
2–3 mos	**2,030**	74 (4)	93 (91–95)	
≥4 mos	**23**	3 (13)	76 (14–93)	
Omicron-predominant period				
Unvaccinated (Ref)	**3,911**	1,890 (48)	—	—
Any mRNA vaccine, 2 doses	**3,619**	979 (27)	55 (50–60)	0.01
<2 mos	**88**	22 (25)	71 (51–83)	
2–3 mos	**294**	69 (23)	65 (53–74)	
4 mos	**150**	42 (28)	58 (38–71)	
≥5 mos	**3,087**	846 (27)	54 (48–59)	
Any mRNA vaccine, 3 doses	**2,833**	276 (10)	88 (86–90)	<0.001
<2 mos	**1,261**	103 (8)	91 (88–93)	
2–3 mos	**1,383**	137 (10)	88 (85–90)	
≥4 mos	**189**	36 (19)	78 (67–85)	

Abbreviations: ED = emergency department; ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision*; Ref = referent group; UC = urgent care; VE = vaccine effectiveness.

* VE was calculated as [1 − odds ratio] x 100%, estimated using a test-negative design, conditioned on calendar week and geographic area, and adjusted for age, local virus circulation (percentage of SARS-CoV-2–positive results from testing within the counties surrounding the facility on the date of the encounter), propensity to be vaccinated (calculated separately for each VE estimate), and other factors. Generalized boosted regression tree methods were used to estimate the propensity to be vaccinated based on sociodemographic characteristics, underlying medical conditions, and facility characteristics.

† Medical events with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after admission were included. Recipients of Janssen vaccine, 1 or >3 doses of an mRNA vaccine, and those for whom <14 days had elapsed since receipt of any dose were excluded.

§ Vaccination status was documented in electronic health records and immunization registries and was defined as having received the listed number of doses of an mRNA-based COVID-19 vaccine ≥14 days before the medical event index date. Index date was defined as the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before the medical event or the admission date if testing only occurred after the admission. Persons categorized as having received 3 vaccine doses include those who received a third dose in their primary series or received a booster dose after their 2 dose primary series; the third dose could have been either a 100-μg or 50-μg dose of Moderna vaccine or a 30-μg dose of the Pfizer-BioNTech vaccine.

¶ California, Colorado, Indiana, Minnesota, New York, Oregon, Texas, Utah, Washington, and Wisconsin.

** Partners contributing data on medical events and estimated dates of Omicron predominance were in California (December 21), Colorado (December 19), Indiana (December 26), Minnesota and Wisconsin (December 25), New York (December 18), Oregon (December 24), Texas (December 16), Utah (December 24), and Washington (December 24). The study period began in September 2021 for partners located in Texas.

†† p-value for test of linear trendline fitted to VE estimates across ordinal categories of time since vaccination (<2 months = 0; 2–3 months = 1, 4 months = 2, ≥5 months = 3).

third dose. The finding of lower VE for 2 or 3 doses during the Omicron-predominant period is consistent with previous reports from the VISION network and others¶¶¶,**** (*2*,*7*). Waning of VE after receipt of a third dose of mRNA vaccine has also been observed in Israel (*8*) and in preliminary reports from the VISION Network (*2*). This analysis enhances an earlier VISION Network report (*2*) by extending the Omicron study period to January 22, 2022, providing a more detailed breakdown of time since vaccination, and using an analytic technique that better controls for potential confounding by calendar week and geographic area. By comparing COVID-19 test-positive case-patients with COVID-19 test-negative control patients in the same geographic area and for whom encounter index dates occurred within the same week, bias in

¶¶¶ https://www.medrxiv.org/content/10.1101/2021.12.14.21267615v1
**** https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v3

TABLE 3. Characteristics of hospitalizations among adults with COVID-19–like illness,* by mRNA COVID-19 vaccination status† and SARS-CoV-2 test result — 10 states,§ August 2021–January 2022¶

Characteristic	Total no. (column %)	mRNA COVID-19 vaccination status, no. (row %)			SMD††	SARS-CoV-2 test result, no. (row %)		SMD††
		Unvaccinated	Vaccinated (2 doses)	Vaccinated (3 doses)**		Negative	Positive	
All hospitalizations	**93,408 (100)**	40,125 (43)	42,326 (45)	10,957 (12)	—	72,308 (77)	21,100 (23)	—
Variant predominance period								
B.1.617.2 (Delta)	**83,045 (89)**	36,214 (44)	38,707 (47)	8,124 (10)	0.24	65,090 (78)	17,955 (22)	0.15
B.1.1.529 (Omicron)	**10,363 (11)**	3,911 (38)	3,619 (35)	2,833 (27)		7,218 (70)	3,145 (30)	
Site								
Baylor Scott & White Health	**17,110 (18)**	8,688 (51)	7,182 (42)	1,240 (7)	0.67	13,772 (80)	3,338 (20)	0.43
Columbia University	**3,491 (4)**	1,494 (43)	1,723 (49)	274 (8)		2,908 (83)	583 (17)	
HealthPartners	**1,096 (1)**	253 (23)	777 (71)	66 (6)		966 (88)	130 (12)	
Intermountain Healthcare	**8,070 (9)**	3,741 (46)	3,299 (41)	1,030 (13)		5,643 (70)	2,427 (30)	
Kaiser Permanente Northern California	**23,236 (25)**	4,967 (21)	13,264 (57)	5,005 (22)		19,952 (86)	3,284 (14)	
Kaiser Permanente Northwest	**4,170 (5)**	1,702 (41)	1,988 (48)	480 (12)		3,371 (81)	799 (19)	
Regenstrief Institute	**25,131 (27)**	13,891 (55)	9,415 (37)	1,825 (7)		16,897 (67)	8,234 (33)	
University of Colorado	**11,104 (12)**	5,389 (49)	4,678 (42)	1,037 (9)		8,799 (79)	2,305 (21)	
Age group, yrs								
18–44	**17,919 (19)**	11,649 (65)	5,550 (31)	720 (4)	0.75	12,998 (73)	4,921 (27)	0.32
45–64	**25,620 (27)**	13,426 (52)	10,470 (41)	1,724 (7)		18,278 (71)	7,342 (29)	
65–74	**20,947 (22)**	7,369 (35)	10,471 (50)	3,107 (15)		16,775 (80)	4,172 (20)	
75–84	**18,316 (20)**	5,003 (27)	9,874 (54)	3,439 (19)		15,215 (83)	3,101 (17)	
≥85	**10,606 (11)**	2,678 (25)	5,961 (56)	1,967 (19)		9,042 (85)	1,564 (15)	
Sex								
Male§§	**42,175 (45)**	18,619 (44)	18,465 (44)	5,091 (12)	0.03	31,609 (75)	10,566 (25)	0.13
Female	**51,233 (55)**	21,506 (42)	23,861 (47)	5,866 (11)		40,699 (79)	10,534 (21)	
Race/Ethnicity								
White, non-Hispanic	**60,285 (65)**	24,582 (41)	27,842 (46)	7,861 (13)	0.28	47,171 (78)	13,114 (22)	0.16
Hispanic	**11,752 (13)**	5,559 (47)	5,194 (44)	999 (9)		8,680 (74)	3,072 (26)	
Black, non-Hispanic	**10,360 (11)**	5,447 (53)	4,200 (41)	713 (7)		8,077 (78)	2,283 (22)	
Other, non-Hispanic¶¶	**7,199 (8)**	2,379 (33)	3,722 (52)	1,098 (15)		5,845 (81)	1,354 (19)	
Unknown	**3,812 (4)**	2,158 (57)	1,368 (36)	286 (8)		2,535 (67)	1,277 (33)	
Chronic respiratory condition* **								
Yes§§	**59,525 (64)**	24,741 (42)	27,360 (46)	7,424 (12)	0.10	46,548 (78)	12,977 (22)	0.06
No	**33,883 (36)**	15,384 (45)	14,966 (44)	3,533 (10)		25,760 (76)	8,123 (24)	
Chronic nonrespiratory condition†††								
Yes§§	**79,433 (85)**	31,480 (40)	37,798 (48)	10,155 (13)	0.36	63,475 (80)	15,958 (20)	0.32
No	**13,975 (15)**	8,645 (62)	4,528 (32)	802 (6)		8,833 (63)	5,142 (37)	
Immunocompromised status§§§								
Yes§§	**19,401 (21)**	5,988 (31)	9,755 (50)	3,658 (19)	0.33	16,969 (87)	2,432 (13)	0.32
No	**74,007 (79)**	34,137 (46)	32,571 (44)	7,299 (10)		55,339 (75)	18,668 (25)	
Total vaccinated	**53,283 (57)**	—	42,326 (79)	10,957 (21)		48,518 (91)	4,765 (9)	

See table footnotes on the next page.

VE estimates resulting from temporal and spatial variations in virus circulation and vaccine coverage was reduced.

The findings in this report are subject to at least seven limitations. First, because this study was designed to estimate VE against COVID-19–associated ED/UC visits or hospitalizations, VE estimates from this study do not include COVID-19 infections that were not medically attended. Second, the median interval from receipt of a third dose to medical encounters was 49 days; thus, the observed performance of a third dose is limited to a relatively short period after vaccination. Third, the small number of COVID-19 test-positive patients in the most remote time-since-vaccination groups reduced the precision of the VE estimates for those groups (e.g., ≥5 months). Fourth, variations in waning of VE by age group, immunocompromised status, other indicators of underlying health status, or vaccine product have not yet been examined. This study could not distinguish whether a third dose was received as an additional dose as part of a primary series (as recommended for immunocompromised persons) or as a booster dose after completion of a primary series. Further research should evaluate waning VE of a third primary dose among immunocompromised adults compared with waning of VE after a booster dose among immunocompetent adults. Fifth, despite adjustments to account for differences between

TABLE 3. (*Continued*) Characteristics of hospitalizations among adults with COVID-19–like illness,* by mRNA COVID-19 vaccination status† and SARS-CoV-2 test result — 10 states,§ August 2021–January 2022¶

Characteristic	Total no. (column %)	mRNA COVID-19 vaccination status, no. (row %)			SMD††	SARS-CoV-2 test result, no. (row %)		SMD††
		Unvaccinated	Vaccinated (2 doses)	Vaccinated (3 doses)**		Negative	Positive	
Vaccine product								
Pfizer-BioNTech	**31,460 (59)**	—	24,382 (78)	7,078 (22)	—	28,339 (90)	3,121 (10)	0.15
Moderna	**21,349 (40)**	—	17,850 (84)	3,499 (16)		19,731 (92)	1,618 (8)	
Combination of mRNA products	**474 (1)**	—	94 (20)	380 (80)		448 (95)	26 (5)	
No. of doses received (interval from receipt of most recent dose to hospitalization)								
2 (<2 mos)	**1,662 (3)**	—	1,662 (100)	—	—	1,591 (96)	71 (4)	0.42
2 (2–3 mos)	**3,084 (6)**	—	3,084 (100)	—		2,861 (93)	223 (7)	
2 (4 mos)	**3,279 (6)**	—	3,279 (100)	—		3,045 (93)	234 (7)	
2 (≥5 mos)	**34,301 (64)**	—	34,301 (100)	—		30,535 (89)	3,766 (11)	
3 (<2 mos)	**7,332 (14)**	—	—	7,332 (100)		7,111 (97)	221 (3)	
3 (2–3 mos)	**3,413 (6)**	—	—	3,413 (100)		3,202 (94)	211 (6)	
3 (≥4 mos)	**212 (0)**	—	—	212 (100)		173 (82)	39 (18)	

Abbreviations: ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision*; SMD = standardized mean or proportion difference.

* Medical events with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after admission were included. Recipients of Janssen vaccine, 1 or >3 doses of an mRNA vaccine, and those for whom 1–13 days had elapsed since receipt of any dose were excluded.

