

## Use of Ebola Vaccines — Worldwide, 2021–2023

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### Abstract

Ebola virus disease (Ebola) is a rare but severe illness in humans, with an average case fatality rate of approximately 50%. Two licensed vaccines are currently available against *Orthoebolavirus zairense*, the virus that causes Ebola: the 1-dose rVSVΔG-ZEBOV-GP (ERVEBO [Merck]) and the 2-dose regimen of Ad26.ZEBOV and MVA-BN-Filo (Zabdeno/Mvabea [Johnson & Johnson]). The Strategic Advisory Group of Experts on Immunization recommends the use of 1-dose ERVEBO during Ebola outbreaks, and in 2021, a global stockpile of ERVEBO was established to ensure equitable, timely, and targeted access to vaccine doses for future Ebola outbreaks. This report describes the use of Ebola vaccines and the role of the stockpile developed and managed by the International Coordinating Group (ICG) on Vaccine Provision during 2021–2023. A total of 145,690 doses have been shipped from the ICG stockpile since 2021. However, because outbreaks since 2021 have been limited and rapidly contained, most doses (139,120; 95%) shipped from the ICG stockpile have been repurposed for preventive vaccination of high-risk groups, compared with 6,570 (5%) used for outbreak response. Repurposing doses for preventive vaccination could be prioritized in the absence of Ebola outbreaks to prevent transmission and maximize the cost-efficiency and benefits of the stockpile.

### Introduction

*Orthoebolavirus zairense*, the virus responsible for Ebola virus disease (Ebola), has caused the largest filovirus outbreaks worldwide; the average Ebola case fatality rate is approximately 50% (1). Currently, two licensed vaccines are recommended for the prevention of Ebola caused by *Orthoebolavirus zairense*: the 1-dose rVSVΔG-ZEBOV-GP (ERVEBO [Merck]) and the 2-dose Ad26.ZEBOV and MVA-BN-Filo (Zabdeno/Mvabea

[Johnson & Johnson]) (2). ERVEBO was licensed by the European Medicines Agency and the Food and Drug Administration in 2019 and is indicated for use in persons aged >12 months (2,3). It has a shelf life of 3 years. The vaccine has also been approved in Burundi, Central African Republic, Côte d'Ivoire, Democratic Republic of the Congo (DRC), Ghana, Guinea, Republic of the Congo, Rwanda, Sierra Leone, Uganda, and Zambia (Merck regulatory department, personal communication, December 6, 2023) (2). In 2021, the Strategic Advisory Group of Experts on Immunization recommended using ERVEBO in ring vaccination during Ebola outbreaks, because it confers protection after 1 dose (4). Zabdeno/Mvabea

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is recommended for preventive vaccination in areas at lower risk for Ebola (or areas neighboring an outbreak) because the full regimen requires 2 doses administered 56 days apart (4).

ERVEBO was shown to be safe and effective during clinical trials and has likely played an important role in limiting Ebola morbidity and mortality during outbreaks since it was first introduced (2). In a study conducted in Ebola treatment facilities in DRC, 56% of unvaccinated patients died from Ebola, compared with 25% of patients vaccinated before symptom onset (5). Ensuring timely availability of Ebola vaccine doses in the event of a major Ebola outbreak is crucial to limiting its spread and protecting global health security.

In 2021, a global stockpile of ERVEBO was established under the International Coordinating Group (ICG) on Vaccine Provision to ensure equitable and timely access to vaccine doses for Ebola outbreaks\* (6). Upon the establishment of the ICG stockpile, the global agreement was to maintain the stockpile at 500,000 doses (6). Gavi, the Vaccine Alliance (<https://www.gavi.org>), supports the procurement of vaccine and operational costs to countries for vaccination (6). Whereas the availability of doses for outbreak response is the primary objective of the

stockpile, ICG has approved requests for targeted preventive vaccination of high-risk groups, including health care workers and frontline workers in countries at risk for Ebola outbreaks. This report describes the use of Ebola vaccines and the role of the ICG vaccine stockpile during 2021–2023.

## Methods

Data on past Ebola outbreaks were obtained from the World Health Organization (WHO) Regional Office for Africa's weekly Outbreak and Emergencies situation reports (1). Information on Ebola vaccine stockpile requests and deliveries during 2021–2023 was obtained from the ICG Secretariat. Data on the stockpile size were obtained from UNICEF Supply Division's ICG Ebola vaccine stockpile report dated January 19, 2024 (7). This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.†

## Results

Ebola vaccine was first used during clinical trials in the 2014–2015 West African outbreak, then under a compassionate use protocol in Guinea during 2015, and again in the 2018–2020 eastern DRC outbreak. Since 2015, when Ebola vaccines were first deployed in outbreak response, recorded

\*The ICG Ebola vaccine stockpile is managed by the ICG on Vaccine Provision comprising Médecins sans Frontières, the International Federation of Red Cross and Red Crescent Societies, UNICEF, and the World Health Organization. These organizations support maintenance and decisions regarding vaccine allocations from the ICG on Vaccine Provision's stockpile of Ebola vaccine. <https://www.who.int/groups/icg/about>

† 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.

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Ebola outbreaks have varied in frequency, size, and origin, with recent outbreaks more often linked to reintroduction through viral persistence<sup>§</sup> (four of five outbreaks since 2021) than to zoonotic spillover (Table 1).

The ICG Ebola vaccine stockpile reached the goal of 500,000 doses in 2022 and, as of December 2023, holds 518,890 doses. In total, 208,390 (40%) doses from the current stockpile are scheduled to expire in 2024. Doses from the ICG stockpile were first deployed in 2021 in DRC for outbreak response. During 2021–2023, a total of 145,690 ERVEBO doses were shipped through requests from the ICG stockpile. Among 11 requests to ICG during this period, 10 were approved or partially approved, and one request was declined<sup>¶</sup> (Table 2). All requests to ICG for outbreak response (three of 11) were delivered within 1 week of being received. Longer times to delivery were noted for shipments intended for preventive vaccination because of the additional planning and engagement around those activities.

The number of doses shipped from the stockpile has increased annually, from 4,800 doses in 2021, to 13,870 doses in 2022, and 127,020 doses in 2023. During this period, 42,620 doses expired. Most doses shipped (139,120; 95%) were repurposed for preventive vaccination. Five percent (6,570) of doses were shipped for outbreak response use. DRC has received the largest number of vaccine doses (111,000; 76%), followed by Uganda (23,460; 16%) and Guinea-Bissau (11,170; 8%).

## Discussion

The ICG stockpile provides equitable access to vaccines that can be shipped quickly in the event of an Ebola outbreak. The relatively small number of doses used for outbreak response (6,570; 5% of doses shipped) reflects the smaller size and rapid containment of Ebola outbreaks since 2021. North Kivu, DRC, has received and administered more doses than any other geographic area worldwide since 2018, which might have contributed to the rapid containment of subsequent outbreaks in that area (1).

After approvals of vaccine for preventive use by ICG in 2022, WHO, in early 2023, circulated an internal memo on behalf of ICG informing at-risk countries of the availability of vaccines for preventive vaccination of health care workers

<sup>§</sup> Person-to-person transmission of Ebola virus that persisted in immunologically privileged sites (sites that are able to tolerate the introduction of antigen without eliciting an inflammatory immune response, including the eyes, placenta, fetus, testicles, and central nervous system) or body fluids after recovery from acute infection in humans, in contrast to outbreaks originating from zoonotic spillover, which is the transmission of virus from an animal to a human.

<sup>¶</sup> The request to ICG that was not approved lacked justification that the security forces to be vaccinated were involved in Ebola outbreak response and were at risk. ICG invited the country to resubmit the application prioritizing staff members involved in Ebola response activities.

and frontline workers. Preventive vaccination campaigns have targeted health care workers and frontline workers in at-risk countries, given their increased risk for exposure because of their frequent contact with patients (8). The addition of preventive Ebola vaccination of these workers could reduce total cases, hospitalizations, and deaths in Ebola outbreaks by an estimated 14%–38% compared with nonpharmaceutical interventions and ring vaccination alone (8).

The variability of Ebola outbreak size and time to containment makes predicting future vaccine needs challenging. Repurposing doses for preventive vaccination of targeted groups can protect high-risk persons as well as make use of doses with a shorter shelf life. More than 200,000 short-shelf-life doses in the ICG stockpile due to expire in 2024 could be redirected for preventive vaccination. In addition to focusing on reactive (outbreak response) vaccination, early planning for preventive vaccination with short-shelf-life doses could be incorporated into future stockpile management strategies. Additional studies accounting for the variability in outbreak size could guide planning to maximize the cost-efficiency of stockpile management.

The frequency of recent outbreaks, especially those linked to viral persistence, highlights the need for innovative strategies to protect Ebola survivors and prevent reintroductions. One such strategy is to offer postoutbreak immunization to close contacts of survivors, including new sex partners and other groups at risk for transmission because of viral persistence (9). Additional avenues to expand preventive vaccination among high-risk populations could be explored in countries at risk for outbreaks. Demand-generation activities\*\* incorporating findings from community engagement and vaccine acceptance studies in targeted risk groups could accompany vaccination campaigns and help develop targeted engagement plans. Investments and advocacy for preventive vaccination against Ebola are crucial for health system preparedness and resiliency. Currently, Gavi, WHO, and UNICEF are coordinating with other partners to develop a learning agenda<sup>††</sup> to help guide research prioritization and funding decisions for Ebola vaccine use.

## Limitations

The findings in this report are subject to at least two limitations. First, whereas the Ebola vaccine has reduced morbidity and mortality during outbreaks, the impact of Ebola vaccines on preventing outbreaks is difficult to ascertain because of the

\*\* Activities that aim to increase public awareness of and coverage with the vaccine and might include public education campaigns, health care worker education and engagement, community outreach, targeted messaging to high-risk groups, and increased access to the vaccine.

†† A set of prioritized vaccine implementation research questions and activities to guide evidence-building and decision-making around the Ebola vaccine.

**TABLE 1. Characteristics of reported Ebola virus disease outbreaks — World Health Organization, African Region, 2014–2023\***

Start date–end date	Total no. of cases	Total no. of deaths (CFR, %)	Country or countries	Region/Province	Origin
Mar 23, 2014–Jun 10, 2016	28,610	11,308 (40)	Guinea, Liberia, and Sierra Leone	NA	Zoonotic spillover
Jul 23–Oct 20, 2014	20	8 (40)	Nigeria	Lagos	Human transmission from West Africa outbreak
Jul 26–Nov 21, 2014	69	49 (71)	DRC	Equateur	Zoonotic Spillover
Aug 23–Oct 17, 2014	8	6 (75)	Senegal	Dakar	Human transmission from West Africa outbreak
Oct 23–Dec 6, 2014	1	0 (—)	Mali	Bamako and Kayes	Human transmission from West Africa outbreak
May 11–Jul 2, 2017	8	4 (50)	DRC	Bas Uele	Zoonotic spillover
May 8–Jul 24, 2018	54	33 (61)	DRC	Equateur	Zoonotic spillover
Jun 1–Nov 18, 2020	130	55 (42)	DRC	Equateur	Zoonotic spillover and viral persistence
Aug 1, 2018–Jun 25, 2020	3,470	2,287 (66)	DRC and Uganda	North Kivu, South Kivu, and Ituri	Zoonotic spillover
Feb 7–May 3, 2021	12	6 (50)	DRC	North Kivu	Viral persistence
Feb 14–Jun 19, 2021	23	12 (52)	Guinea	N'Zérékoré	Viral persistence
Oct 8–Dec 16, 2021	11	9 (82)	DRC	North Kivu	Viral persistence
Apr 23–Jul 4, 2022	5	5 (100)	DRC	Equateur	Zoonotic spillover <sup>†</sup>
Aug 22–Sep 27, 2022	1	1 (100)	DRC	North Kivu	Viral persistence <sup>§</sup>

**Abbreviations:** CFR = case fatality rate; DRC = Democratic Republic of the Congo; NA = not applicable.

\* Outbreak data obtained from the World Health Organization Regional Office for Africa weekly Outbreak and Emergencies situation reports was compared with data from CDC available online. <https://www.cdc.gov/vhf/ebola/history/chronology.html> (Accessed January 9, 2024).