† Vaccination was defined as having received the listed number of doses of an mRNA-based COVID-19 vaccine ≥14 days before the medical event index date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before medical event or the admission date if testing only occurred after the admission.

§ California, Colorado, Indiana, Minnesota, New York, Oregon, Texas, Utah, Washington, and Wisconsin.

¶ Partners contributing data on medical events and estimated date of Omicron predominance were in California (December 21), Colorado (December 19), Indiana (December 26), Minnesota and Wisconsin (December 25), New York (December 18), Oregon (December 24), Texas (December 16), Utah (December 24), and Washington (December 24). The study period began in September 2021 for partners located in Texas.

** Persons categorized as having received 3 vaccine doses include those who have received a third dose in their primary series or have received a booster dose following their 2-dose primary series; the third dose could have been either a 100-μg or 50-μg dose of Moderna vaccine or a 30-μg dose of the Pfizer-BioNTech vaccine.

†† An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between medical events for vaccinated versus unvaccinated patients. When calculating SMDs for differences of characteristics across mRNA COVID-19 vaccination status, the SMD was calculated as the average of the absolute value of the SMD for unvaccinated versus vaccinated with 2 doses and the absolute value of the SMD for unvaccinated versus vaccinated with 3 doses. All SMDs are reported as the absolute SMD.

§§ Indicates the referent group used for SMD calculations for dichotomous variables.

¶¶ Other race includes Asian, Native Hawaiian or other Pacific islander, American Indian or Alaska Native, Other not listed, and multiple races.

*** Chronic respiratory condition was defined using ICD-9 and ICD-10 as the presence of discharge codes for asthma, chronic obstructive pulmonary disease, or other lung disease.

††† Chronic nonrespiratory condition was defined using ICD-9 and CD-10 as the presence of discharge codes for heart failure, ischemic heart disease, hypertension, other heart disease, stroke, other cerebrovascular disease, diabetes type I or II, other diabetes, metabolic disease, clinical obesity, clinically underweight, renal disease, liver disease, blood disorder, immunosuppression, organ transplant, cancer, dementia, neurologic disorder, musculoskeletal disorder, or Down syndrome.

§§§ Immunocompromised status was defined using ICD-9 and ICD-10 as the presence of discharge codes for solid malignancy, hematologic malignancy, rheumatologic or inflammatory disorder, other intrinsic immune condition or immunodeficiency, or organ or stem cell transplant.

unvaccinated and vaccinated persons, VE estimates might have been biased by residual differences between these groups with respect to immunocompromised status and other health conditions, as well as from unmeasured behaviors (e.g., mask use and close contact with persons with COVID-19). For example, insufficient adjustment for immunocompromised status might have biased the estimates of VE downward among persons most remote from receipt of a third dose. Sixth, genetic characterization of patients' viruses was not available, and analyses relied on dates when the Omicron variant became locally predominant based on surveillance data; therefore, the Omicron period of predominance in this study likely includes some medical encounters associated with the Delta variant. Finally, although the facilities in this study serve heterogeneous populations in 10 states, the findings might not be generalizable to the U.S. population.

These findings underscore the importance of receiving a third dose of mRNA COVID-19 vaccine to prevent both COVID-19–associated ED/UC encounters and COVID-19 hospitalizations among adults. The finding that protection conferred by mRNA vaccines waned in the months after receipt of a third vaccine dose reinforces the importance of further consideration of additional doses to sustain or improve protection against COVID-19–associated ED/UC encounters and COVID-19 hospitalizations. All eligible persons should remain up to date with recommended COVID-19 vaccinations to best protect against COVID-19–associated hospitalizations and ED/UC visits.

Summary

What is already known about this topic?

Protection against COVID-19 after 2 doses of mRNA vaccine wanes, but little is known about durability of protection after 3 doses.

What is added by this report?

Vaccine effectiveness (VE) against COVID-19–associated emergency department/urgent care (ED/UC) visits and hospitalizations was higher after the third dose than after the second dose but waned with time since vaccination. During the Omicron-predominant period, VE against COVID-19–associated ED/UC visits and hospitalizations was 87% and 91%, respectively, during the 2 months after a third dose and decreased to 66% and 78% by the fourth month after a third dose. Protection against hospitalizations exceeded that against ED/UC visits.

What are the implications for public health practice?

All eligible persons should remain up to date with recommended COVID-19 vaccinations to best protect against COVID-19–associated hospitalizations and ED/UC visits.

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References

1. Fowlkes A, Gaglani M, Groover K, Thiese MS, Tyner H, Ellingson K; HEROES-RECOVER Cohorts. Effectiveness of COVID-19 vaccines in preventing SARS-CoV-2 infection among frontline workers before and during B.1.617.2 (Delta) variant predominance—eight U.S. locations, December 2020–August 2021. MMWR Morb Mortal Wkly Rep 2021;70:1167–9. PMID:34437521 https://doi.org/10.15585/mmwr.mm7034e4
2. Thompson MG, Natarajan K, Irving SA, et al. Effectiveness of a third dose of mRNA vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance—VISION Network, 10 States, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:139–45. PMID:35085224 https://doi.org/10.15585/mmwr.mm7104e3
3. Tartof SY, Slezak JM, Fischer H, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet 2021;398:1407–16. PMID:34619098 https://doi.org/10.1016/S0140-6736(21)02183-8
4. Tenforde MW, Self WH, Naioti EA, et al.; IVY Network Investigators; IVY Network. Sustained effectiveness of Pfizer-BioNTech and Moderna vaccines against COVID-19 associated hospitalizations among adults—United States, March–July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1156–62. PMID:34437524 https://doi.org/10.15585/mmwr.mm7034e2
5. Bruxvoort KJ, Sy LS, Qian L, et al. Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants of SARS-CoV-2: test negative case-control study. BMJ 2021;375:e068848. PMID:34911691 https://doi.org/10.1136/bmj-2021-068848
6. Thompson MG, Stenehjem E, Grannis S, et al. Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. N Engl J Med 2021;385:1355–71. PMID:34496194 https://doi.org/10.1056/NEJMoa2110362
7. Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 Omicron and Delta variants. JAMA 2022. PMID:35060999 https://doi.org/10.1001/jama.2022.0470
8. Barda N, Dagan N, Cohen C, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet 2021;398:2093–100. PMID:34756184 https://doi.org/10.1016/S0140-6736(21)02249-2

Effectiveness of Maternal Vaccination with mRNA COVID-19 Vaccine During Pregnancy Against COVID-19–Associated Hospitalization in Infants Aged <6 Months — 17 States, July 2021–January 2022

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COVID-19 vaccination is recommended for persons who are pregnant, breastfeeding, trying to get pregnant now, or who might become pregnant in the future, to protect them from COVID-19.[§] Infants are at risk for life-threatening complications from COVID-19, including acute respiratory failure (*1*). Evidence from other vaccine-preventable diseases suggests that maternal immunization can provide protection to infants, especially during the high-risk first 6 months of life, through passive transplacental antibody transfer (*2*). Recent studies of COVID-19 vaccination during pregnancy suggest the possibility of transplacental transfer of SARS-CoV-2–specific antibodies that might provide protection to infants (*3*–*5*); however, no epidemiologic evidence currently exists for the protective benefits of maternal immunization during pregnancy against COVID-19 in infants. The Overcoming COVID-19 network conducted a test-negative, case-control study at 20 pediatric hospitals in 17 states during July 1, 2021–January 17, 2022, to assess effectiveness of maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy against COVID-19 hospitalization in infants. Among 379 hospitalized infants aged <6 months (176 with COVID-19 [case-infants] and 203 without COVID-19 [control-infants]), the median age was 2 months, 21% had at least one underlying medical condition, and 22% of case- and control-infants were born premature (<37 weeks gestation). Effectiveness of maternal vaccination during pregnancy against COVID-19 hospitalization in infants aged <6 months was 61% (95% CI = 31%–78%). Completion of a 2-dose mRNA COVID-19 vaccination series during pregnancy might help prevent COVID-19 hospitalization among infants aged <6 months.

Using a test-negative, case-control study design, vaccine performance was assessed by comparing the odds of having completed a 2-dose primary mRNA COVID-19 vaccination series during pregnancy among mothers of case-infants and control-infants (those with negative SARS-CoV-2 test results) (*6*). Participating infants were aged <6 months and admitted outside of their birth hospitalization to one of 20 pediatric hospitals during July 1, 2021–January 17, 2022. During this period, the SARS-CoV-2 Delta variant was the predominant variant in the United States through mid-December, after which Omicron became predominant.[¶] Case-infants were hospitalized with COVID-19 as the primary reason for admission or had clinical symptoms consistent with acute COVID-19,[**] and case-infants had a positive SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) or antigen test result. No case-infant received a diagnosis of multisystem inflammatory syndrome. Control-infants were those hospitalized with or without COVID-19 symptoms and with negative SARS-CoV-2 RT-PCR or antigen test results. Enrolled control-infants were matched to case-infants by site and were hospitalized within 3–4 weeks of a case-infant's admission date. Baseline demographic characteristics, clinical information, and SARS-CoV-2 testing history were obtained through parent or guardian interviews performed by trained study personnel during hospitalization or after discharge, and electronic medical record review of the infant's record. Mothers were asked about their COVID-19 vaccination history, including number of doses and whether a dose had been received

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§ https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/pregnancy.html

¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions
** Symptomatic COVID-19–like illness was defined as one or more of the following: fever, cough, shortness of breath, gastrointestinal symptoms (e.g., diarrhea, vomiting, or "stomachache"), use of respiratory support (high-flow oxygen by nasal cannula, new invasive or noninvasive ventilation) for the acute illness, or new pulmonary findings on chest imaging consistent with pneumonia. Four case-infants tested at an outside hospital or other facility had some missing data on positive test results and were not retested at the study hospital.

during pregnancy, location where vaccine was received, vaccine manufacturer, and availability of a COVID-19 vaccination card. Study personnel reviewed documented sources, including state vaccination registries, electronic medical records, or other sources (e.g., documentation from primary care providers) to verify vaccination status.

Mothers were considered vaccinated against COVID-19 if they completed a 2-dose series of either Pfizer-BioNTech or Moderna mRNA COVID-19 vaccine, based on source documentation or by plausible self-report (provision of vaccination dates and location). Maternal COVID-19 vaccination status was categorized as 1) unvaccinated (mothers who did not receive COVID-19 vaccine before their infants' hospitalization) or 2) vaccinated[††] (mothers who completed their 2-dose primary mRNA COVID-19 vaccine series during pregnancy ≥14 days before delivery). SARS-CoV-2 infection status of the mother during pregnancy or after delivery was not documented in this evaluation. Mothers were excluded if they were partially vaccinated during pregnancy (1 dose during pregnancy and none before pregnancy) or vaccinated after pregnancy (71), received Janssen (Johnson & Johnson) COVID-19 vaccine (four), received 2 doses of COVID-19 vaccination before pregnancy (seven), or received >2 doses of COVID-19 vaccine ≥14 days before delivery (10).

Descriptive statistics (Pearson chi-square tests and Fisher's exact tests for categorical outcomes or Wilcoxon rank-sum tests for continuous outcomes) were used to compare characteristics of case- and control-infants; p-values <0.05 were considered statistically significant. Effectiveness of maternal vaccination (i.e., vaccine effectiveness [VE]) against infant COVID-19 hospitalization was calculated using the equation VE = 100% × (1 – adjusted odds ratio of completing 2-doses of COVID-19 mRNA vaccines during pregnancy among mothers of case-infants and control-infants), determined from logistic regression models. Models were adjusted for infant age and sex, U.S. Census region, calendar time of admission, and race/ethnicity (*6*). Other factors were assessed (e.g., infant's underlying health conditions, Social Vulnerability Index, and behavioral factors) but were not included in the final model because they did not change the odds ratio of vaccination by >5% or because data on many infants were not available (e.g., breastfeeding history, prematurity, or child care attendance). In a secondary analysis, effectiveness of maternal receipt of the second dose of COVID-19 vaccination early in pregnancy (within the first 20 weeks) and late in pregnancy (21 weeks through 14 days before delivery) was assessed. Statistical analyses were conducted using SAS (version 9.4; SAS Institute). Procedures were approved as public health surveillance by each participating site and CDC and were conducted consistent with applicable federal law and CDC policy.[§§]

During July 1, 2021–January 17, 2022, among 483 eligible infants in 20 pediatric hospitals in 17 states, 104 (22%) were excluded; 71 excluded infants were born to mothers partially vaccinated during pregnancy or vaccinated after delivery, 10 were born to mothers who received a third vaccine dose ≥14 days before delivery, and 23 were excluded for other reasons.[¶¶] Among the remaining 379 hospitalized infants (176 case-infants and 203 control-infants), the median age was 2 months, 80 (21%) had at least one underlying medical condition, and 72 (22%) were born premature (Table 1). Among case-infants, 16% of mothers had received 2 COVID-19 vaccine doses during pregnancy, whereas 32% of control-infant mothers were vaccinated. Case- and control-infants had similar prevalences of underlying medical conditions (20% and 23%, respectively; p = 0.42) and prematurity (23% and 21%, respectively; p = 0.58). Case-infants were more commonly non-Hispanic Black (18%) and Hispanic (34%) than were control-infants (9% and 28%, respectively).

Among case-infants, 43 (24%) were admitted to an intensive care unit (ICU) (Table 2). A total of 25 (15%) case-infants were critically ill and received life support during hospitalization, including mechanical ventilation, vasoactive infusions, or extracorporeal membrane oxygenation (ECMO); among these critically ill infants, one (0.4%) died. Of the 43 case-infants admitted to an ICU, 88% had mothers who were unvaccinated. The mothers of the one case-infant who required ECMO and one case-infant who died were both unvaccinated.

VE of a completed 2-dose maternal primary mRNA COVID-19 vaccination series during pregnancy against COVID-19–associated hospitalization in infants aged <6 months was 61% (95% CI = 31% to 78%) (Table 3). Among 93 mothers classified as vaccinated, 90 (97%) had documented dates of vaccination. Effectiveness of a completed 2-dose COVID-19 vaccination series early in pregnancy (first 20 weeks) was 32% (95% CI = –43% to 68%), although the

[††] Mothers were defined as vaccinated after completing their 2-dose primary mRNA COVID-19 vaccine series during pregnancy, including both doses received during pregnancy or the first dose received before pregnancy and the second dose, completing their primary series, received during pregnancy. Data on maternal moderately or severely immunocompromising conditions were not recorded for mothers of enrolled infants to determine whether mothers needed an additional mRNA COVID-19 vaccine dose to complete their primary series.

[§§] 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.

[¶¶] Other reasons for excluding infants from the analysis included May or June hospital admission (two); birth to mothers who received Janssen (Johnson & Johnson) COVID-19 vaccine (four), who received their second dose of vaccine <14 days before delivery (three), who received a 2-dose primary mRNA COVID-19 vaccine before pregnancy (seven), or with unknown vaccination status (one); infants who received a positive SARS-CoV-2 test result but were admitted for non–COVID-19 reasons (four); and SARS-CoV-2 testing >10 days after illness onset or >3 days from hospitalization (two).

TABLE 1. Characteristics of infants aged <6 months hospitalized with COVID-19 (case-infants) and without COVID-19 (control-infants) — 20 pediatric hospitals, 17 states,* July 2021–January 2022

Characteristic (no. missing)	Case status, n/N† (column %)		
	Case-infants (N = 176)	Control-infants (N = 203)	p-value§
Median age, mos (IQR)	2 (1–3)	2 (1–3)	0.96
Age group, mos			
0–2	129 (73.3)	153 (75.4)	0.64
3–5	47 (26.7)	50 (24.6)	
Sex			
Female	84 (47.7)	83 (40.9)	0.18
Race and ethnicity			
Black, non-Hispanic	32 (18.2)	19 (9.4)	0.02
White, non-Hispanic	56 (31.8)	82 (40.4)	
Other, non-Hispanic	10 (5.7)	21 (10.3)	
Hispanic, any race	60 (34.1)	56 (27.6)	
Unknown	18 (10.2)	25 (12.3)	
Social Vulnerability Index,¶ (IQR) (1)	0.71 (0.39–0.86)	0.61 (0.29–0.83)	0.06
U.S. Census region*			
Northeast	30 (17.1)	29 (14.3)	0.08
Midwest	44 (25.0)	60 (29.6)	
South	54 (30.7)	42 (20.7)	
West	48 (27.3)	72 (35.5)	
Month of admission			
July	10 (5.7)	5 (2.5)	0.14
August	23 (13.1)	26 (12.8)	
September	16 (9.1)	25 (12.3)	
October	10 (5.7)	21 (10.3)	
November	18 (10.2)	30 (14.8)	
December	59 (33.5)	51 (25.1)	
January**	40 (22.7)	45 (22.2)	
Underlying health condition in infants			
At least one underlying condition (5)	34/174 (19.5)	46/200 (23.0)	0.42
Respiratory disorder (6)	9/174 (5.2)	9/199 (4.5)	0.77
Cardiovascular system disorder (5)	15/174 (8.6)	19/200 (9.5)	0.77
Neurologic/Neuromuscular disorder (5)	4/174 (2.3)	7/200 (3.5)	0.49
Immunosuppression or autoimmune (5)	0/174 (—)	2/200 (1.0)	0.50
Other chronic conditions†† (6)	18/174 (10.3)	23/199 (11.6)	0.71
Preterm birth (born <37 weeks gestation) (50)	34/146 (23.3)	38/183 (20.8)	0.58
Maternal vaccination during pregnancy§§	28 (15.9)	65 (32.0)	<0.01
Timing of maternal vaccination¶¶ (3)			
Early pregnancy (first 20 weeks)	17/165 (10.3)	26/164 (15.9)	0.14
Late pregnancy (21 weeks–14 days before delivery)	9/157 (5.7)	38/176 (21.6)	<0.01
Maternal vaccine type			
Pfizer-BioNTech	20 (71.4)	35 (53.9)	0.11
Moderna	8 (28.6)	30 (46.2)	
Behavioral factors***			
Breastfeeding (103)	76/138 (55.1)	90/138 (65.2)	0.09
Child care (108)	6/135 (4.4)	9/136 (6.6)	0.43

Abbreviation: SVI = Social Vulnerability Index.

* Infants were enrolled from 20 pediatric hospitals in 17 states. *Northeast*: Boston Children's Hospital (Massachusetts), Cooperman Barnabas Medical Center (New Jersey), and Children's Hospital of Philadelphia (Pennsylvania); *Midwest:* Akron Children's Hospital (Ohio), Nationwide (Ohio), Children's Mercy Kansas City (Missouri), Mayo Clinic (Minnesota), Riley Children's (Indiana), Lurie Children's Hospital (Illinois), Minnesota Masonic (Minnesota), and Children's Hospital of Michigan (Michigan); *South:* Arkansas Children's Hospital (Arkansas), University of North Carolina at Chapel Hill Children's Hospital (North Carolina), Medical University of South Carolina Children's Health (South Carolina), Texas Children's Hospital (Texas), Children's Hospital of New Orleans (Louisiana), and Children's Healthcare of Atlanta, Emory (Georgia); *West:* Children's Hospital Colorado (Colorado), Children's Hospital Los Angeles (California), and University of California San Diego-Rady Children's Hospital (California).

† If N is less than total.

§ Testing for statistical significance was conducted using the Pearson chi-square test and Fisher's exact test for comparisons with fewer than five observations. Wilcoxon rank-sum tests were used to compare continuous data.

¶ CDC/Agency for Toxic Substances and Disease Registry SVI documentation is available at https://www.atsdr.cdc.gov/placeandhealth/svi/index.html. Median SVI for case-infants and control-infants are based on 2018 U.S. SVI data. The SVI ranges from 0 to 1.0, with higher scores indicating greater social vulnerability. One control-infant was missing an SVI score.

** January numbers do not reflect the entire month. Patients included were admitted through January 17, 2022.

†† Other chronic conditions included rheumatologic/autoimmune disorder, hematologic disorder, renal or urologic dysfunction, gastrointestinal/hepatic disorder, metabolic or confirmed or suspected genetic disorder, or atopic or allergic condition.

§§ COVID-19 vaccination status included the following two categories: 1) unvaccinated (mothers who did not receive COVID-19 vaccine doses before their infant's hospitalization) or 2) vaccinated (mothers who completed their 2-dose primary mRNA COVID-19 vaccination series during pregnancy and ≥14 days before delivery).

¶¶ Timing of vaccination is based on date of receipt of the second dose of a 2-dose primary mRNA COVID-19 vaccine series during pregnancy.

*** Behavioral factors are reported during interview with mother or proxy. Breastfeeding included any breastfeeding (either exclusive or partial).

TABLE 2. Clinical outcomes and severity among case-infants aged <6 months hospitalized with COVID-19, by maternal vaccination status during pregnancy* — 20 pediatric hospitals, 17 states,† July 2021–January 2022

Characteristic (no. unknown)	Maternal vaccination status during pregnancy, n/N (%)		
	Total (N = 176)	Unvaccinated (n = 148)	Vaccinated (2-doses of mRNA COVID-19 vaccine) (n = 28)
Intensive care unit admission	**43/176 (24.4)**	38/148 (25.7)	5/28 (17.9)
Critically ill infants on life support (4)	**25/172 (14.5)**	21/144 (14.6)	4/28 (14.3)
Invasive mechanical ventilation (4)	**11/172 (6.4)**	10/144 (6.9)	1/28 (3.6)
Noninvasive mechanical ventilation (4)	**18/172 (10.5)**	15/144 (10.4)	3/28 (10.7)
Vasoactive infusions (4)	**6/172 (3.5)**	5/144 (3.5)	1/28 (3.6)
Extracorporeal membrane oxygenation (4)	**1/172 (0.6)**	1/144 (0.7)	0/28 (—)
Infants with discharge data, n/total N (%)	**170/176 (96.6)**	142/148 (96.0)	28/28 (100)
Hospital length of stay, median days§ (IQR) (8)	**2 (1–3)**	2 (1–3)	2 (1–5)
Died before discharge (6)	**1/170 (0.6)**	1/142 (0.7)	0/28 (—)

* COVID-19 vaccination status included the following two categories: 1) unvaccinated (mothers who did not receive COVID-19 vaccine doses before their infant's hospitalization) or 2) vaccinated (mothers who completed their 2-dose primary mRNA COVID-19 vaccination series during pregnancy and ≥14 days before delivery).

† Infants were enrolled from 20 pediatric hospitals in 17 states. *Northeast*: Boston Children's Hospital (Massachusetts), Cooperman Barnabas Medical Center (New Jersey), and Children's Hospital of Philadelphia (Pennsylvania); *Midwest:* Akron Children's Hospital (Ohio), Nationwide (Ohio), Children's Mercy Kansas City (Missouri), Mayo Clinic (Minnesota), Riley Children's (Indiana), Lurie Children's Hospital (Illinois), Minnesota Masonic (Minnesota), and Children's Hospital of Michigan (Michigan); *South:* Arkansas Children's Hospital (Arkansas), University of North Carolina at Chapel Hill Children's Hospital (North Carolina), Medical University of South Carolina Children's Health (South Carolina), Texas Children's Hospital (Texas), Children's Hospital of New Orleans (Louisiana), and Children's Healthcare of Atlanta, Emory (Georgia); *West:* Children's Hospital Colorado (Colorado), Children's Hospital Los Angeles (California), and University of California San Diego-Rady Children's Hospital (California).