<sup>†</sup> Zoonotic spillover is the transmission of virus from an animal to a human.

<sup>§</sup> Person-to-person transmission of Ebola virus from virus that persisted in immunologically privileged sites (sites that are able to tolerate the introduction of antigen without eliciting an inflammatory immune response, including the eyes, placenta, fetus, testicles, and central nervous system) or body fluids after recovery from acute infection.

**TABLE 2. Requests to the International Coordinating Group on Vaccine Provision for Ebola vaccine deliveries from global stockpile, by country and year — worldwide, 2021–2023**

Country	Year	No. of doses requested	No. of doses shipped	Vaccination strategy	Target groups	Days from request to delivery	Approval status
DRC	2021	4,800	4,800	Outbreak response	Ring vaccination	6	Approved
	2022	1,570	1,770	Outbreak response	Ring vaccination	7	Approved
	2022	962	962*	Outbreak response	Ring vaccination	2	Approved
	2023	75,000	21,670	Preventive campaign	Frontline workers <sup>†</sup>	20	Approved
	2023	82,647	82,760	Preventive campaign	Frontline workers	30	Approved
Uganda	2022	12,000	12,060	Preventive campaign	Frontline workers	25	Approved
	2023	17,096	11,400	Preventive campaign	Frontline workers and security forces	118	Partially approved
Guinea-Bissau	2023	10,963	11,170	Preventive campaign	Health care and frontline workers and support staff members	48	Approved
Switzerland	2022	40	40	Preventive campaign	International frontline workers	0	Approved
	2023	20	20	Preventive campaign	International frontline workers	0	Approved
Kenya	2022	2,000	0	Preventive campaign	Security forces	NA	Not approved <sup>§</sup>

**Abbreviations:** DRC = Democratic Republic of the Congo; ICG = International Coordinating Group; NA = not applicable.

\* Doses shifted from Equateur province to North Kivu province in DRC from previously shipped doses approved by ICG.

<sup>†</sup> Frontline workers are generally considered to be personnel directly involved in essential, public-facing roles related to health services or outbreak response; countries might define this group differently.

<sup>§</sup> The request to ICG that was not approved lacked justification that the security forces to be vaccinated were involved in Ebola outbreak response and were at risk. ICG invited the country to resubmit the application prioritizing staff members involved in Ebola response activities.

infrequent occurrence of the disease. Second, important data are lacking regarding the duration of protection, vaccine effectiveness in outbreak situations, and the need for booster doses. These data will be needed to guide decision-making regarding vaccination strategies and should be a focus for future research.

### Implications for Public Health Practice

The availability of licensed Ebola vaccines is an important advancement in Ebola prevention and global health security. In the absence of large-scale outbreaks, the demand for vaccines lags behind the current supply of doses, and preventive vaccination could be considered for high-risk groups. Investments,

## References

## Summary

## What is already known about this topic?

The International Coordinating Group on Vaccine Provision established an Ebola vaccine stockpile in 2021 to ensure equitable, rapid access to vaccines during an outbreak.

## What is added by this report?

Since 2021, the absence of large Ebola virus disease (Ebola) outbreaks has resulted in fewer vaccine doses being used for outbreak response. Out of the 145,690 doses shipped from the stockpile through 2023, 95% (139,120) have been repurposed for preventive vaccination, and 5% (6,570) were used in outbreak response.

## What are the implications for public health practice?

Repurposing doses for preventive vaccination could be prioritized in the absence of Ebola outbreaks to prevent transmission and maximize the cost-efficiency and benefits of the stockpile.

advocacy, and additional research to inform preventive vaccination are crucial for health system preparedness and resiliency. Focus on working with countries at risk for Ebola outbreaks to identify high-risk groups and generate demand for preventive vaccination is important for optimizing the use of the stockpile. Ensuring the availability of sufficient Ebola vaccine doses for emergency outbreak response remains the priority of ICG.

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## SARS-CoV-2 Viral Shedding and Rapid Antigen Test Performance — Respiratory Virus Transmission Network, November 2022–May 2023

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### Abstract

As population immunity to SARS-CoV-2 evolves and new variants emerge, the role and accuracy of antigen tests remain active questions. To describe recent test performance, the detection of SARS-CoV-2 by antigen testing was compared with that by reverse transcription–polymerase chain reaction (RT-PCR) and viral culture testing during November 2022–May 2023. Participants who were enrolled in a household transmission study completed daily symptom diaries and collected two nasal swabs (tested for SARS-CoV-2 via RT-PCR, culture, and antigen tests) each day for 10 days after enrollment. Among participants with SARS-CoV-2 infection, the percentages of positive antigen, RT-PCR, and culture results were calculated each day from the onset of symptoms or, in asymptomatic persons, from the date of the first positive test result. Antigen test sensitivity was calculated using RT-PCR and viral culture as references. The peak percentage of positive antigen (59.0%) and RT-PCR (83.0%) results occurred 3 days after onset, and the peak percentage of positive culture results (52%) occurred 2 days after onset. The sensitivity of antigen tests was 47% (95% CI = 44%–50%) and 80% (95% CI = 76%–85%) using RT-PCR and culture, respectively, as references. Clinicians should be aware of the lower sensitivity of antigen testing compared with RT-PCR, which might lead to false-negative results. This finding has implications for timely initiation of SARS-CoV-2 antiviral treatment, when early diagnosis is essential; clinicians should consider RT-PCR for persons for whom antiviral treatment is recommended. Persons in the community who are at high risk for severe COVID-19 illness and eligible for antiviral treatment should seek testing from health care providers with the goal of obtaining a more sensitive diagnostic test than antigen tests (i.e., an RT-PCR test).

### Introduction

SARS-CoV-2 rapid antigen tests were developed and received Food and Drug Administration Emergency Use

Authorization early during the COVID-19 pandemic.\* These tests were initially rolled out broadly in the United States to diagnose cases and isolate persons who received positive test results to aid in preventing onward spread at a time when population SARS-CoV-2 immunity was low, and rates of severe COVID-19–associated outcomes were high. In addition, demands for testing exceeded supply, and long turnaround times for reverse transcription–polymerase chain reaction (RT-PCR) test results contributed to ongoing transmission. Wide access to antigen tests was made possible through U.S. government initiatives implemented to prevent transmission.<sup>†,§</sup> After the emergence of the Omicron variant in late 2021, at-home antigen test use began to increase sharply (1,2).

Studies conducted during circulation of SARS-CoV-2 pre-Delta and Delta variants illustrated that antigen tests have high specificity, but lower sensitivity when compared with RT-PCR tests, thereby missing a substantial number of infections but correlating more closely with viral culture results (3–6). Viral culture, although not frequently used for routine patient care, is able to detect actively replicating virus (thus identifying when a person is likely to be infectious), whereas RT-PCR cannot distinguish between replicating virus and viral fragments. Most of these studies included few participants with vaccine- or infection-induced immunity. SARS-CoV-2 variants and population immunity have evolved since many of the studies assessing antigen tests were performed; thus, the role that antigen tests should play in diagnosing SARS-CoV-2 infection remains an active question. The objective of this investigation was to reevaluate the performance characteristics of SARS-CoV-2 antigen tests with those of RT-PCR and viral culture tests during a period with greater population immunity and more recently circulating SARS-CoV-2 Omicron variants.

\* <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-antigen-test-help-rapid-detection-virus-causes>

† <https://www.covid.gov/tools-and-resources/resources/tests>

§ <https://www.whitehouse.gov/wp-content/uploads/2021/01/National-Strategy-for-the-COVID-19-Response-and-Pandemic-Preparedness.pdf>

## Methods

This evaluation included participants enrolled in an antigen test substudy within a case-ascertained household transmission study during November 2022–May 2023<sup>¶</sup> (7). Index patients with confirmed SARS-CoV-2 infection and their household contacts were enrolled within 7 days of illness onset in the index patient. Participants completed baseline surveys including demographic characteristics, COVID-19 signs or symptoms (symptoms),\*\* vaccination,<sup>††</sup> and self-reported previous infection. Participants (index patients and contacts) also provided a blood specimen for SARS-CoV-2 anti-N antibody detection<sup>§§</sup> (8,9). For 10 days after enrollment, all participants completed daily COVID-19 symptom diaries and collected two nasal swabs each day. One swab was self-collected in viral transport media, stored in refrigerator for up to 72 hours, then collected by a study team member and stored at  $-12^{\circ}\text{F}$  ( $-80^{\circ}\text{C}$ ) until aliquoted for automated RT-PCR (Hologic Panther Fusion)<sup>¶¶</sup> and viral culture,<sup>\*\*\*</sup> and the other swab was used for at-home antigen testing.<sup>†††</sup> Participants interpreted and reported their antigen test results in their daily symptom diary. For this analysis, SARS-CoV-2 infection was defined as at least one positive RT-PCR test result during the study period; onset was defined as the first day of symptoms or, if the participant remained asymptomatic, day of first positive test result.

<sup>¶</sup> The Respiratory Virus Transmission Network sites that participated in the antigen substudy were located in Arizona, Colorado, New York, Tennessee, and Wisconsin. Persons who received test results positive for SARS-CoV-2 were recruited from participating medical centers, community testing sites, actively surveilled cohorts, and public health registries at five sites.

\*\* Elicited COVID-19 symptoms included fever (including feeling feverish and chills), cough, sore throat, runny nose, nasal congestion, fatigue (including feeling run-down), wheezing, trouble breathing (including shortness of breath), chest tightness (including chest pain), loss of smell or loss of taste, headache, abdominal pain, diarrhea, vomiting, and muscle or body aches.

<sup>††</sup> Vaccination history was self-reported and then verified by study team using state vaccination registries, electronic medical records, and pharmacy records.

<sup>§§</sup> Detection of antinucleocapsid antibodies from a dried blood spot collected at baseline was considered serological evidence of previous SARS-CoV-2 infection. Simultaneous detection and differentiation of total binding antibody (immunoglobulin [Ig]M, IgG, and IgA) to SARS-CoV-2 2019-nCoV WHU02 strain nucleocapsid protein, Wuhan-Hu-1 strain spike protein receptor binding domain, and Wuhan-Hu-1 strain spike protein trimer in capillary (finger stick) dried blood was performed using the ProcartaPlex Immunoassay multiplex custom panel (Invitrogen) deployed on the MAGPIX System (Luminex).