§ Hospital length of stay was missing for eight case-infants born to unvaccinated mothers.

TABLE 3. Effectiveness* of maternal 2-dose primary mRNA COVID-19 vaccination against COVID-19-associated hospitalization in infants aged <6 months, by timing of maternal vaccination during pregnancy† — 20 pediatric hospitals, 17 states,§ July 2021–January 2022

Timing of maternal vaccination during pregnancy†	No. vaccinated¶/Total (%)		Vaccine effectiveness,* % (95% CI)
	Case-infants	Control-infants	
Any time	28/176 (15.9)	65/203 (32.0)	61 (31 to 78)
Early (first 20 weeks)	17/165 (10.3)	26/164 (15.9)	32 (–43 to 68)
Late (21 weeks' gestation through 14 days before delivery)	9/157 (5.7)	38/176 (21.6)	80 (55 to 91)

* Vaccine effectiveness estimates were based on odds of antecedent maternal vaccination during pregnancy in case-infants versus control-infants, adjusted for U.S. Census region, admission date (biweekly intervals), continuous age, sex, and race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic of any race, or unknown).

† Timing of vaccination is based on date of receipt of the second dose of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy. Gestational age was missing for seven of 90 (7.8%) infants born to vaccinated mothers with known timing of the second dose, and for these infants classification of vaccination timing was based on gestational age of 40 weeks.

§ Infants were enrolled from 20 pediatric hospitals in 17 states. *Northeast*: Boston Children's Hospital (Massachusetts), Cooperman Barnabas Medical Center (New Jersey), and Children's Hospital of Philadelphia (Pennsylvania); *Midwest:* Akron Children's Hospital (Ohio), Nationwide (Ohio), Children's Mercy Kansas City (Missouri), Mayo Clinic (Minnesota), Riley Children's (Indiana), Lurie Children's Hospital (Illinois), Minnesota Masonic (Minnesota), and Children's Hospital of Michigan (Michigan); *South:* Arkansas Children's Hospital (Arkansas), University of North Carolina at Chapel Hill Children's Hospital (North Carolina), Medical University of South Carolina Children's Health (South Carolina), Texas Children's Hospital (Texas), Children's Hospital of New Orleans (Louisiana), and Children's Healthcare of Atlanta, Emory (Georgia); *West:* Children's Hospital Colorado (Colorado), Children's Hospital Los Angeles (California), and University of California San Diego-Rady Children's Hospital (California).

¶ COVID-19 vaccination status included the following two categories: 1) unvaccinated (mothers who did not receive COVID-19 vaccine doses before their infant's hospitalization) or 2) vaccinated (mothers who completed their 2-dose primary mRNA COVID-19 vaccination series during pregnancy and ≥14 days before delivery).

confidence interval was wide and should be interpreted with caution, and later in pregnancy (21 weeks through 14 days before delivery) was 80% (95% CI = 55% to 91%).

Discussion

During July 2021–January 2022, maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy was associated with reduced risk for COVID-19 hospitalization among infants aged <6 months in a real-world evaluation at 20 U.S. pediatric hospitals during a period of Delta and Omicron variant circulation. Among 176 infants aged <6 months hospitalized with COVID-19, 148 (84%) were born to mothers who were not vaccinated during pregnancy. Although booster doses are recommended for pregnant women, VE of maternal booster doses received during pregnancy could not be assessed because of small sample size, which likely underestimated VE. Overall, these findings indicate that maternal vaccination during pregnancy might help protect against COVID-19 hospitalization among infants aged <6 months.

COVID-19 during pregnancy is associated with severe illness and death (*7*), and pregnant women with COVID-19 are more likely to experience preterm birth, stillbirth, and other pregnancy complications (*8*). Vaccination is recommended for pregnant women to prevent COVID-19, including severe illness and death. COVID-19 vaccination is safe and effective when administered during pregnancy (*9*,*10*). Receipt of COVID-19 vaccination during pregnancy is associated with detectable maternal antibodies in maternal sera at delivery, breast milk, and infant sera indicating transfer of maternal antibodies (*3*–*5*). The higher VE point estimates among infants born to women vaccinated later in pregnancy are consistent with the possibility of transplacental transfer of SARS-CoV-2–specific antibodies that might provide protection to infants. The optimal timing of maternal vaccination for the transfer

Summary

What is already known about this topic?

COVID-19 vaccination during pregnancy is recommended to prevent severe illness and death in pregnant women. Infants are at risk for COVID-19–associated complications, including respiratory failure and other life-threatening complications.

What is added by this report?

Effectiveness of maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy against COVID-19 hospitalization among infants aged <6 months was 61% (95% CI = 31% to 78%). Effectiveness of completion of the primary COVID-19 vaccine series early and later in pregnancy was 32% (95% CI = –43% to 68%) and 80% (95% CI = 55% to 91%), respectively.

What are the implications for public health practice?

Completion of a 2-dose mRNA COVID-19 vaccination series during pregnancy might help prevent COVID-19 hospitalization among infants aged <6 months.

of antibodies to protect the infant is currently uncertain, and the direct effect of maternal COVID-19 vaccination in preventing severe COVID-19 in infants has not previously been described. Further, with infants not currently age-eligible for vaccination and infant hospitalization rates remaining at the highest levels of the pandemic,*** this study suggests that maternal COVID-19 vaccination during pregnancy might protect infants aged <6 months from COVID-19–related hospitalization.

The findings in this report are subject to at least seven limitations. First, VE could not be assessed directly against specific variants. Second, the sample was too small to assess VE by pregnancy trimester of vaccination, and the small sample size resulted in wide confidence intervals for some estimates that should be interpreted with caution. Third, the analysis did not assess whether pregnant women were infected with SARS-CoV-2 before or during pregnancy, which might have provided maternal antibodies. Fourth, residual confounding such as additional differences in behaviors between vaccinated and unvaccinated mothers, including whether mothers had prenatal care, that might affect risk for infection cannot be excluded, and potential confounders (e.g., breastfeeding, child care attendance, and prematurity) could not be accounted for in the model because this information was not available for all infants. Fifth, because this analysis included self-reported data for a few participants, maternal vaccination status might be misclassified for a few infants, or there might be imperfect recollection of whether the mother completed COVID-19 vaccination during pregnancy. Sixth, immunocompromising maternal conditions were not collected to determine whether mothers needed an additional mRNA COVID-19 vaccine dose to complete their primary series. Finally, VE of maternal booster doses received during pregnancy could not be assessed because of small sample size.

Completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy was associated with reduced risk for COVID-19–associated hospitalization among infants aged <6 months, and protection was higher among infants whose mothers were vaccinated later in pregnancy. Additional evaluation should examine timing of vaccination before pregnancy compared with during pregnancy. CDC recommends that women who are pregnant, are breastfeeding, are trying to get pregnant now, or might become pregnant in the future get vaccinated and stay up to date with COVID-19 vaccination.†††

*** https://gis.cdc.gov/grasp/covidnet/COVID19_5.html

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References

1. Hobbs CV, Woodworth K, Young CC, et al.; Overcoming COVID-19 Investigators. Frequency, characteristics and complications of COVID-19 in hospitalized infants. Pediatr Infect Dis J 2022;41:e81–6. PMID:34955519 https://doi.org/10.1097/INF.0000000000003435
2. Marchant A, Sadarangani M, Garand M, et al. Maternal immunisation: collaborating with mother nature. Lancet Infect Dis 2017;17:e197–208. PMID:28433705 https://doi.org/10.1016/S1473-3099(17)30229-3
3. Nir O, Schwartz A, Toussia-Cohen S, et al. Maternal-neonatal transfer of SARS-CoV-2 immunoglobulin G antibodies among parturient women treated with BNT162b2 messenger RNA vaccine during pregnancy. Am J Obstet Gynecol MFM 2022;4:100492. PMID:34547533 https://doi.org/10.1016/j.ajogmf.2021.100492
4. Trostle ME, Aguero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. Am J Obstet Gynecol MFM 2021;3:100481. PMID:34562636 https://doi.org/10.1016/j.ajogmf.2021.100481
5. Yang YJ, Murphy EA, Singh S, et al. Association of gestational age at coronavirus disease 2019 (COVID-19) vaccination, history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and a vaccine booster dose with maternal and umbilical cord antibody levels at delivery. Obstet Gynecol 2021. Epub December 28, 2021. PMID:34963127 https://doi.org/10.1097/AOG.0000000000004693
6. Olson SM, Newhams MM, Halasa NB, et al.; Overcoming Covid-19 Investigators. Effectiveness of BNT162b2 vaccine against critical Covid-19 in adolescents. N Engl J Med 2022;NEJMoa2117995. PMID:35021004 https://doi.org/10.1056/NEJMoa2117995
7. Zambrano LD, Ellington S, Strid P, et al.; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1641–7. PMID:33151921 https://doi.org/10.15585/mmwr.mm6944e3
8. Woodworth KR, Olsen EO, Neelam V, et al.; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team; COVID-19 Pregnancy and Infant Linked Outcomes Team (PILOT). Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy—SET-NET, 16 jurisdictions, March 29–October 14, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1635–40. PMID:33151917 https://doi.org/10.15585/mmwr.mm6944e2
9. Dagan N, Barda N, Biron-Shental T, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. Nat Med 2021;27:1693–5. PMID:34493859 https://doi.org/10.1038/s41591-021-01490-8
10. Shimabukuro TT, Kim SY, Myers TR, et al.; CDC v-safe COVID-19 Pregnancy Registry Team. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med 2021;384:2273–82. PMID:33882218 https://doi.org/10.1056/NEJMoa2104983

Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, July 2021–January 2022

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The first U.S. case of COVID-19 attributed to the Omicron variant of SARS-CoV-2 (the virus that causes COVID-19) was reported on December 1, 2021 (*1*), and by the week ending December 25, 2021, Omicron was the predominant circulating variant in the United States.* Although COVID-19–associated hospitalizations are more frequent among adults,† COVID-19 can lead to severe outcomes in children and adolescents (*2*). This report analyzes data from the Coronavirus Disease 19–Associated Hospitalization Surveillance Network (COVID-NET)§ to describe COVID-19–associated hospitalizations among U.S. children (aged 0–11 years) and adolescents (aged 12–17 years) during periods of Delta (July 1–December 18, 2021) and Omicron (December 19, 2021–January 22, 2022) predominance. During the Delta- and Omicron-predominant periods, rates of weekly COVID-19–associated hospitalizations per 100,000 children and adolescents peaked during the weeks ending September 11, 2021, and January 8, 2022, respectively. The Omicron variant peak (7.1 per 100,000) was four times that of the Delta variant peak (1.8), with the largest increase observed among children aged 0–4 years.¶ During December 2021, the monthly hospitalization rate among unvaccinated adolescents aged 12–17 years (23.5) was six times that among fully vaccinated adolescents (3.8). Strategies to prevent COVID-19 among children and adolescents, including vaccination of eligible persons, are critical.**

COVID-NET conducts population-based surveillance for laboratory-confirmed COVID-19–associated hospitalizations in 99 counties across 14 states.†† Among residents of a predefined surveillance catchment area, COVID-19–associated hospitalizations are defined as receipt of a positive SARS-CoV-2 real-time reverse transcription–polymerase chain reaction (RT-PCR) or rapid antigen detection test result during hospitalization or during the 14 days before admission. This analysis describes weekly hospitalization rates during the weeks ending July 3, 2021–January 22, 2022, to coincide with a period during which detailed clinical data (e.g., intensive care unit [ICU] admission) were available (monthly, July 1–December 31, 2021). Unadjusted weekly COVID-19–associated hospitalization rates were calculated by dividing the total number of hospitalized patients by the population estimates within each age group for the counties included in the surveillance catchment area.§§ ICU admission rates were similarly calculated using 2-week periods. All rates were estimated per 100,000 population for children, adolescents, or both.

Among adolescents aged 12–17 years, hospitalization rates were calculated by COVID-19 vaccination status, which was determined both for hospitalized patients and the catchment population using linkage to state immunization information systems data.¶¶ Monthly incidence was calculated by summing the total number of hospitalized adolescents who were fully vaccinated (≥14 days after final dose in primary series) for each day of the month and dividing by the sum of fully vaccinated adolescents in the underlying population for each day of the month;

* https://covid.cdc.gov/covid-data-tracker/#variant-proportions

† https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html

§ https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html

¶ COVID-NET hospitalization data are preliminary and subject to change as more data become available. In particular, case counts and rates for recent hospital admissions are subject to lag.

** https://www.cdc.gov/coronavirus/2019-ncov/vaccines/your-vaccination.html

†† California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

§§ Rates are calculated using the National Center for Health Statistics vintage 2020 bridged-race postcensal population estimates for the counties included in surveillance (https://www.cdc.gov/nchs/nvss/bridged_race.htm).

¶¶ The Food and Drug Administration granted emergency use authorization for the Pfizer-BioNTech COVID-19 vaccine for adolescents aged 12–15 years on May 10, 2021. The earliest date that adolescents in this age group could have met the definition for being a fully vaccinated COVID-19 patient was June 14, 2021.

the same method was used to calculate incidence in unvaccinated adolescents.*** Rate ratios (RRs) and 95% CIs were calculated.

Trained surveillance staff members conducted medical chart abstractions for all pediatric COVID-NET patients using a standardized case report form through November 2021. Because of the large number of cases during December 2021, some sites examined clinical outcome data on a representative sample of hospitalized children.††† Data on indicators of severe disease were collected (i.e., hospital length of stay, ICU admission, use of invasive mechanical ventilation [IMV],§§§ and in-hospital death), as were data on primary reason for admission¶¶¶ and symptoms that were present when the patient was admitted**** (*3*). Proportions were compared between periods of Delta predominance (July 1–December 18, 2021) and Omicron predominance (December 19–31, 2021); a variant that accounted for >50% of sequenced isolates was considered to be predominant.†††† A similar analysis was completed by vaccination status among adolescents, the only pediatric age group for whom a COVID-19 vaccine had been approved throughout the surveillance period. Wilcoxon rank-sum tests were used to compare medians, and chi-square or Fisher's exact tests were used to compare proportions; p-values <0.05 were considered statistically significant. Percentages were weighted to account for the probability of selection for sampled cases and further adjusted to account for nonresponse (defined as an incomplete chart review). Data were analyzed using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§§§

During the Delta- and Omicron-predominant periods, pediatric weekly hospitalization rates peaked during the weeks ending September 11, 2021, and January 8, 2022, respectively; the Omicron variant peak (7.1 per 100,000 children and adolescents) was four times that of the Delta variant peak (1.8). Hospitalization rates among children aged 0–4 years were approximately five times as high during the peak week of the Omicron period (15.6) than during the Delta period (2.9) (RR = 5.4; 95% CI = 4.0–7.2) (Figure); RRs were also increased among children aged 5–11 years (Delta = 1.1; Omicron = 2.4; RR = 2.3; 95% CI = 1.5–3.6) and adolescents aged 12–17 years (Delta = 1.7; Omicron = 5.9; RR = 3.5; 95% CI = 2.5–5.0). Peak ICU admission rates for children and adolescents were 1.4 times higher during Omicron predominance (2-week period ending December 31, 2021 [1.5]) than during Delta predominance (2-week period ending September 11, 2021 [1.1]). During December 2021, when both variants were circulating, the rates of hospitalization were 23.5 and 3.8 per 100,000 among unvaccinated and fully vaccinated adolescents, respectively (RR = 6.3; 95% CI = 4.4–8.6).

Complete clinical data were available for 1,834¶¶¶¶ and 266***** hospitalized children and adolescents in the Delta-predominant (July 1–December 18, 2021) and Omicron-predominant (December 19, 2021–December 31, 2021) periods, respectively. The proportions of hospitalized children and adolescents requiring ICU admission (Delta = 27.8%; Omicron = 20.2%) or IMV (Delta = 6.3%; Omicron = 2.3%) were significantly lower during the Omicron period (Table 1). No significant difference was detected between the Delta- and Omicron-predominant periods in the proportion of patients

*** Fully vaccinated adolescents with COVID-19–associated hospitalizations were defined as those who had received the final dose in their primary series ≥14 days before receiving a positive SARS-CoV-2 test result associated with their hospitalization. Adolescents who received only 1 vaccine dose ≥14 days before the SARS-CoV-2 test date or had received a single dose of vaccine <14 days before the positive SARS-CoV-2 test results were considered partially vaccinated; they were not included in rates and were grouped with unvaccinated adolescents in other analyses. Unvaccinated adolescents were defined as those who did not meet the criteria for being fully or partially vaccinated. Additional COVID-NET methods for determining vaccination status have been described previously (https://www.medrxiv.org/cgi/content/short/2021.08.27.21262356v1).

††† Colorado, Georgia, New Mexico, and Utah sampled 50% of patients during the month of December. All other sites included 100% of cases. To produce random samples of hospitalized patients for medical record abstraction, random numbers (1–100) are automatically generated and assigned to each patient as their data are entered into the surveillance database. Percentages are weighted to account for the probability of selection for sampled patients.

§§§ ICU admission and IMV are not mutually exclusive categories, and patients could have received both.

¶¶¶ Among sampled patients, COVID-NET collects data on the primary reason for admission to differentiate hospitalizations of patients with laboratory-confirmed SARS-CoV-2 infection who are likely admitted primarily for COVID-19 illness rather than for other reasons. During chart review, if the surveillance officer finds that the chief complaint or history of present illness mentions fever/respiratory illness, COVID-19-like illness, or a suspicion for COVID-19, then the case is categorized as COVID-19 related illness as the primary reason for admission.

**** COVID-19–related symptoms included respiratory symptoms (congestion or runny nose, cough, hemoptysis or bloody sputum, shortness of breath or respiratory distress, sore throat, upper respiratory infection, influenza-like illness, and wheezing) and nonrespiratory symptoms (abdominal pain, altered mental status or confusion, anosmia or decreased smell, chest pain, conjunctivitis, diarrhea, dysgeusia or decreased taste, fatigue, fever or chills, headache, muscle aches or myalgias, nausea or vomiting, rash, and seizures), and among those aged <2 years, included apnea, cyanosis, decreased vocalization or stridor, dehydration, hypothermia, inability to eat or poor feeding, and lethargy. Symptoms are abstracted from the medical chart and might not be complete.

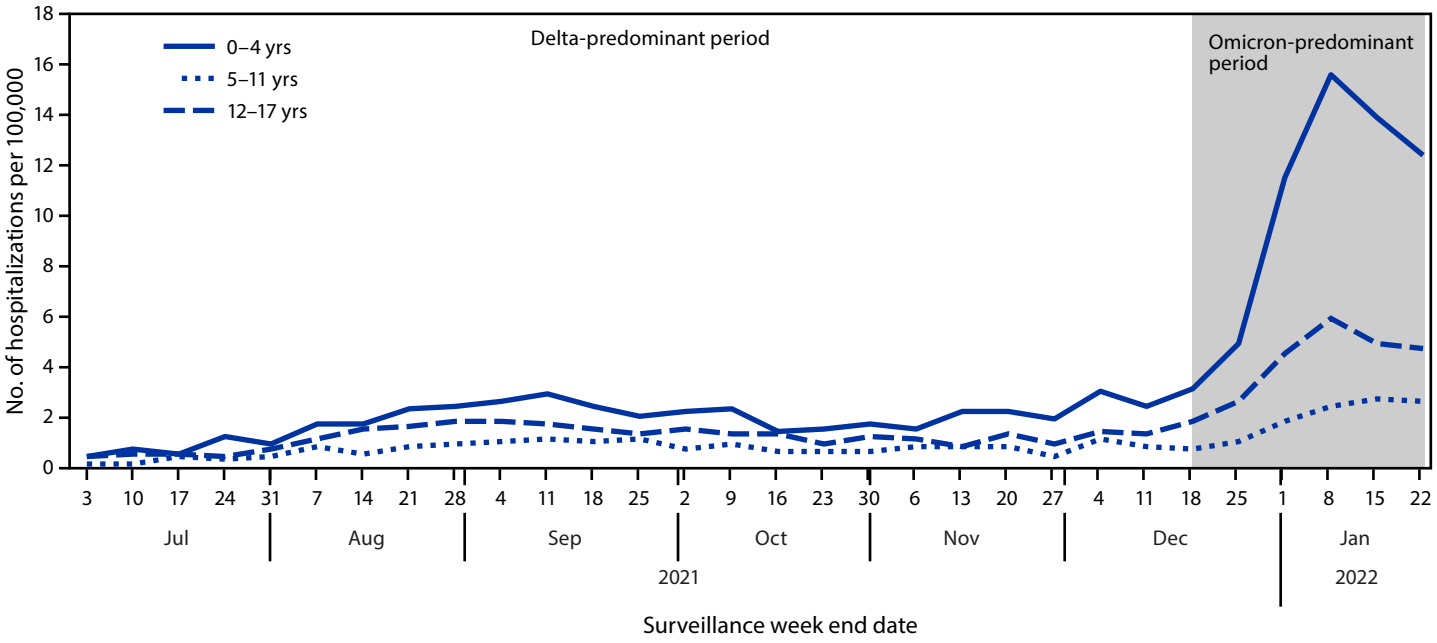
†††† Delta became the predominant (>50%) variant circulating in the United States the week ending July 3, 2021. By the week ending December 18, 2021, Omicron accounted for 38% of circulating variants; Omicron became the predominant variant the week ending December 25 at 74%.

§§§§ 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.

¶¶¶¶ Among the 1,943 sampled children and adolescents with COVID-19–associated hospitalizations during July 1–December 18, 2021, a total of 1,834 (94.4%) had data available on hospital length of stay, ICU admission, receipt of IMV, and in-hospital death at the time of reporting.

***** Among the 281 sampled children and adolescents with COVID-19–associated hospitalizations during December 19–31, 2021, a total of 266 (94.7%) had data available on hospital length of stay, ICU admission, receipt of IMV, and in-hospital death at the time of reporting.

FIGURE. Weekly COVID-19–associated hospitalization rates* among children and adolescents aged 0–17 years, by age group — COVID-NET, 14 states,† July 3, 2021–January 22, 2022



Abbreviation: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network.
* Number of patients with laboratory-confirmed COVID-19–associated hospitalizations per 100,000 population; rates are subject to change as additional data are reported.
† COVID-NET sites are in the following 14 states: California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah. Starting the week ending December 4, 2021, Maryland data are removed from weekly rate calculations.

with COVID-19–related symptoms recorded at admission (87.7% versus 86.9%) or with COVID-19 as the primary reason for admission (81.3% versus 81.6%).

The proportion of hospitalized adolescents who were fully vaccinated was significantly lower during the Delta-predominant period (8.3%) than during the Omicron-predominant period (22.2%) (Table 1), consistent with increasing adolescent vaccination coverage during the surveillance period. During July 1–December 31, 2021, 42.4% of hospitalized unvaccinated adolescents were non-Hispanic Black adolescents (Table 2). A higher proportion of unvaccinated adolescents (70.3%) than fully vaccinated adolescents (40.8%) had COVID-19 as a primary reason for admission. A significantly higher proportion of unvaccinated adolescents were admitted to the ICU (30.3%) than were those who were vaccinated (15.5%).