<sup>¶¶</sup> RT-PCR results were interpreted as categorically positive or negative according to the FDA-authorized parameters of the Hologic Panther Fusion SARS-CoV-2 assay, as utilized for in vitro diagnostic purposes. <https://www.fda.gov/media/136156/download/attachment>

<sup>\*\*\*</sup> Viral culture was performed on Vero E6 cells expressing both ACE2 and TMPRSS2. Cells were infected with serial dilutions of virus in Dulbecco's Modified Eagle Medium (DMEM) containing ciprofloxacin, and cytopathic effect (CPE) was visually observed during a period of 5 days. Observation of CPE was considered positive for viral culture.

<sup>†††</sup> Quidel QuickVue At-Home COVID-19 Test (available as over-the-counter). <https://www.fda.gov/media/146312/download>

Among participants who ever received a positive RT-PCR test result and had one or more paired RT-PCR and antigen results reported, the percentage of positive antigen, RT-PCR, and viral culture results was calculated for each day relative to onset. The percentage of positive antigen test results was stratified by symptom and fever status. Sensitivity of antigen testing among paired samples collected from 2 days before until 10 days after onset was computed using two references: 1) same-day positive RT-PCR result and 2) same-day positive culture result, stratified by overall symptom status and presence of fever alone or fever or cough. Wilson score intervals were used for calculating 95% CIs around percentage of positive test results. Cluster-robust bootstrapping was used to calculate 95% CIs around sensitivity to account for within-participant correlation. All analyses were performed in RStudio (version 4.2.3; RStudio). This study was reviewed and approved by the Vanderbilt University Institutional Review Board.<sup>§§§</sup>

## Results

### Characteristics of Study Participants

Among 354 participants in 129 households, 236 (67%) received a positive SARS-CoV-2 RT-PCR test result and were included in this investigation (Table). Participants ranged in age from 2 months to 83 years (median = 36 years; IQR = 17–50 years), 133 (56%) were non-Hispanic White persons, and 140 (59%) were female. Ninety-two (40%) participants reported receipt of a COVID-19 vaccine  $\leq 12$  months before enrollment; 82 (35%) had received  $\geq 2$  doses, but the most recent dose was  $> 12$  months before enrollment; 57 (24%) were unvaccinated (including those who had only ever received 1 dose); and vaccination status was unknown for five participants. A total of 102 (43%) participants had self-reported or serologic evidence of previous SARS-CoV-2 infection. At least one COVID-19 symptom was reported by 219 (93%) participants, including 182 (77%) who reported cough and 156 (66%) who reported fever.

### SARS-CoV-2 Test Results

Among the 236 SARS-CoV-2–infected participants (i.e., those who received a positive RT-PCR test result), 2,244 antigen results were reported and included in analyses. Overall, 143 (61%) participants received one or more positive culture result, and 164 (69%) received one or more positive antigen test result.

The highest percentage of positive antigen (59%; 95% CI = 51%–67%) and RT-PCR (83%; 95% CI = 76%–88%) test results occurred 3 days after onset (Figure 1). The

<sup>§§§</sup> 45 C.F.R. part 46.114; 21 C.F.R. part 56.114.

**TABLE. Characteristics of participants infected with SARS-CoV-2\* (N = 236) — Respiratory Virus Transmission Network, November 2022–May 2023**

Characteristic	No. (%)
Age at enrollment, yrs, median (IQR)	36 (17–50)
<b>Age group, yrs</b>	
0–4	22 (9)
5–11	15 (6)
12–17	23 (10)
18–49	114 (48)
50–64	44 (20)
≥65	18 (7)
<b>Gender</b>	
Female	140 (59)
Male	95 (40)
Nonbinary/Transgender	1 (<1)
<b>Race and ethnicity†</b>	
Black or African American	17 (7)
White	133 (57)
Hispanic or Latino	69 (29)
Other	14 (6)
Unknown/Refused	3 (1)
<b>SVI, median (IQR)§</b>	0.43 (0.19–0.80)
<b>Any chronic medical condition</b>	110 (47)
<b>Vaccination status¶</b>	
Unvaccinated	57 (24)
Vaccinated >12 mos before enrollment	82 (35)
Vaccinated ≤12 mos before enrollment	92 (40)
Unknown	5 (<1)
<b>Any previous SARS-CoV-2 infection**</b>	102 (43)
<b>Any COVID-19 symptoms††</b>	219 (93)
Any cough	182 (77)
Any fever	156 (66)
One or more positive viral cultures	143 (61)
One or more positive antigen tests	164 (69)

**Abbreviations:** RT-PCR = reverse transcription–polymerase chain reaction; SVI = social vulnerability index.

\* SARS-CoV-2 infection defined as having received at least one positive RT-PCR result during study testing.

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

§ SVI was determined using the 2020 U.S. Census Bureau decennial tract location of the home. SVI uses 16 census variables to indicate the relative vulnerability of every census tract to a hazardous event with values closer to 1 representing highly vulnerable areas and values closer to 0 representing least vulnerable areas.

¶ Vaccination history was self-reported and then verified by study team. Participants were considered vaccinated within 12 months before enrollment if they had received ≥2 doses and the most recent dose was received between 14 days and 12 months before enrollment; vaccinated >12 months before enrollment if they had received ≥2 doses and the most recent dose was received >12 months before enrollment; and unvaccinated if they received <2 doses before enrollment.

\*\* By self-report or serologic evidence. Previous SARS-CoV-2 infection was defined as self-report of a previous infection ≥1 month before enrollment or by detection of antinucleocapsid antibodies from a dried blood spot collected at baseline.

†† Elicited COVID-19 signs and symptoms included fever (including feeling feverish or chills), cough, sore throat, runny nose, nasal congestion, fatigue (including feeling run-down), wheezing, trouble breathing (including shortness of breath), chest tightness (including chest pain), loss of smell or loss of taste, headache, abdominal pain, diarrhea, vomiting, and muscle or body aches.

highest percentage of positive viral culture results (52%; 95% CI = 43%–61%) occurred 2 days after onset. Among the 219 symptomatic participants, the highest percentage of positive antigen test results was 65% (95% CI = 57%–73%) at 3 days after onset among those who experienced any COVID-19 symptom and 80% (95% CI = 68%–88%) at 2 days after onset among those who reported fever.

### Sensitivity of Antigen Testing

Compared with same-day collected RT-PCR and culture results, the overall sensitivities of daily antigen test results were 47% (95% CI = 44%–50%) and 80% (95% CI = 76%–85%), respectively (Figure 2) (Supplementary Table, <https://stacks.cdc.gov/view/cdc/153544>). When stratified by symptoms experienced on the day of specimen collection, antigen test sensitivity increased with occurrence of any COVID-19 symptoms (56% and 85% compared with RT-PCR and culture, respectively) and peaked on days that fever was reported (77% and 94% compared with RT-PCR and culture, respectively). Compared with RT-PCR and culture results, sensitivity of antigen testing was low on days when no symptoms were reported (18% and 45%, respectively).

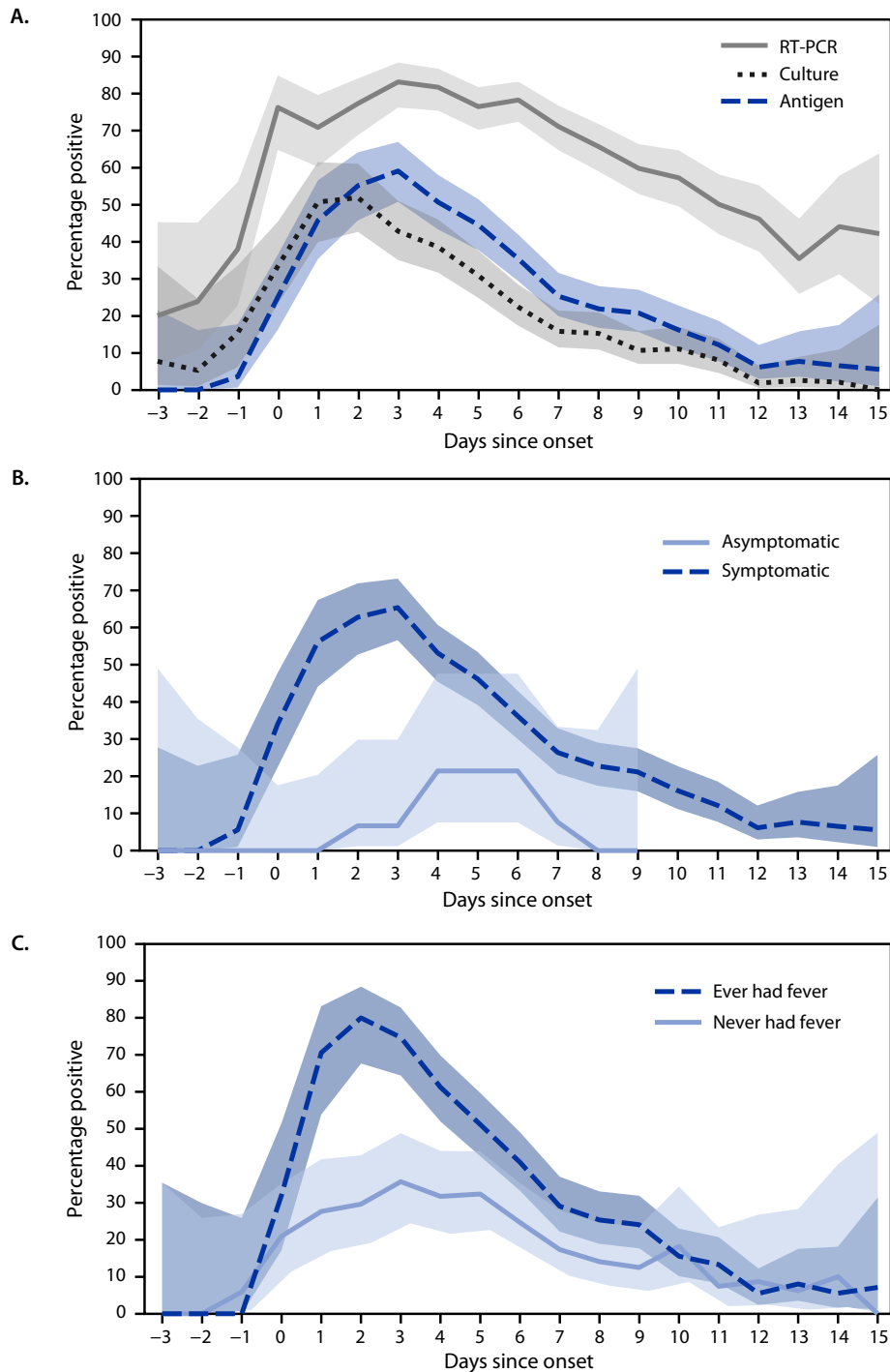
### Discussion

Among participants enrolled in a household transmission study during a period of increased disease- and vaccine-induced immunity, and when circulating viruses differed antigenically from the ancestral SARS-CoV-2 strain, antigen and culture tests detected a similar proportion of SARS-CoV-2 infections, but detection by RT-PCR was higher than that by either antigen or culture. Similarly, paired antigen test sensitivity was low compared with RT-PCR (47%), but relatively high compared with culture (80%). The sensitivity of antigen testing was higher when symptoms were present on the test day and peaked on days when participants reported fever. Although viral culture is not an absolute marker of transmissibility, this pattern suggests that positive antigen test results could indicate transmissible virus; thus, antigen tests might aid persons with COVID-19 in determining when they are no longer infectious once symptoms begin to resolve.

The findings from this investigation remain similar to those reported in other studies throughout the COVID-19 pandemic (3–6). For example, considering the current study's sensitivity results, an early 2021 study comparing antigen testing with RT-PCR and culture found similar antigen test sensitivity compared with culture (84%), but slightly higher sensitivity compared with RT-PCR (64%) (3). The sensitivity difference between these two studies could be attributed to many



**FIGURE 1.** Percentage\* of rapid antigen, reverse transcription–polymerase chain reaction, and viral culture test results that were positive for SARS-CoV-2 (A) and percentage of antigen test results that were positive, by symptom status† (B) and presence of fever (C) each day since onset§ among participants infected with SARS-CoV-2¶ — Respiratory Virus Transmission Network, November 2022–May 2023



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

\* With 95% CIs indicated by shaded areas.

† Elicited COVID-19 signs and symptoms included fever (including feeling feverish or chills), cough, sore throat, runny nose, nasal congestion, fatigue (including feeling run-down), wheezing, trouble breathing (including shortness of breath), chest tightness (including chest pain), loss of smell or loss of taste, headache, abdominal pain, diarrhea, vomiting, and muscle or body aches.

§ Date of symptom onset or, for asymptomatic persons, date of first positive test result.

¶ SARS-CoV-2 infection defined as having received at least one positive RT-PCR test result during study testing.

factors, including differences in participant immunity, infecting variants, the limit of detection of the reference RT-PCR, or sampling methods.

Minimizing false negative test results is important because additional modalities, including antiviral medications, are available to prevent severe outcomes. Antiviral treatments for SARS-CoV-2 infection should be started as soon as possible, and within 5–7 days of symptom onset.<sup>¶¶¶</sup> Therefore, persons who are at higher risk for severe illness and eligible for antiviral treatment would benefit from a more accurate diagnostic test. In most clinical scenarios in the United States, this approach means a SARS-CoV-2 RT-PCR test would be a better diagnostic test to minimize the risk for a false-negative result. Alternatively, if RT-PCR tests are not available or accessible, clinicians and patients should follow FDA's serial antigen testing recommendations to help optimize diagnostic test performance.<sup>\*\*\*\*</sup>

### Limitations

The findings in this report are subject to at least three limitations. First, participants included in this analysis might not represent all U.S. persons infected with SARS-CoV-2 and represent those with mild to moderate illness. These findings might not apply to persons with more severe COVID-19 illness. Second, one commercially available antigen test was used in this study; results might not apply to all available antigen tests. Finally, because of the parent study design, onset for asymptomatic participants (i.e., the day of the first positive test result), could be biased if household members were not enrolled early enough to record the earliest positive test result.

### Implications for Public Health Practice

As COVID-19 becomes endemic and public focus shifts from stopping transmission to preventing severe illness,<sup>†††</sup> diagnostic testing should emphasize use of the best tests to identify infection in persons who would benefit from treatment. The low sensitivity of antigen testing among persons with asymptomatic infections illustrates that these tests should only be used once symptoms are present. Conversely, the higher sensitivity when symptoms are present (especially cough or fever) supports the need to stay at home when symptomatic, irrespective of test result.<sup>§§§§</sup> The low sensitivity of antigen

### Summary

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

During the COVID-19 pandemic, rapid antigen tests were found to detect potentially transmissible SARS-CoV-2 infection, but antigen tests were less sensitive than reverse transcription–polymerase chain reaction (RT-PCR) testing.

#### What is added by this report?

During November 2022–May 2023, among persons infected with SARS-CoV-2, sensitivity of rapid antigen tests was 47% compared with RT-PCR and 80% compared with viral culture. Antigen tests continue to detect potentially transmissible infection but miss many infections identified by positive RT-PCR test results.

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

Rapid antigen tests can aid in identifying infectiousness of persons infected with SARS-CoV-2 and providing access to diagnostic testing for persons with COVID-19 symptoms. Persons in the community eligible for antiviral treatment should seek more sensitive diagnostic tests from a health care provider. Clinicians should consider RT-PCR testing for persons for whom antiviral treatment is recommended.

tests compared with RT-PCR tests has implications for timely initiation of anti-SARS-CoV-2 treatment when early and accurate diagnosis is important. With several treatment options available, clinicians should consider more sensitive RT-PCR tests for accurate diagnosis in persons at higher risk for severe illness to minimize delays in treatment initiation. Persons in the community who are at high risk for severe COVID-19 illness and eligible for antiviral treatment should seek testing from health care providers with the goal of obtaining a more sensitive diagnostic test than antigen tests (i.e., an RT-PCR test).

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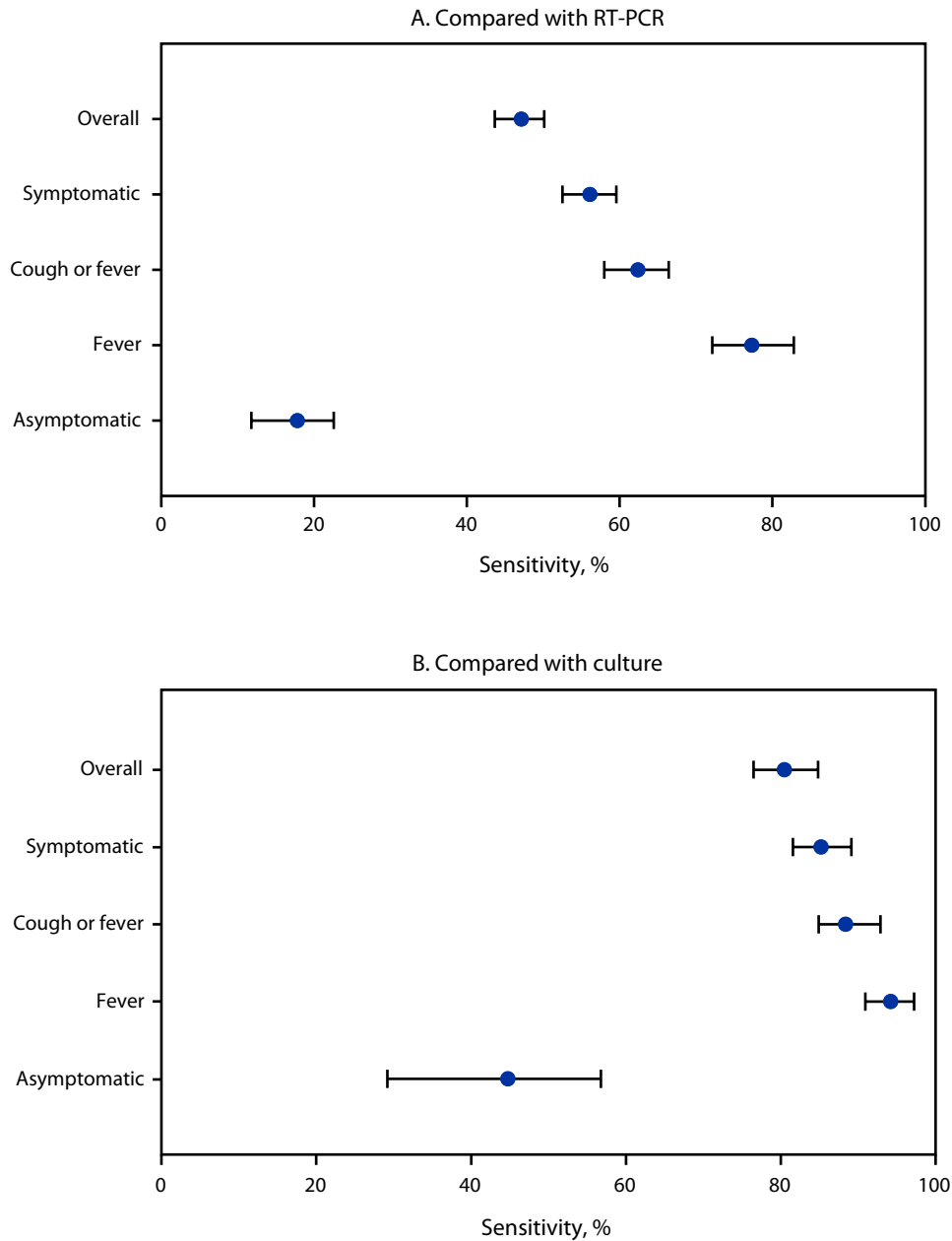
<sup>¶¶¶</sup> <https://www.cdc.gov/coronavirus/2019-ncov/your-health/treatments-for-severe-illness.html>

<sup>\*\*\*\*</sup> <https://www.fda.gov/medical-devices/safety-communications/home-covid-19-antigen-tests-take-steps-reduce-your-risk-false-negative-results-fda-safety>

<sup>†††</sup> <https://www.cdc.gov/respiratory-viruses/whats-new/changing-threat-covid-19.html>

<sup>§§§§</sup> <https://www.cdc.gov/respiratory-viruses/prevention/precautions-when-sick.html>

**FIGURE 2. Sensitivity\*** of rapid antigen tests results for diagnosing SARS-CoV-2 infection compared with reverse transcription–polymerase chain reaction (A) and viral culture (B), overall and by presence of symptoms† — Respiratory Virus Transmission Network, November 2022–May 2023



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

\* With 95% CIs indicated by error bars.

† Elicited COVID-19 signs and symptoms included fever (including feeling feverish or chills), cough, sore throat, runny nose, nasal congestion, fatigue (including feeling run-down), wheezing, trouble breathing (including shortness of breath), chest tightness (including chest pain), loss of smell or loss of taste, headache, abdominal pain, diarrhea, vomiting, and muscle or body aches.

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# Investigation of Presumptive HIV Transmission Associated with Receipt of Platelet-Rich Plasma Microneedling Facials at a Spa Among Former Spa Clients — New Mexico, 2018–2023

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## Abstract

HIV transmitted through cosmetic injection services via contaminated blood has not been previously documented. During summer 2018, the New Mexico Department of Health (NMDOH) was notified of a diagnosis of HIV infection in a woman with no known HIV risk factors who reported exposure to needles from cosmetic platelet-rich plasma microneedling facials (vampire facials) received at a spa in spring 2018. An investigation of the spa's services began in summer 2018, and NMDOH and CDC identified four former spa clients, and one sexual partner of a spa client, all of whom received HIV infection diagnoses during 2018–2023, despite low reported behavioral risks associated with HIV acquisition. Nucleotide sequence analysis revealed highly similar HIV strains among all cases. Although transmission of HIV via unsterile injection practices is a known risk, determining novel routes of HIV transmission among persons with no known HIV risk factors is important. This investigation identified an HIV cluster associated with receipt of cosmetic injection services at an unlicensed facility that did not follow recommended infection control procedures or maintain client records. Requiring adequate infection control practices and maintenance of client records at spa facilities offering cosmetic injection services can help prevent the transmission of HIV and other bloodborne pathogens and ensure adequate traceback and notification in the event of adverse clinical outcomes, respectively.