Discussion

The Omicron variant, which is associated with increased transmissibility and partial escape from infection- or vaccine-induced immunity, replaced Delta as the predominant variant in the United States in late December 2021 (*1*). Once the Omicron variant became predominant, peak population-based COVID-19–associated hospitalization rates among children and adolescents were four times as high as rates during the peak of the Delta period. Children aged 0–4 years, who were ineligible for vaccination during this time, experienced the largest increase in hospitalization rates. Observed indicators of severe COVID-19 among children and adolescents, in addition to the potential for longer-term sequelae (*4*,*5*), highlight the importance of multicomponent strategies to reduce the incidence of COVID-19, including vaccination of eligible persons and other prevention measures.†††††

Among adolescents aged 12–17 years, the only pediatric age group for whom a COVID-19 vaccine was approved throughout the study period, December hospitalization rates among unvaccinated adolescents were approximately six times those among fully vaccinated adolescents, suggesting that vaccines were highly effective in preventing serious COVID-19 illness. Vaccination eligibility was expanded to include children aged 5–11 years on November 2, 2021. As of December 31, 2021, 54% of the population aged 12–17 years and 16% of those aged 5–11 years had completed a COVID-19 primary vaccination series.§§§§§ Increasing vaccination coverage among both age groups can reduce COVID-19–associated hospitalizations (*6*);

††††† https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html
§§§§§ https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends

TABLE 1. Demographic and clinical characteristics and outcomes among children and adolescents aged 0–17 years with laboratory-confirmed COVID-19–associated hospitalizations,* by date of admission — COVID-NET, 14 states,† July 1–December 31, 2021

Characteristic	No. of hospitalized children (%)			
	Total			
	Jul 1–Dec 31	Jul 1–Dec 18	Dec 19–31	p-value§
Total	**2,100 (100.0)¶**	**1,834 (82.3)¶**	**266 (17.7)¶**	—
Age, yrs, median (IQR)	**7 (1–14)**	7 (1–14)	3.5 (0.4–13)	<0.001
Age group, yrs				
0–4	**920 (44.6)**	778 (42.5)	142 (54.2)	0.003
5–11	**460 (21.5)**	417 (22.5)	43 (16.9)	
12–17	**720 (33.9)**	639 (34.9)	81 (28.9)	
Sex				
Male	**1,081 (51.7)**	934 (51.2)	147 (54.2)	0.38
Female	**1,019 (48.3)**	900 (48.8)	119 (45.8)	
Race and ethnicity**				
Hispanic	**463 (21.8)**	420 (23.1)	43 (15.7)	<0.001
Black, non-Hispanic	**736 (35.8)**	619 (33.4)	117 (47.1)	
White, non-Hispanic	**670 (31.3)**	598 (32.6)	72 (25.5)	
Asian or Pacific Islander, non-Hispanic	**82 (3.9)**	71 (3.9)	11 (3.7)	
All other races††	**47 (2.3)**	41 (2.3)	6 (2.1)	
Unknown race and ethnicity	**102 (5.0)**	85 (4.8)	17 (5.9)	
Primary reason for admission§§				
Likely related to COVID-19	**1,703 (81.3)**	1,489 (81.3)	214 (81.6)	0.19
Obstetrics	**63 (2.9)**	57 (3.0)	6 (2.2)	
Inpatient surgery	**53 (2.6)**	43 (2.5)	10 (3.3)	
Psychiatric admission requiring medical care	**118 (5.6)**	108 (5.9)	10 (4.0)	
Trauma	**75 (3.5)**	67 (3.7)	8 (2.8)	
Other reason	**78 (3.8)**	62 (3.3)	16 (6.1)	
Unknown reason	**6 (0.3)**	6 (0.3)	0 (—)	
COVID-19–related symptoms at admission¶¶				
Yes	**1,832 (87.6)**	1,604 (87.7)	228 (86.9)	0.72
No	**264 (12.4)**	228 (12.3)	36 (13.1)	
Hospitalization outcomes				
Length of hospital stay, days, median (IQR)	**3 (1–5)**	3 (2–5)	2 (1–5)	0.15
ICU admission***	**562 (26.4)**	510 (27.8)	52 (20.2)	0.01
Invasive mechanical ventilation***	**118 (5.6)**	112 (6.3)	6 (2.3)	0.01
In-hospital death	**11 (0.5)**	11 (0.6)	0 (—)	0.38
Vaccination status (among patients aged 12–17 yrs)				
Fully vaccinated†††	**71 (9.9)**	53 (8.3)	18 (22.2)	<0.001
Unvaccinated	**647 (90.1)**	584 (91.7)	63 (77.8)	

See table footnotes on the next page.

enhanced outreach strategies are needed to address disparities in vaccination coverage by race/ethnicity.

Consistent with national hospital surveillance data (*7*), the findings in this report indicate that the Omicron-predominant period had higher rates of pediatric COVID-19 hospitalizations than the Delta-predominant period. No differences were found between the Delta- and Omicron-predominant periods in the proportion of hospitalizations that were likely to be related to COVID-19. Findings suggest that incidental admissions do not account for the increase in hospitalization rates observed during the Omicron period. Throughout the COVID-19 pandemic, admissions for reasons other than COVID-19 have been recorded (*8*,*9*), and during both the Delta- and Omicron-predominant periods, incidental admissions were more likely among fully vaccinated adolescents. Reasons for admission should continue to be monitored as more children and adolescents become fully vaccinated.

The findings in this report are subject to at least six limitations. First, COVID-19–associated hospitalizations might have been missed because of testing practices and test availability. Second, the period of Omicron variant predominance with available detailed clinical data is brief (December 19–31, 2021) and does not capture the peak of hospitalizations during the Omicron period; in addition, the Delta variant was still circulating in late December. Third, accounting for seasonality in comparisons of Delta and Omicron predominant periods was not possible. Fourth, the number of hospitalized children eligible for vaccination remained low at the time of reporting, and hospitalization rates stratified by vaccination status are subject to error if misclassification of vaccination status occurred. Fifth, because children aged 5–11 years could not meet the

TABLE 1. (*Continued*) Demographic and clinical characteristics and outcomes among children and adolescents aged 0–17 years with laboratory-confirmed COVID-19–associated hospitalizations,* by date of admission — COVID-NET, 14 states,† July 1–December 31, 2021

Abbreviations: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network; ICU = intensive care unit.

* Data are from a weighted sample of hospitalized children and adolescents with completed medical record abstractions. Sample sizes presented are unweighted with weighted percentages.

† Includes persons admitted to a hospital with an admission date during July 1–December 31, 2021. Maryland contributed data through November 26, 2021. Counties included in COVID-NET surveillance: California (Alameda, Contra Costa, and San Francisco counties); Colorado (Adams, Arapahoe, Denver, Douglas, and Jefferson counties); Connecticut (Middlesex and New Haven counties); Georgia (Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, and Rockdale counties); Iowa (one county represented); Maryland (Allegany, Anne Arundel, Baltimore, Baltimore City, Calvert, Caroline, Carroll, Cecil, Charles, Dorchester, Frederick, Garrett, Harford, Howard, Kent, Montgomery, Prince George's, Queen Anne's, St. Mary's, Somerset, Talbot, Washington, Wicomico, and Worcester counties); Michigan (Clinton, Eaton, Genesee, Ingham, and Washtenaw counties); Minnesota (Anoka, Carver, Dakota, Hennepin, Ramsey, Scott, and Washington counties); New Mexico (Bernalillo, Chaves, Doña Ana, Grant, Luna, San Juan, and Santa Fe counties); New York (Albany, Columbia, Genesee, Greene, Livingston, Monroe, Montgomery, Ontario, Orleans, Rensselaer, Saratoga, Schenectady, Schoharie, Wayne, and Yates counties); Ohio (Delaware, Fairfield, Franklin, Hocking, Licking, Madison, Morrow, Perry, Pickaway, and Union counties); Oregon (Clackamas, Multnomah, and Washington counties); Tennessee (Cheatham, Davidson, Dickson, Robertson, Rutherford, Sumner, Williamson, and Wilson counties); and Utah (Salt Lake County).

§ Proportions between the Delta and Omicron predominance periods were compared with chi-square tests or Fisher's exact tests (as appropriate), and medians were compared with the Wilcoxon rank-sum test; p-values <0.05 were considered statistically significant.

¶ Data are missing for <5% of observations for all variables.

** If ethnicity was unknown, non-Hispanic ethnicity was assumed.

†† Includes non-Hispanic persons reported as other or multiple races.

§§ Among sampled patients, COVID-NET collects data on the primary reason for admission to differentiate hospitalizations of patients with laboratory-confirmed SARS-CoV-2 infection who are likely admitted primarily for COVID-19 illness rather than for other reasons. During chart review, if the surveillance officer finds that the chief complaint or history of present illness mentions fever or respiratory illness, COVID-19–like illness, or suspected COVID-19, then the case is categorized as COVID-19–related illness as the primary reason for admission. Reasons for admission that are likely primarily not related to COVID-19 include the following categories: obstetrics/labor and delivery, inpatient surgery or procedures, psychiatric admission requiring acute medical care, trauma, other, or unknown. Reasons categorized as "other" are reviewed by two physicians to determine whether the admission is likely COVID-19 related.

¶¶ COVID-19–related symptoms included respiratory symptoms (congestion or runny nose, cough, hemoptysis or bloody sputum, shortness of breath or respiratory distress, sore throat, upper respiratory infection, influenza-like illness, and wheezing) and nonrespiratory symptoms (abdominal pain, altered mental status or confusion, anosmia or decreased smell, chest pain, conjunctivitis, diarrhea, dysgeusia or decreased taste, fatigue, fever or chills, headache, muscle aches or myalgias, nausea or vomiting, rash, and seizures), and among those aged <2 years, included apnea, cyanosis, decreased vocalization or stridor, dehydration, hypothermia, inability to eat or poor feeding, and lethargy. Symptoms are abstracted from the medical chart and might not be complete.

*** ICU admission and invasive mechanical ventilation are not mutually exclusive categories, and patients could have received both.

††† Fully vaccinated adolescents with COVID-19–associated hospitalizations were defined as those who had received the final dose in their primary series ≥14 days before receiving a positive SARS-CoV-2 test result associated with their hospitalization. Adolescents who received only 1 vaccine dose ≥14 days before the SARS-CoV-2 test date or had received a single dose of vaccine <14 days before the positive SARS-CoV-2 test results were considered partially vaccinated; they were not included in rates and were grouped with unvaccinated adolescents in other analyses. COVID-NET sites, through agreements with state health departments and other partners, collect COVID-19 vaccination information on COVID-19–associated hospitalizations through state-based vaccine registries. When possible, sites collect COVID-19 vaccination status on all persons with COVID-19 cases who are hospitalized, including the number of vaccine doses received, the vaccine product, and dates of vaccination administration.

definition for being fully vaccinated until December 7, 2021, vaccination among this age group was not considered in this study. However, vaccinations could have affected hospitalization rates during the Omicron period. Further, boosters among adolescents aged 12–17 years could not be examined because the recommendation was so recent. Finally, the COVID-NET catchment areas include approximately 10% of the U.S. population; thus, these findings might not be generalizable to the entire United States.