## Introduction

During summer 2018, the index patient, a woman aged 40–50 years, was evaluated after receiving a positive rapid HIV test result while abroad. Upon evaluation, the patient received a positive HIV antigen/antibody rapid test result, with positive confirmatory results\* the same day, indicating stage 1 HIV infection.<sup>†</sup> The patient reported no injection drug use, recent blood transfusions, or recent sexual contact with anyone other than her current sexual partner, who received a negative HIV

test result after the patient's diagnosis. However, the patient did report exposure to needles during a platelet-rich plasma (PRP) microneedling procedure in spring 2018 at spa A in New Mexico. The procedure involves drawing a client's blood, separating the blood into its components of plasma and cells, and using single-use disposable or multiuse sterile equipment to inject the PRP into the face for cosmetic purposes, such as skin rejuvenation and reducing the appearance of acne scars (*1*).

## Investigation and Results

NMDOH and CDC investigated cosmetic injection services as a possible transmission route for HIV. The period for active case finding was from spring 2018, when the initial patient received the procedure, to fall 2018 when spa A closed. Spa A's owner operated without appropriate licenses at multiple locations and did not have an appointment scheduling system that stored client contact information. Investigators compiled and cross-referenced names and telephone numbers from spa A client consent forms, handwritten appointment records, and telephone contacts to create a list of potentially affected clients. The investigative team was not permitted to collect specimens from spa A at the time of the inspection in September 2018, because the inspection was conducted under the purview of the New Mexico Regulation and Licensing Department, which did not have authority to collect specimens. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.<sup>§</sup>

## Identification of Clients at Risk

The investigative team identified 59 clients at risk for exposure, including 20 who received PRP with microneedling at spa A, and 39 who received other injection services (e.g., onabotulinumtoxinA [botox]) during the case-finding period. Investigators cross-referenced the client list with the New Mexico state HIV registry and identified one spa A client who received a diagnosis of HIV in 2012.

\* Positive HIV-1 and HIV-2 antibody plus HIV-1 p24 antigen test, a negative HIV-1/2 differentiation antibody test, and a detectable HIV-1 RNA qualitative test.

<sup>†</sup> [https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm?s\\_cid%20=%20rr6303a1\\_w](https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm?s_cid%20=%20rr6303a1_w)

<sup>§</sup> 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.

During 2018–2023, current and former spa A clients who received new HIV diagnoses were reported to NMDOH from clinical providers throughout the state. During this period, a spa A–related HIV case was defined as a new HIV diagnosis in a patient with previous receipt of blood product or any injection services provided by spa A’s owner<sup>‡</sup> from 2017 until closure of the unlicensed operation in fall 2018, or who had sexual contact with a person who received such spa services. Cases were included only if an HIV nucleotide sequence demonstrated molecular linkage to other HIV sequences from persons with infections associated with spa A.

**Characteristics of Patients**

By spring 2023, five patients had been identified, including four women and one man who was a sexual partner of one of the four women patients and never received any services from spa A. Blood specimens from the five patients and a former client with a 2012 HIV diagnosis were submitted to CDC for nucleotide sequence analysis to ascertain cluster association and determine case status; all five patients were confirmed to have spa A–related cases. Medical record reviews and clinician interviews were conducted for all confirmed patients. Three patients were interviewed by NMDOH. Patients ranged in age from 40–60 years. HIV diagnoses occurred during

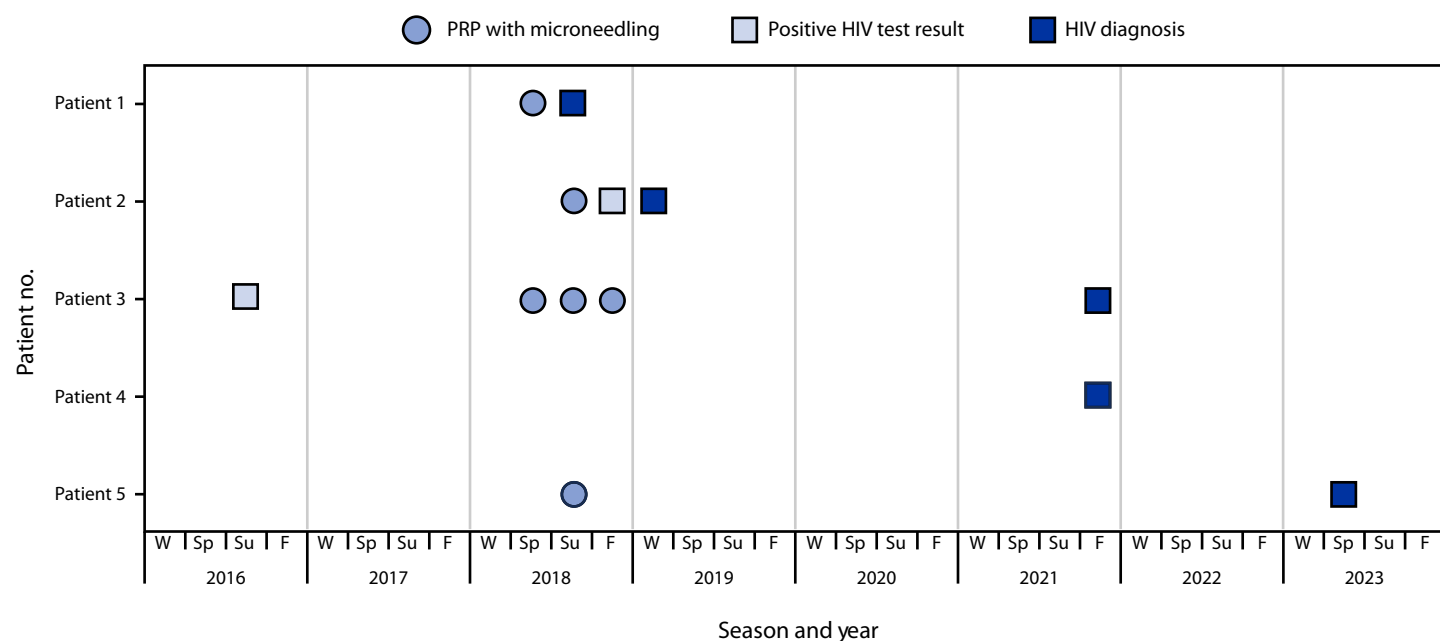
summer 2018 through spring 2023 (Figure 1) (Table). Two patients had stage 1 disease, and three had stage 3 disease at the time of diagnosis\*\* (2). All four female patients had received PRP with microneedling at spa A.

Four of the five patients with confirmed spa A–related HIV infections received at least one PRP with microneedling facial treatment at spa A during May–September 2018. Two of the patients in this cluster (a man and a woman) were engaged in a sexual relationship before and after their diagnoses. Sexual partners of two other patients received negative HIV test results after their partners’ diagnoses, and the remaining patient reported having no sexual partner at the time of diagnosis. Before receiving a diagnosis of confirmed HIV infection, two of the five patients had previously received a positive rapid HIV test result during routine evaluations for life insurance, one in summer 2016, and the other in fall 2018; however, only one patient reported being notified of the positive screening test result and subsequently had their HIV diagnosis confirmed by a primary care provider in winter 2019. The other patient received a confirmed HIV diagnosis after hospitalization with an AIDS-defining illness in fall 2021. One patient received their HIV diagnosis in spring 2023 after hospitalization with an AIDS-defining illness.

\*\* <https://www.cdc.gov/mmwr/pdf/rr/rr6303.pdf>

<sup>‡</sup> Or spa A owner’s associates in a location other than the spa.

**FIGURE 1. Receipt of platelet-rich plasma and microneedling facial treatments at spa A and HIV screening and diagnosis test results among five patients with HIV infection — New Mexico, 2016–2023**



**Abbreviations:** F = fall; PRP = platelet-rich plasma; Sp = spring; Su = summer; W = winter.

**TABLE. Characteristics of patients with confirmed HIV infection associated with receipt of cosmetic injection services at spa A — New Mexico, 2018–2023**

Characteristic	Patient no.				
	1	2	3	4*	5
Sex	Woman	Woman	Woman	Man	Woman
Age range, yrs <sup>†</sup>	40–50	40–50	50–60	40–50	40–50
Season and year of HIV screening and diagnosis	Summer 2018	Positive screen: fall 2018; diagnosis: winter 2019	Positive screen: summer 2016; diagnosis: fall 2021	Fall 2021	Spring 2023
HIV stage <sup>†,§</sup>	Stage 1	Stage 1	Stage 3	Stage 3	Stage 3
Spa A services received; season and year received	PRP with microneedling; spring 2018	PRP with microneedling; summer 2018	PRP with microneedling (multiple procedures); spring and summer 2018	None; NA	PRP with microneedling; summer 2018

**Abbreviations:** NA = not available; PRP = platelet-rich plasma.

\* This patient was the sexual partner of a spa A client who received a diagnosis of HIV infection after receiving PRP with microneedling at spa A.

<sup>†</sup> At time of HIV diagnosis.

<sup>§</sup> <https://www.cdc.gov/mmwr/pdf/rr/rr6303.pdf>

The two patients who were engaged in a sexual relationship had stage 3 or chronic HIV infections, indicating that their infections were likely attributed to exposures before receipt of cosmetic injection services. The other three patients in this cluster had no known social contact with one another, and no specific mechanism for transmission among these patients was confirmed. Evidence suggests that contamination from an undetermined source at the spa during spring and summer 2018 resulted in HIV-1 transmission to these three patients.

### Evaluation of HIV Sequences

Whole blood specimens collected from all patients and the former client living with HIV since 2012 were used to generate HIV-1 polymerase (*pol*), *gag*, and envelope (*env*) sequences to evaluate sequence relatedness using established protocols (3,4). HIV-1 subtype B was determined using the online subtyping tool COMET (5). Maximum likelihood phylogenetic analysis was employed to compare the *pol*, *gag*, and *env* sequences from this investigation with genetically similar sequences from GenBank, the National Institutes of Health genetic sequence database (<https://www.ncbi.nlm.nih.gov/genbank>), and with 46 local control sequences from routine HIV surveillance in New Mexico in 2018 and 2023 for *pol*. Additional *pol* sequences derived from blood specimens collected by commercial laboratories from three patients within 3 weeks of diagnosis were included in phylogenetic analyses. HIV-1 subtype J sequences were used as an outgroup<sup>††</sup> for the phylogenetic analyses. Phylogenetic analyses showed that *gag*, *pol*, and *env* sequences from all patients clustered together strongly in a monophyletic clade with high confidence (Figure 2). Sequences from the former client living with HIV, who was not receiving

antiretroviral therapy at the time of specimen collection, did not cluster with any New Mexico sequences.

### Investigation of Spa A

In fall 2018, on-site inspection of spa A revealed multiple unsafe infection control practices. A centrifuge, a heating dry bath, and a rack of unlabeled tubes containing blood were located on a kitchen counter. Unlabeled tubes of blood and medical injectables (i.e., botox and lidocaine) were stored in the kitchen refrigerator along with food. Unwrapped syringes were found in drawers, on counters, and discarded in regular trash cans. An autoclave (steam sterilizer) was not found on the premises. Procedure equipment was surface cleaned using ammonium chloride disinfecting spray and benzalkonium chloride disinfecting wipes after each client visit, and disposable electric desiccator tips were cleaned by alcohol immersion and reused.

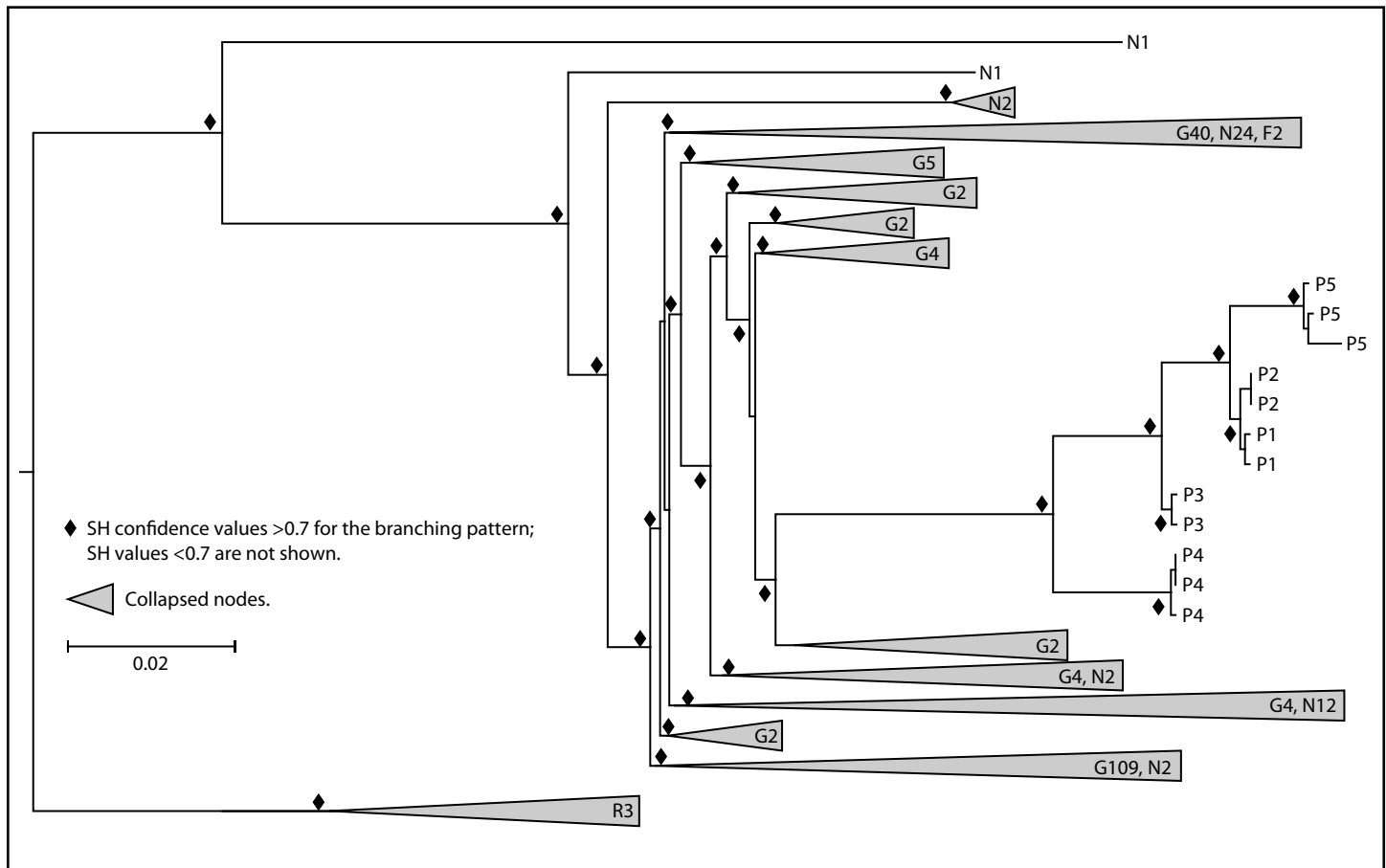
### Public Health Response

Because Spanish was the first language of many spa A clients, and available client information was limited, NMDOH's public health response comprised multiple approaches. Direct calls were made to known spa A clients to encourage testing for bloodborne pathogens. Several Health Alert Notifications were sent to providers in New Mexico to ask patients receiving new diagnoses of HIV infection about spa services received before their diagnosis.<sup>§§</sup> NMDOH communicated the risk for HIV transmission attributed to spa A's unsterile injection services to the Office of Border Health/Border Infectious Disease Surveillance Group, neighboring jurisdictions through CDC's Epidemic Information Exchange, and published four

<sup>††</sup> A more distantly related group that serves as a reference group when determining the evolutionary relationships.

<sup>§§</sup> <https://www.nmhealth.org/publication/view/general/8339/>

FIGURE 2. Maximum likelihood phylogeny\* of HIV polymerase sequences† from spa A patients 1–5‡ and client receiving diagnosis of HIV infection in 2012, compared with sequences from GenBank and local HIV surveillance databases — New Mexico, 2018–2023



**Abbreviations:** F = former client; G = genetically related; N = New Mexico controls; P = patients 1–5; R = reference sequence; SH = Shimodaira-Hasegawa.

\* Collapsed nodes are those with >1 sequence with total number of sequences indicated. Longer branch is associated with higher number of nucleotide substitutions per site. Scale bar for branch length is shown as the number of nucleotide substitutions per site.

† HIV-1 subtype J reference sequences are used as the outgroup.

‡ Each patient had 2 or 3 sequences included in the analysis.

press releases during 2018–2023<sup>§§</sup> with information on free testing for current and former spa A clients at state public health offices. NMDOH organized and advertised bloodborne pathogen testing events for current and former spa A clients via social media, radio, newspaper, and television in both English and Spanish. Members of the NMDOH investigative team canvassed community health centers and businesses in predominantly Spanish-speaking neighborhoods to distribute testing information for current and former spa A clients. As a result of these activities, 198 former spa A clients and their sexual partners were tested during 2018–2023. No additional

HIV infections were identified, nor were any hepatitis B or hepatitis C infections detected. Free testing remains available for former spa A clients, and the investigation and public health response are continuing.

## Discussion

This investigation is the first to associate HIV transmission with nonsterile cosmetic injection services. A common exposure to spa A among clients without behaviors associated with HIV acquisition helped identify a possible cluster association, and analysis of additional data suggested that HIV transmission likely occurred via receipt of PRP with microneedling facial procedures; however, the source of contamination remains unknown. Although the investigative team was not permitted to collect specimens from spa A, evidence from this investigation supports the likely transmission of HIV through

<sup>§§</sup> September 11, 2018: <https://www.nmhealth.org/news/alert/2018/9/?view=709>; September 21, 2018: <https://www.nmhealth.org/news/information/2018/9/?view=712>; April 29, 2019: <https://www.nmhealth.org/news/alert/2019/4/?view=762>; July 5, 2023: <https://www.nmhealth.org/news/alert/2023/7/?view=1988>



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

Transmission of HIV through cosmetic injection services via contaminated blood has not been previously documented; however, transmission of HIV via unsterile injection practices is a known risk. Determining novel routes of HIV transmission among persons with no known HIV risk factors is important.

**What is added by this report?**

Investigation of multiple HIV infections among persons with no known HIV risk factors who received platelet-rich plasma with microneedling (vampire facials) at an unlicensed New Mexico spa revealed likely HIV transmission associated with these cosmetic injection services.

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

In the absence of known HIV risk factors, clinical and public health staff members might consider cosmetic injection services as a route of HIV transmission. Requiring adequate infection control practices at spa facilities offering cosmetic injection services can help prevent the transmission of HIV and other bloodborne pathogens. Maintenance of client records could facilitate investigations of suspected transmission at such facilities.

poor infection control practices. This cluster could potentially include additional persons with undiagnosed HIV infection or with a diagnosis of infection but no available sequence for analysis (3,6).

Incomplete spa client records posed a substantial challenge during this investigation, necessitating a large-scale outreach approach to identify potential cases, as opposed to direct communication with all clients. Requiring maintenance of sufficient client records to ensure adequate traceback by regulated businesses that provide injection services could ensure adequate capability to conduct traceback. NMDOH continues to elicit feedback from former spa A clients to improve future messaging.

**Implications for Public Health Practice**

This investigation underscores the importance of determining possible novel sources of HIV transmission among persons with no known HIV risk factors. Requiring adequate infection control practices at spa facilities offering cosmetic injection services can help prevent the transmission of HIV and other bloodborne pathogens. Maintenance of client records could facilitate investigations of suspected transmission at such facilities.

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# Use of an Additional Updated 2023–2024 COVID-19 Vaccine Dose for Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024

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## Abstract

COVID-19 remains an important public health threat, despite overall decreases in COVID-19–related severe disease since the start of the COVID-19 pandemic. COVID-19–associated hospitalization rates remain higher among adults aged ≥65 years relative to rates in younger adults, adolescents, and children; during October 2023–January 2024, 67% of all COVID-19–associated hospitalizations were among persons aged ≥65 years. On September 12, 2023, CDC’s Advisory Committee on Immunization Practices (ACIP) recommended updated (2023–2024 Formula) COVID-19 vaccination with a monovalent XBB.1.5-derived vaccine for all persons aged ≥6 months to protect against severe COVID-19–associated illness and death. Because SARS-CoV-2 continues to circulate throughout the year, and because of the increased risk for COVID-19–related severe illness in persons aged ≥65 years, the protection afforded by updated vaccines against JN.1 and other currently circulating variants, and the expected waning of vaccine-conferred protection against disease, on February 28, 2024, ACIP recommended all persons aged ≥65 years receive 1 additional dose of the updated (2023–2024 Formula) COVID-19 vaccine. Implementation of these recommendations is expected to enhance immunity that might have waned and decrease the risk for severe COVID-19–associated outcomes, including death, among persons aged ≥65 years.

## Introduction

Since June 2020, CDC’s Advisory Committee on Immunization Practices (ACIP) has convened 39 public meetings to review data and consider recommendations related to the use of COVID-19 vaccines (1). On September 12, 2023, ACIP recommended that all persons aged ≥6 months receive updated (2023–2024 Formula) monovalent, XBB.1.5 component (updated) COVID-19 vaccination to protect against severe COVID-19–associated illness and death (2).