Coinciding with emerging predominance of the Omicron variant, rates of COVID-19–associated hospitalization among children and adolescents increased rapidly during the last 2 weeks of December 2021, especially among those aged 0–4 years. Moreover, among adolescents, hospitalization rates were higher among those who were unvaccinated. Vaccination of eligible persons, in addition to other prevention strategies such as masking, are critical to reducing the incidence of severe COVID-19 among children and adolescents.¶¶¶¶ All persons who are eligible for vaccination should receive and stay up to date with COVID-19 vaccines to reduce the risk for severe disease for themselves and others with whom they come into contact, including children who are currently too young to be vaccinated.******

¶¶¶¶ https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html

****** https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

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TABLE 2. Demographic and clinical characteristics and outcomes among fully vaccinated* and unvaccinated adolescents aged 12–17 years with laboratory-confirmed COVID-19–associated hospitalizations,† by date of admission — COVID-NET, 14 states,§ July 1–December 31, 2021

	No. of hospitalized adolescents (%)						
	Unvaccinated	Vaccinated		Unvaccinated		Vaccinated	
	Total						
Characteristic	Jul 1–Dec 31		p-value¶	Jul 1–Dec 18	Dec 19–31	Jul 1–Dec 18	Dec 19–31
Total	**647 (100.0)****	**71 (100.0)****	—	**584 (90.2)****	**63 (9.8)****	**53 (74.6)****	**18 (25.4)****
Age, yrs, median (IQR)	**15 (14–16)**	**15 (14–16)**	0.75	15 (14–17)	14 (13–16)	15 (14–16)	15 (14–16)
Sex							
Male	**298 (46.0)**	**25 (35.2)**	0.08	266 (45.5)	32 (50.8)	20 (37.7)	5 (27.7)
Female	**349 (54.0)**	**46 (64.8)**		318 (54.5)	31 (49.2)	33 (62.3)	13 (72.3)
Race and ethnicity††							
Hispanic	**148 (22.9)**	**14 (19.7)**	0.006	136 (23.3)	12 (19.0)	12 (22.6)	2 (11.1)
Black, non-Hispanic	**274 (42.4)**	**17 (24.0)**		240 (41.1)	34 (53.9)	11 (20.8)	6 (33.4)
White, non-Hispanic	**162 (25.0)**	**32 (45.0)**		154 (26.4)	8 (12.7)	25 (47.1)	7 (38.8)
Asian or Pacific Islander, non-Hispanic	**14 (2.2)**	**1 (1.4)**		10 (1.7)	4 (6.4)	1 (1.9)	0 (—)
All other races§§	**20 (3.1)**	**2 (2.8)**		19 (3.3)	1 (1.6)	1 (1.9)	1 (5.5)
Unknown race and ethnicity	**29 (4.5)**	**5 (7.1)**		25 (4.3)	4 (6.4)	3 (5.7)	2 (11.2)
Primary reason for admission¶¶							
Likely related to COVID-19	**454 (70.3)**	**29 (40.8)**	<0.001	413 (70.8)	41 (65.0)	19 (35.8)	10 (55.5)
Obstetrics	**40 (6.2)**	**0 (—)**		36 (6.2)	4 (6.4)	0 (—)	0 (—)
Inpatient surgery	**15 (2.3)**	**7 (9.8)**		13 (2.2)	2 (3.2)	5 (9.4)	2 (11.1)
Psychiatric admission requiring medical care	**79 (12.2)**	**27 (38.1)**		72 (12.4)	7 (11.1)	24 (45.3)	3 (16.8)
Trauma	**40 (6.2)**	**4 (5.6)**		35 (6.0)	5 (8.0)	3 (5.7)	1 (5.5)
Other reason	**16 (2.5)**	**4 (5.6)**		12 (2.1)	4 (6.3)	2 (3.8)	2 (11.1)
Unknown reason	**2 (0.3)**	**0 (—)**		2 (0.3)	0 (—)	0 (—)	0 (—)
COVID-19–related symptoms at admission***							
Yes	**536 (83.0)**	**53 (74.6)**	0.08	487 (83.4)	49 (79.0)	37 (69.8)	16 (88.9)
No	**110 (17.0)**	**18 (25.4)**		97 (16.6)	13 (21.0)	16 (30.2)	2 (11.1)
Hospitalization outcomes							
Length of hospital stay, days, median (IQR)	**4 (2–7)**	**3 (1–8)**	0.55	4 (2–6.5)	4 (2–8)	3 (2–9)	3 (1–5)
ICU admission†††	**196 (30.3)**	**11 (15.5)**	0.009	184 (31.6)	12 (19.1)	8 (15.1)	3 (16.6)
Invasive mechanical ventilation†††	**42 (6.5)**	**6 (8.4)**	0.54	41 (7.1)	1 (1.6)	5 (9.4)	1 (5.5)
In-hospital death	**5 (0.8)**	**2 (2.8)**	0.10	5 (0.9)	0 (—)	2 (3.8)	0 (—)

See table footnotes on the next page.

Summary

What is already known about this topic?

COVID-19 can cause severe illness in children and adolescents.

What is added by this report?

Coinciding with increased circulation of the Omicron variant, COVID-19–associated hospitalization rates among children and adolescents aged 0–17 years increased rapidly in late December 2021, especially among children aged 0–4 years who are not yet eligible for vaccination. Throughout the periods of Delta and Omicron predominance, hospitalization rates remained lower among fully vaccinated adolescents aged 12–17 years than among unvaccinated adolescents.

What are the implications for public health practice?

Strategies to prevent COVID-19 among children and adolescents, including vaccination of eligible persons, are critical.

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TABLE 2. (*Continued*) Demographic and clinical characteristics and outcomes among fully vaccinated* and unvaccinated adolescents aged 12–17 years with laboratory-confirmed COVID-19–associated hospitalizations,† by date of admission — COVID-NET, 14 states,§ July 1–December 31, 2021

Abbreviations: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network; ICU = intensive care unit.

* Fully vaccinated adolescents with COVID-19–associated hospitalizations were defined as those who had received the final dose in their primary series ≥14 days before receiving a positive SARS-CoV-2 test result associated with their hospitalization. Adolescents who received only 1 vaccine dose ≥14 days before the SARS-CoV-2 test date or had received a single dose of vaccine <14 days before the positive SARS-CoV-2 test results were considered partially vaccinated; they were not included in rates and were grouped with unvaccinated adolescents in other analyses. COVID-NET sites, through agreements with state health departments and other partners, collect COVID-19 vaccination information on COVID-19–associated hospitalizations through state-based vaccine registries. When possible, sites collect COVID-19 vaccination status on all persons with COVID-19 cases who are hospitalized, including the number of vaccine doses received, the vaccine product, and dates of vaccination administration.

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††† ICU admission and invasive mechanical ventilation are not mutually exclusive categories, and patients could have received both.

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References

1. CDC COVID-19 Response Team. SARS-CoV-2 B.1.1.529 (Omicron) variant—United States, December 1–8, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1731–4. PMID:34914670 https://doi.org/10.15585/mmwr.mm7050e1
2. Delahoy MJ, Ujamaa D, Whitaker M, et al.; COVID-NET Surveillance Team. Hospitalizations associated with COVID-19 among children and adolescents—COVID-NET, 14 states, March 1, 2020–August 14, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1255–60. PMID:34499627 https://doi.org/10.15585/mmwr.mm7036e2
3. Woodruff RC, Campbell AP, Taylor CA, et al. Risk factors for severe COVID-19 in children. Pediatrics 2021;e2021053418. PMID:34935038 https://doi.org/10.1542/peds.2021-053418
4. Feldstein LR, Rose EB, Horwitz SM, et al.; Overcoming COVID-19 Investigators; CDC COVID-19 Response Team. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334–46. PMID:32598831 https://doi.org/10.1056/NEJMoa2021680
5. Barrett CE, Koyama AK, Alvarez P, et al. Risk for newly diagnosed diabetes >30 days after SARS-CoV-2 infection among persons aged <18 years—United States, March 1, 2020–June 28, 2021. MMWR Morb Mortal Wkly Rep 2022;71:59–65. PMID:35025851 https://doi.org/10.15585/mmwr.mm7102e2
6. Olson SM, Newhams MM, Halasa NB, et al.; Overcoming Covid-19 Investigators. Effectiveness of BNT162b2 vaccine against critical Covid-19 in adolescents. N Engl J Med 2022;NEJMoa2117995. PMID:35021004 https://doi.org/10.1056/NEJMoa2117995
7. Iuliano AD, Brunkard JM, Boehmer TK, et al. Trends in disease severity and health care utilization during the early Omicron variant period compared with previous SARS-CoV-2 high transmission periods—United States, December 2020–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:146–52. PMID:35085225 https://doi.org/10.15585/mmwr.mm7104e4
8. Havers FP, Whitaker M, Self JL, et al.; COVID-NET Surveillance Team. Hospitalization of adolescents aged 12–17 years with laboratory-confirmed COVID-19—COVID-NET, 14 states, March 1, 2020–April 24, 2021. MMWR Morb Mortal Wkly Rep 2021;70:851–7. PMID:34111061 https://doi.org/10.15585/mmwr.mm7023e1
9. Wanga V, Gerdes ME, Shi DS, et al. Characteristics and clinical outcomes of children and adolescents aged <18 years hospitalized with COVID-19—six hospitals, United States, July–August 2021. MMWR Morb Mortal Wkly Rep 2021;70:1766–72. PMID:34968374 https://doi.org/10.15585/mmwr.mm705152a3

Notes from the Field

Outbreak of COVID-19 Among a Highly Vaccinated Population Aboard a U.S. Navy Ship After a Port Visit — Reykjavik, Iceland, July 2021

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On July 27, 2021, a fully vaccinated* crew member on a U.S. Navy ship who had been symptomatic with cough and congestion for 4 days was evaluated in the ship's onboard medical department and received a positive test result† for SARS-CoV-2, the virus that causes COVID-19. The ship had approximately 350 personnel on board§; COVID-19 vaccination rate was >98%.¶ The ship had been on an 8-week deployment with port visits in Norway (July 13–14) and in Reykjavik, Iceland (July 18–21). Masking and physical distancing mandates on the ship were relaxed while at sea but were immediately reimplemented upon identification of the crew member's positive test result. During the deployment, personnel had permission to go ashore only during the Iceland port visit and only if they were fully vaccinated. Before July 27, no one had been evaluated at the onboard medical department for respiratory symptoms. Although reported COVID-19 incidence was low in Iceland just before the port visit (17.5 per 100,000 population on July 18), incidence increased approximately elevenfold, to 219.5 per 100,000 on July 27 with emergence of the B.1.617.2 (Delta) variant.** At the onset of the COVID-19 pandemic, outbreaks on some U.S. Navy ships led to attack rates greater than 25% (*1*) of the crew in the confined environment. In this outbreak during Delta variant predominance, the combination of a high vaccination rate with prevention strategies resulted in a lower (6.3%) attack rate of COVID-19 than seen at the onset of the pandemic.

After identification of the initial case on July 27, all ship personnel were notified to report to the onboard medical department if they had any COVID-19–like signs or symptoms,†† resulting in diagnoses of an additional 11 COVID-19 cases that day. The ship immediately instituted prevention measures, including mask use, physical distancing, increased cleaning, isolation of the 12 initial patients, testing of 69 close contacts,§§ and testing and quarantine of six unvaccinated persons (two of whom were also close contacts). On July 28 and 29, six additional cases were identified through testing. Nasal swabs from these 18 persons with positive antigen test results were sent off the ship for reverse transcription–polymerase chain reaction (RT-PCR) testing and all were positive for SARS-CoV-2.¶¶ Further analysis determined 17 of the 18 specimens were Delta variant AY.9 lineage; 16 of the 17 were identical.*** During this same time frame at the end of July, Delta AY.9 was identified in 8% of specimens in Iceland and fewer than 1% of specimens in Norway and the United States.††† The 18 infected persons were removed from the ship on July 31 to reduce the ship's health care requirements and to prevent further transmission. Four additional cases of COVID-19 were identified during August 1–7 (including three diagnosed aboard the ship and one postdeployment) with onset July 28–August 5. The overall attack rate was 6.3%. The ship returned to its home port on August 3, concluding its deployment as scheduled.

Among the 22 infected personnel identified, all were fully vaccinated, and all were symptomatic. Most (91%) were aged <40 years (average age = 30.2 years). No patient required hospitalization or supplemental oxygen and no deaths occurred. Before the outbreak was identified on July 27, 13 (59%) of the 22 infected personnel had been symptomatic for a median of 3 days (range = 1–5 days) aboard the ship with no masking or physical distancing protocols in place (Figure). During the 15-day outbreak period (July 22–August 5), 91 personnel received rapid antigen testing.