As of February 3, 2024, approximately 6.7 million COVID-19–associated hospitalizations and 1.1 million COVID-19–associated deaths had occurred in the United States (3). Although the overall risk for COVID-19–associated hospitalization and death has decreased, severe illness related to

COVID-19 continues to be a public health problem, especially among older adults. COVID-19–associated hospitalization rates remain higher among adults aged ≥65 years relative to rates among younger adults, adolescents, and children. During October 2023–January 2024, 67% of all COVID-19–associated hospitalizations were among persons aged ≥65 years (4). Further, COVID-19 death rates during January 1, 2023–January 31, 2024, were highest among adults aged ≥75 years, followed by adults aged 65–74 years (5,6). Whereas approximately 98%–99% of the U.S. population has measurable antibody titers against SARS-CoV-2 from infection, vaccination, or both (hybrid immunity), adults aged ≥65 years are less likely to have immunity resulting from infection (including immunity from infection only or hybrid immunity), compared with adults aged 30–49 years and 50–64 years (7). In addition, immunosenescence, the age-related decline in the functioning of the immune system, results in a less complete immune response to novel antigens and a reduced ability to develop robust immunity after infections or vaccination (8). The pool of naive T-cells diminishes with age, and this insufficient naive T-cell pool affects the ability to generate neutralizing antibody responses and cytotoxic T-cells in response to SARS-CoV-2 (9).

Thus, adults aged ≥65 years are more likely than are younger adults, adolescents, and children to rely upon vaccination to increase immunity that might have waned and might need more frequent vaccine doses to maintain protection. Coverage with the updated COVID-19 vaccine among adults aged ≥65 years was 42% as of February 3, 2024 (10,11). Adults in this age group are more concerned about COVID-19 disease and had higher confidence in COVID-19 vaccine safety and vaccine importance than did younger adults (5). A nationally representative survey conducted during November 2023–January 2024 indicated that 68.4% of adults aged ≥65 years who had received an updated COVID-19 vaccine dose definitely would get another updated vaccine if it were recommended, 27.2% probably would or are unsure if they would get another updated vaccine, and 4.4% said they probably or definitely would not. COVID-19 vaccines are currently on the commercial market, but access-related barriers and disparities in vaccine coverage remain (5); in the absence of any recommendations for an

additional dose, access to vaccine would be limited among persons unable to pay out of pocket for the vaccine.\*

On February 28, 2024, ACIP voted to recommend that all persons aged  $\geq 65$  years receive 1 additional dose of any updated COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech). This recommendation was based on continuing SARS-CoV-2 circulation throughout the year, increased risk for severe illness attributable to COVID-19 in adults aged  $\geq 65$  years, protection provided by the updated vaccines against JN.1 and other currently circulating variants, the expected waning of SARS-CoV-2 immunity, and additional implementation considerations, including facilitating clear communication and equitable access to vaccine (5).

## Methods

In 2018, ACIP adopted the Evidence to Recommendations framework to guide the development of vaccine recommendations. Since November 2023, the ACIP COVID-19 work group met seven times to discuss the current policy question, i.e., whether adults aged  $\geq 65$  years should receive an additional dose of updated COVID-19 vaccine. Work group membership included ACIP voting members, representatives of ACIP ex officio and liaison organizations, and scientific consultants with expertise in public health, immunology, medical specialties, and immunization safety and effectiveness. Work group discussion topics included COVID-19 disease surveillance and epidemiology; COVID-19 vaccination coverage; and the safety, effectiveness, feasibility of implementation, and cost effectiveness of COVID-19 vaccines. This report summarizes the ACIP recommendation for an additional dose of the updated COVID-19 vaccine for persons aged  $\geq 65$  years and the rationale, including evidence reviewed by the work group and presented to ACIP (<https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-additional-dose-adults-etr.html>).

## Vaccine Effectiveness and Safety

No clinical trial immunogenicity data on an additional dose of the updated COVID-19 vaccines exist; however, the initial dose elicits a robust neutralizing antibody response and provides protection against JN.1 and other circulating variants (12,13). Early vaccine effectiveness (VE) estimates demonstrate that updated COVID-19 vaccination provided increased protection against symptomatic SARS-CoV-2 infection and

COVID-19–associated emergency department and urgent care visits and hospitalization, compared with receipt of no updated vaccine dose (12,14). Although these early VE estimates show no substantial waning, based on data on effectiveness of original and bivalent COVID-19 vaccines, waning of vaccine-conferred immunity is expected. Effectiveness of an additional dose in older adults has been demonstrated for previously recommended additional original COVID-19 vaccine doses (15). Among adults aged  $\geq 50$  years who were eligible to receive a second original monovalent mRNA COVID-19 vaccine booster dose, VE against COVID-19–associated emergency department and urgent care encounters during the SARS-CoV-2 Omicron BA.2/BA.2.12.1 period  $\geq 120$  days after the third dose was 32% but increased to 66%  $\geq 7$  days after the fourth dose. VE against COVID-19–associated hospitalization  $\geq 120$  days after the third dose was 55% but increased to 80%  $\geq 7$  days after the fourth dose (15). In addition, in a large cohort of nursing home residents during circulation of SARS-CoV-2 Omicron subvariants, receipt of a second original monovalent mRNA COVID-19 booster dose  $\leq 60$  days earlier was 74% effective against severe COVID-19–related outcomes (including hospitalization or death) and 90% effective against death, compared with receipt of a single booster dose (16).

COVID-19 vaccines have a favorable safety profile as demonstrated by robust safety surveillance during 3 years of COVID-19 vaccine use (17). Anaphylactic reactions have rarely been reported after receipt of COVID-19 vaccines (18). A rare risk for myocarditis and pericarditis exists, predominately in males aged 12–39 years (19). No new safety concerns have been identified for the updated COVID-19 vaccine (5). Among adults aged  $\geq 65$  years, overall reactogenicity after COVID-19 vaccination is less frequent and less severe than among adolescents and younger adults (20). A statistical signal for ischemic stroke after Pfizer-BioNTech bivalent mRNA COVID-19 vaccine was detected in the CDC Vaccine Safety Datalink among persons aged  $\geq 65$  years, and information about this detection has been presented at previous ACIP meetings. Ongoing efforts to evaluate the signal have not identified any clear and consistent evidence of a safety concern for ischemic stroke with bivalent mRNA COVID-19 vaccines either when given alone or when given simultaneously with influenza vaccines (21). A recent VE study indicated that the bivalent COVID-19 vaccine was 47% effective in preventing COVID-19 related thromboembolic events (ischemic stroke, myocardial infarction, and deep vein thrombosis) among persons aged  $\geq 65$  years (22).

\* Section 2713(a)(2) of the Public Health Service Act, as added by section 1001 of the Affordable Care Act, implemented at 26 CFR 54.9815–2713(a)(1)(ii), 29 CFR 2590.715–2713(a)(1)(ii), and 45 CFR 147.130(a)(1)(ii). This requirement does not apply to grandfathered health plan coverage under section 1251 of the Affordable Care Act, implemented at 26 CFR 54.9815–1251, 29 CFR 2590.715–1272, and 45 CFR 147.140.

## Cost Effectiveness

ACIP considered whether an additional dose of updated COVID-19 vaccine in persons aged  $\geq 65$  years is a reasonable and efficient allocation of resources. The societal incremental cost-effectiveness ratio (ICER) for an additional dose of COVID-19 vaccine in persons aged  $\geq 65$  years was \$255,122 per quality-adjusted life year saved for the base case estimate. ICER values were sensitive to probability of hospitalizations, costs, and seasonality assumptions. Estimates of ICER values that approximate cost effectiveness for those with higher risk for COVID-19–associated hospitalization, such as persons with underlying conditions or those aged  $\geq 75$  years, were more favorable (23).

## Recommendation for Use of an Additional Updated COVID-19 Vaccine Dose in Persons Aged $\geq 65$ Years

On February 28, 2024, ACIP recommended that all persons aged  $\geq 65$  years receive 1 additional dose of any updated COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech).<sup>†</sup> This additional dose should be administered  $\geq 4$  months after the previous dose of updated COVID-19 vaccine. For initial vaccination with Novavax COVID-19 vaccine, the 2-dose series should be completed before administration of the additional dose. Because Novavax COVID-19 vaccine is currently authorized under Emergency Use Authorization, the recommendation for the updated Novavax COVID-19 vaccine is an interim recommendation.

## Persons Aged $\geq 65$ Years with Moderate or Severe Immunocompromise

Persons aged  $\geq 65$  years who are moderately or severely immunocompromised, have completed an initial series, and have received  $\geq 1$  updated COVID-19 vaccine dose should receive 1 additional updated COVID-19 vaccine dose  $\geq 2$  months after the last dose of updated vaccine. Further additional doses may be administered, guided by the clinical judgment of a health care provider and personal preference and circumstances. Any further additional doses should be administered  $\geq 2$  months after the last COVID-19 vaccine dose. Additional clinical considerations, including detailed schedules and tables by age for all age groups and vaccination history for those who are or are not moderately or severely immunocompromised, are available at <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html>.

<sup>†</sup> ACIP voted (11 to one with one abstention) to recommend that persons aged  $\geq 65$  years should receive an additional dose of updated (2023–2024 Formula) COVID-19 vaccine.

## Summary

### What is already known about this topic?

In September 2023, the Advisory Committee on Immunization Practices (ACIP) recommended updated (2023–2024 Formula) COVID-19 vaccination for all persons aged  $\geq 6$  months.

### What is added by this report?

On February 28, 2024, ACIP recommended that all persons aged  $\geq 65$  years receive 1 additional dose of any updated (2023–2024 Formula) COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech).

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

Adults aged  $\geq 65$  years should receive an additional dose of the updated (2023–2024 Formula) COVID-19 vaccine to enhance their immunity and decrease the risk for severe COVID-19–associated illness.

## Reporting Vaccine Adverse Events

Adverse events after vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS). For licensed COVID-19 vaccines administered to persons aged  $\geq 12$  years, reporting is encouraged for any clinically significant adverse event even when whether the vaccine caused the event is uncertain, as well as for vaccination errors. For COVID-19 vaccines given under Emergency Use Authorization, vaccination providers are required to report certain adverse events to VAERS. Additional information is available at <https://vaers.hhs.gov> or by telephone at 1-800-822-7967.

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## Notes from the Field

### Group A *Streptococcus* Bacteremia in Persons Who Inject Drugs — Northern Vermont, January 2020–October 2023

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CDC has recently reported increases in invasive group A *Streptococcus* (GAS) infections.\* Injection of illicit drugs and homelessness are two documented risk factors for invasive GAS infections (1). In 2022 and 2023, the University of Vermont Medical Center (UVMMC) Infection Prevention and Antimicrobial Stewardship programs detected a substantial increase compared with 2020–2021 in community-acquired GAS bacteremia among adult patients seeking care at UVMMC. The programs conducted an investigation to identify opportunities to enhance the delivery of care.

#### Investigation and Outcomes

Cases of invasive GAS infections were identified using reports in the electronic medical record (EMR), using Epic software. A case of GAS bacteremia was defined as *Streptococcus pyogenes* in a blood culture from a UVMMC patient during January 1, 2020–October 31, 2023. A repeat positive culture occurring >30 days after the initial positive culture was considered a recurrent infection and was included in the analysis. Patients meeting the following criteria were excluded: those who transferred to UVMMC with GAS bacteremia, those who had been admitted to the hospital during the previous 7 days, and those whose initial positive culture specimen was obtained ≥48 hours after hospital admission, ≤7 days after surgery, or ≤7 days postpartum. As a quality improvement project aimed at identifying risk factors, developing prevention strategies, and improving patient care for GAS bacteremia, this activity did not require institutional review board review.

Among UVMMC patients, three cases of GAS bacteremia were identified in 2020, four in 2021, 19 in 2022, and 45 during the first 10 months of 2023 (Figure). In comparison, total emergency department patient encounters at UVMMC increased by 19% between 2020–2021 and 2022–2023, and total admissions increased by <2%.

Of the 64 cases identified during 2022–2023, a total of 45 (70%) occurred among 38 patients known to be persons who inject drugs<sup>†</sup> (PWID), based on self-report documented in the

EMR. The remainder of the report focuses on these 38 persons with 45 cases of GAS bacteremia.

Twenty-one (55%) of the 38 patients were female; median patient age was 40.5 years (range = 22–63 years). Among 28 (62%) of the 45 cases, the patient reported experiencing homelessness at the time of GAS bacteremia diagnosis, compared with one of the 19 cases among non-PWID. Among 35 (78%) cases, patients reported active injection drug use at the time of bacteremia; among the remaining 10 (22%) cases, patients reported previous injection drug use and current noninjection illicit drug use. Known xylazine exposure before diagnosis was self-reported in 12 (27%) cases and suspected by a clinician based on the presence of wounds consistent with xylazine use (2) in an additional seven (16%) cases.

Among 44 of the 45 cases, the patients had concurrent skin and soft tissue infections; in 37 (82%) cases, the patients had multiple wounds at the time of diagnosis with GAS bacteremia. Twenty-one of the 38 patients collectively sought aid 59 times (range = one to six visits per person) at UVMMC emergency or urgent care departments for wound care during the 6 months before their diagnosis of GAS bacteremia.

Hospital admission for intravenous antibiotic therapy was recommended for all cases. Among 17 (38%) cases, the patient underwent wound debridement (12 in an operating room and five at bedside). Among 23 (51%) cases, the patient declined admission or left the hospital against medical advice. The average length of admission was 11 days. Two patients died during hospitalization for GAS bacteremia.

#### Preliminary Conclusions and Actions

The precipitous increase in GAS bacteremia at UVMMC followed an increase in involvement of xylazine in fatal opioid overdoses in Vermont, first reported in late 2021.<sup>§,¶</sup> Xylazine causes peripheral vasoconstriction and ischemia and has been associated with necrosis at injection sites and noninjection sites (2). Xylazine can be present in both injected and noninjected drugs.\*\* Xylazine-related wounds might serve as a portal of entry for bacteria into the bloodstream and could, at least in part, explain the increase in GAS bacteremia described in this report. Given the findings of this report and other studies (1), GAS should be considered in PWID with symptoms

\* <https://www.cdc.gov/groupastrep/current-activity.html>

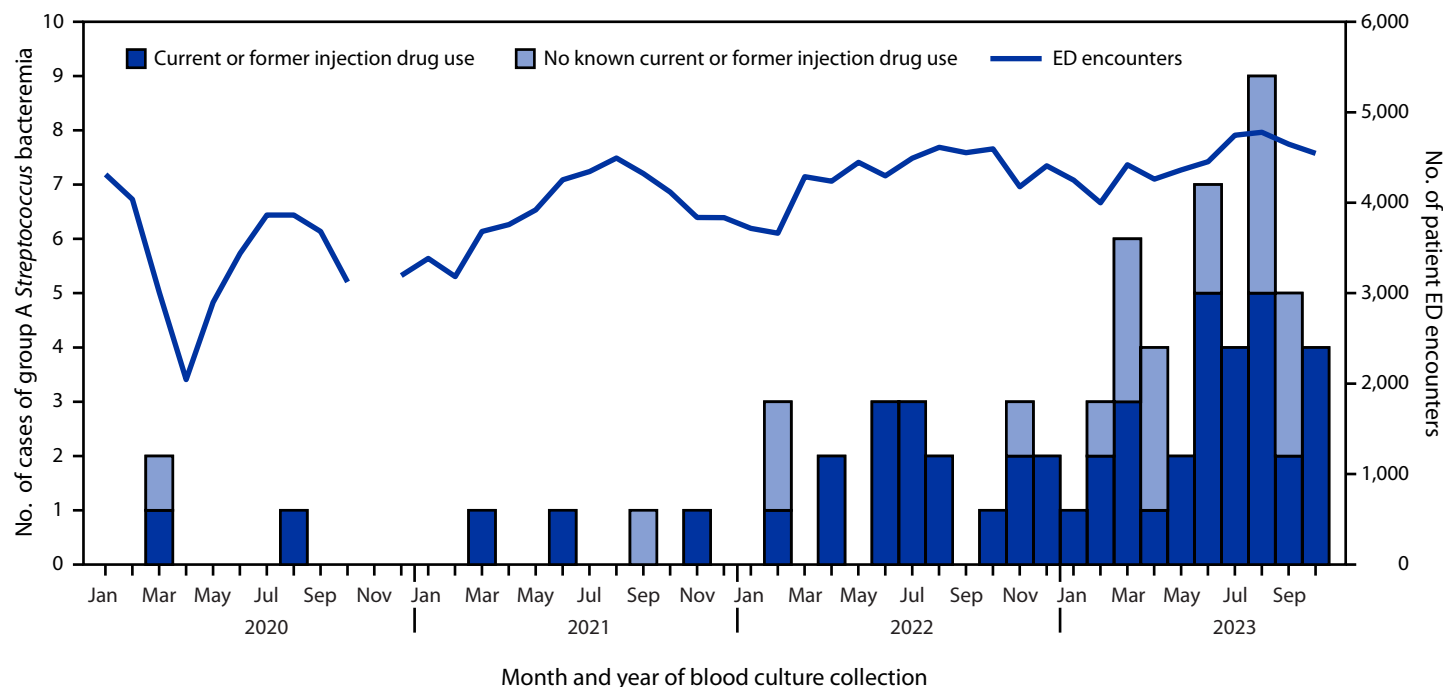
<sup>†</sup> Includes persons who actively engaged in injection drug use at the time of GAS bacteremia diagnosis and those who did so previously.

<sup>§</sup> <https://www.healthvermont.gov/sites/default/files/documents/pdf/ADAP-XylazineBrief.pdf>

<sup>¶</sup> <https://www.cdc.gov/drugoverdose/fatal/dashboard/index.html>

\*\* <https://www.cdc.gov/drugoverdose/deaths/other-drugs/xylazine/faq.html#what>

**FIGURE.** Cases of community-acquired group A *Streptococcus* bacteremia, by month of blood culture collection, patient history of injection drug use, and emergency department encounters — University of Vermont Medical Center, January 2020–October 2023\*<sup>†</sup>



**Abbreviation:** ED = emergency department.

\* Infection and ED encounter data are missing for October 28–November 23, 2020, because of a cyberattack that rendered the University of Vermont Medical Center's electronic medical records unusable.

<sup>†</sup> In October 2021, the Vermont Department of Health reported a greater than twofold increase in the percentage of fatal opioid overdoses with xylazine involvement during the first 7 months of 2021, compared with each of the previous 2 years.

of bacteremia, particularly in persons with wounds. During the 6 months before diagnosis with GAS bacteremia, patients visited emergency or urgent care departments up to six times seeking aid for wound care. Increased access to wound care services in sites accessible to PWID might result in earlier treatment and prevent progression to bacteremia.

In response to these findings, UVMMC is working to improve linkage to care for both opioid use disorder and wound care and is exploring collaborative efforts with local nongovernmental organizations and public health authorities to deliver wound care services in community settings.

### Summary

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

Injection of illicit drugs and homelessness are risk factors for invasive group A streptococcal infections. Xylazine has been associated with necrosis, which could facilitate entry of bacteria into the bloodstream.

#### What is added by this report?

During 2022–2023, the University of Vermont Medical Center experienced a substantial increase in the number of community-acquired group A streptococcal bloodstream infections, predominantly in persons who inject drugs. The increase coincided with the introduction of xylazine into the drug supply. Many patients sought care for wounds before being diagnosed with a bloodstream infection.

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

The availability of wound care services in sites accessible to persons who inject drugs might help prevent bloodstream infections.



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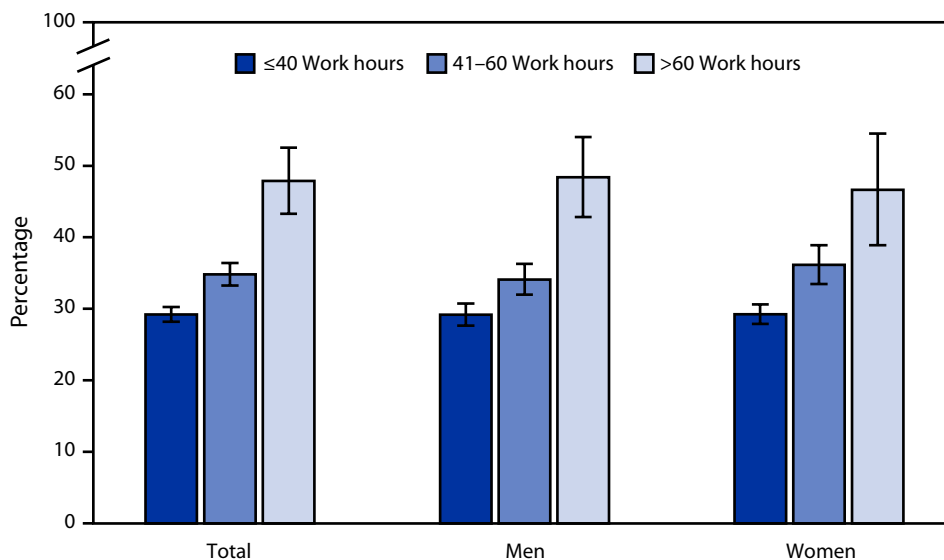
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## QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

### Percentage\* of Employed Adults Aged $\geq 18$ Years Who Slept $< 7$ Hours per 24-Hour Period,<sup>†</sup> by Sex and Number of Work Hours per Week<sup>§</sup> — United States, 2022



\* Estimates were based on household interviews of a sample of the civilian, noninstitutionalized U.S. population, with 95% CIs indicated by error bars.

<sup>†</sup> Based on a response to the question, "On average, how many hours of sleep do you get in a 24-hour period?"

<sup>§</sup> Based on a response to the question, "How many hours did you work last week at all jobs or businesses?"

In 2022, the percentage of employed adults who slept  $< 7$  hours on average during a 24-hour period increased with the number of hours worked per week, including 29% among those who worked  $\leq 40$  hours, 35% among those who worked 41–60 hours, and 48% among those who worked  $> 60$  hours per week. The patterns were similar for men and women.

**Supplementary Table:** <https://stacks.cdc.gov/view/cdc/153722>

**Source:** National Center for Health Statistics, National Health Interview Survey, 2022. <https://www.cdc.gov/nchs/nhis/index.htm>

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For more information on this topic, CDC recommends the following link: [https://www.cdc.gov/sleep/about\\_sleep/sleep\\_hygiene.html](https://www.cdc.gov/sleep/about_sleep/sleep_hygiene.html)

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