* Fully vaccinated was defined as 2 weeks after receipt of a single dose of Ad.26.COV2.S (Janssen [Johnson & Johnson]) vaccine or the second dose of either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccines.

† The Abbott BinaxNOW COVID-19 Ag Card rapid antigen test was used to test personnel aboard the ship. During the deployment, personnel evaluated at the clinic for COVID-19–like symptoms were tested when seen by the ship's medical department.

§ During July 18–August 3, the total number of crew members fluctuated between 346 and 355.

¶ This outbreak occurred 1 month before the August 24, 2021, memo by the U.S. Secretary of Defense mandating vaccines in service members. However, personnel were not authorized to depart the ship for liberty without being fully vaccinated.

** https://www.covid.is/data/ (Accessed December 16, 2021)

†† Fever, chills, rigors, myalgia, headache, sore throat, loss of taste or smell, cough, shortness of breath, or difficulty breathing.

§§ A close contact was defined as anyone within 6 feet of an infected person for a cumulative total of ≥15 minutes within a 24-hour period.

¶¶ Samples were sent to the U.S. Naval Hospital in Rota, Spain, for RT-PCR testing and then sent to Naval Medical Research Center – Frederick on Fort Detrick, Maryland, for genome sequencing and phylogenetic analysis.

*** One of the 17 Delta variant samples had an additional mutation in ORF10 (G29645T, ORF10) resulting in a lysine versus a valine at amino acid V30L. The final sample was not assigned a lineage because of insufficient consensus genome length.

††† Reported data from Outbreak.info's AY.9 Lineage Report. https://outbreak.info/situation-reports?pango%C2%A0=%C2%A0AY.9&loc%C2%A0=%C2%A0ISL&loc%C2%A0=%C2%A0NOR&loc%C2%A0=%C2%A0USA&selected%C2%A0=%C2%A0ISL&overlay%C2%A0=%C2%A0false (Accessed December 31, 2021).

Only one case was identified >14 days after the Iceland port visit, demonstrating very limited spread of infection despite exposure to symptomatic personnel for a median of 3 days in the confined shipboard spaces. In previous U.S. Navy shipboard outbreaks, before COVID-19 vaccines were available, SARS-CoV-2 spread was rapid and extensive, with attack rates of 26.6% (1,271 of 4,779 personnel) on one ship (*1*) and 36.3% (121 of 333) on another (Navy and Marine Corps Public Health Center, unpublished data, 2020). These attack rates were approximately four and six times higher, respectively, than that described in this report.

Summary

What is already known about this topic?

At the onset of the COVID-19 pandemic, outbreaks on some U.S. Navy ships led to attack rates >25% in the confined environment.

What is added by this report?

During July 2021, an outbreak of Delta variant aboard a U.S. Navy ship after a port visit in Iceland resulted in a 6% attack rate. The ship's population was >98% immunized, and although prevention measures (e.g., mask use, extra cleaning, and distancing procedures) were relaxed during the underway period, they were reimplemented upon identification of the first case.

What are the implications for public health practice?

Vaccination, in combination with other prevention strategies, resulted in a much lower attack rate of COVID-19 than seen in the early months of the pandemic.

The findings in this report are subject to at least four limitations. First, shipboard testing was limited to rapid antigen testing, which has a lower sensitivity than RT-PCR testing in asymptomatic persons (*2*). Second, testing relied on persons to report symptoms and close contacts, which is subject to recall bias. Third, this was an outbreak of Delta variant and findings might not be applicable to B.1.1.529 (Omicron) or other variant outbreaks. Finally, this outbreak occurred in a highly vaccinated, young, healthy population, thus limiting generalizability to the overall U.S. population.

This outbreak in the enclosed environment of a ship suggests that high vaccination rates, in combination with COVID-19 prevention measures, can substantially reduce the spread of SARS-CoV-2, despite the high transmissibility of the Delta variant and introduction of SARS-CoV-2 into a congregate setting. Infections among vaccinated persons did occur, which is expected (*3*), but symptoms were mild. Vaccination, in coordination with multicomponent prevention strategies, are critical to limiting SARS-CoV-2 transmission and COVID-19–related illness.

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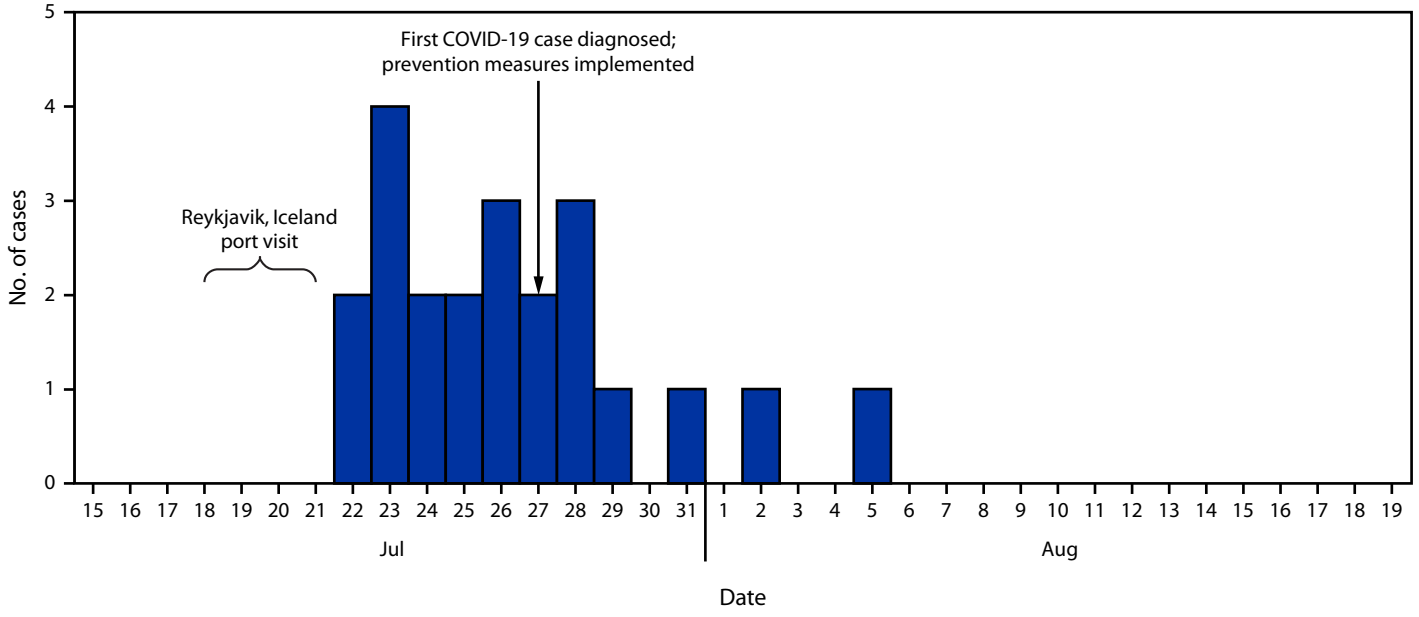
FIGURE. Date of symptom onset or specimen collection* for COVID-19 cases identified during an outbreak on a U.S. Navy ship (N = 22) — Reykjavik, Iceland, July–August 2021†



* Whichever occurred earlier; for all but one case, symptom onset preceded specimen collection.
† Prevention measures included mask use, physical distancing, increased cleaning, canvassing for mild symptoms, and increased testing.

[1]Navy Environmental and Preventive Medicine Unit 7, Rota, Spain; [2]Naval Medical Research Center – Frederick, Fort Detrick, Maryland; [3]Leidos, Reston, Virginia; [4]Navy and Marine Corps Public Health Center, Portsmouth, Virginia.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Kimberly A. Bishop-Lilly reports support from the Armed Forces Health Surveillance Division, Global Emerging Infections Surveillance Branch. No other potential conflicts of interest were disclosed.

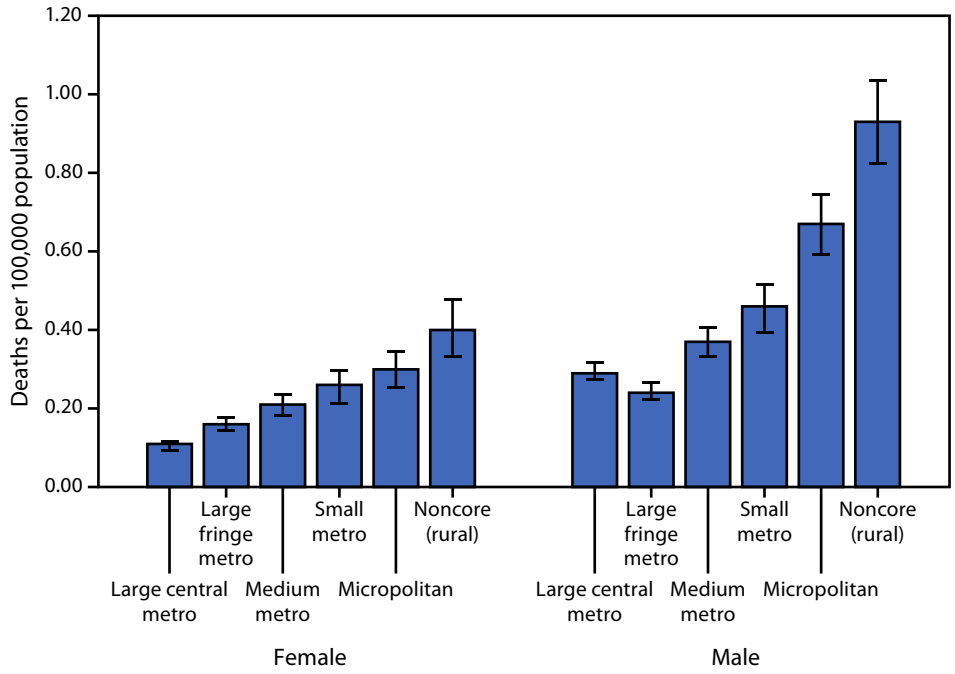
References

1. Kasper MR, Geibe JR, Sears CL, et al. An outbreak of Covid-19 on an aircraft carrier. N Engl J Med 2020;383:2417–26. PMID:33176077 https://doi.org/10.1056/NEJMoa2019375
2. Pollock NR, Jacobs JR, Tran K, et al. Performance and implementation evaluation of the Abbott BinaxNOW rapid antigen test in a high-throughput drive-through community testing site in Massachusetts. J Clin Microbiol 2021;59:e00083–21. PMID:33622768 https://doi.org/10.1128/JCM.00083-21
3. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Death Rates* Attributed to Excessive Cold or Hypothermia,† by Urbanization Level§ and Sex — National Vital Statistics System, 2018–2020



* Crude rate of deaths per 100,000 population; 95% CIs indicated by error bars.
† Deaths attributed to excessive cold or hypothermia were identified using the *International Classification of Diseases, Tenth Revision* underlying cause-of-death code X31 (exposure to excessive natural cold) and multiple cause-of-death code T68 (hypothermia).
§ Urbanization level is based on county of residence using the National Center for Health Statistics Urban-Rural Classification Scheme for Counties. http://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf

During 2018–2020, death rates attributed to excessive cold or hypothermia were generally higher in more rural areas. Among females, the death rate increased from 0.11 per 100,000 for those residing in large central metro areas, to 0.40 for those in noncore (rural) areas. Among males, the death rates were lowest for those residing in large central metro areas (0.29) and large fringe metro areas (0.24), and highest in noncore (rural) areas (0.93). Males had higher death rates than females for each corresponding urbanization level.

Source: National Center for Health Statistics, National Vital Statistics System, Mortality Data, 2018–2020. https://www.cdc.gov/nchs/nvss/deaths.htm

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