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SARS-CoV-2 Rebound With and Without Use of COVID-19 Oral Antivirals

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Abstract

Early treatment with a first-line therapy (nirmatrelvir/ritonavir [Paxlovid] or remdesivir) or second-line therapy (molnupiravir) prevents hospitalization and death among patients with mild-to-moderate COVID-19 who are at risk for severe disease and is recommended by the National Institutes of Health COVID-19 Treatment Guidelines. On May 25, 2023, the Food and Drug Administration approved nirmatrelvir/ritonavir for treatment of adults at high risk for severe disease. Although antiviral therapies are widely available, they are underutilized, possibly because of reports of SARS-CoV-2 rebound after treatment. To enhance current understanding of rebound, CDC reviewed SARS-CoV-2 rebound studies published during February 1, 2020– November 29, 2023. Overall, seven of 23 studies that met inclusion criteria, one randomized trial and six observational studies, compared rebound for persons who received antiviral treatment with that for persons who did not receive antiviral treatment. In four studies, including the randomized trial, no statistically significant difference in rebound rates was identified among persons receiving treatment and those not receiving treatment. Depending on the definition used, the prevalence of rebound varied. No hospitalizations or deaths were reported among outpatients who experienced rebound, because COVID-19 signs and symptoms were mild. Persons receiving antiviral treatment might be at higher risk for rebound compared with persons not receiving treatment because of host factors or treatment-induced viral suppression early in the course of illness. The potential for rebound should not deter clinicians from prescribing lifesaving antiviral treatments when indicated to prevent morbidity and mortality from COVID-19.

Introduction

COVID-19 has caused approximately 6.5 million hospitalizations and 1.1 million deaths in the United States.* Although hospitalizations and deaths are currently much lower than they were during the peak of the pandemic, COVID-19 continues to cause substantial morbidity and mortality. As of December 9, 2023, approximately 23,000 hospitalizations per week were reported among patients with COVID-19, with highest rates among persons aged ≥65 years. Currently, health care providers are positioned to mitigate COVID-19 morbidity and mortality with safe and effective vaccines† and early diagnosis and treatment (*1*).

Antiviral Therapeutics

Early treatment with first-line therapy (nirmatrelvir/ritonavir [Paxlovid] or remdesivir) or second-line therapy (molnupiravir) reduces the prevalence of hospitalization and death among patients with mild-to-moderate COVID-19 who are at risk for severe disease (*2*–*4*), and is recommended by the National

* https://covid.cdc.gov/covid-data-tracker/#datatracker-home (Accessed December 15, 2023).

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

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Institutes of Health (NIH) COVID-19 Treatment Guidelines (*1*). The two oral antivirals, nirmatrelvir/ritonavir and molnupiravir, are widely available but underutilized (*5*). The limited use of these antivirals might be partially attributable to reports of rebound after treatment, especially with nirmatrelvir/ritonavir.[§] However, rebound was reported before the advent of COVID-19 antivirals and was related to immunity and individual level factors (*6*,*7*).

SARS-CoV-2 Rebound

SARS-CoV-2 rebound is typically described as recurrence of signs or symptoms or a new positive viral test result after initial recovery from COVID-19. In May 2022, CDC issued a health advisory alert that described case reports of SARS CoV-2 rebound among patients who completed the recommended 5-day course of nirmatrelvir/ritonavir and noted that rebound was also described among persons who were not treated.[¶] On May 25, 2023, the Food and Drug Administration (FDA) approved nirmatrelvir/ritonavir, which was authorized for emergency use in December 2021, for treatment of mild to moderate COVID-19 among adults aged ≥18 years who are at high risk for severe disease.[**] In their review of data from Evaluation of Protease Inhibition for COVID-19 in High Risk Patients (EPIC-HR), a phase 2/3 randomized controlled trial that examined the efficacy of nirmatrelvir/ritonavir, FDA concluded that there was no consistent association between treatment and rebound (*8*). To enhance current understanding of rebound, CDC reviewed recent literature comparing rebound among COVID-19 patients who did and did not receive antiviral treatment.

Review Methodology

CDC reviewed SARS-CoV-2 rebound studies published during February 1, 2020–November 29, 2023. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses were used (*9*). PubMed, JSTOR, and Google Scholar were searched using keywords "Paxlovid rebound," "SARS-CoV-2 viral rebound," "SARS-CoV-2 rebound," "nirmatrelvir/ritonavir rebound," "molnupiravir rebound," "SARS-CoV-2 infection rebound," "SARS-CoV-2 viral load rebound," "rebound phenomenon," "SARS-CoV-2 viral kinetics," "SARS-CoV-2 virologic rebound," and "SARS-CoV-2 clinical rebound." Searches returned 303 publications that were reviewed[††] (Figure 1); 23 studies met inclusion criteria

[§] https://www.medscape.com/viewarticle/987121?form=fpf
[¶] https://stacks.cdc.gov/view/cdc/117609
[**] https://www.fda.gov/news-events/press-announcements/fda-approves-first-oral-antiviral-treatment-covid-19-adults

[††] Relevant publications were identified based on the titles and abstracts using EndNote (version 20; Clarivate). Two reviewers independently screened all titles and abstracts and hand-searched references of retrieved publications. Disagreements were discussed, and duplicates were removed. Variables extracted from publications included date published, country of study, journal, study design, patient median age, sex, COVID-19 vaccination status, definition of rebound, duration of rebound symptoms, sample size, antiviral treatment type, rebound prevalence, outcome, study limitations, and conclusions.

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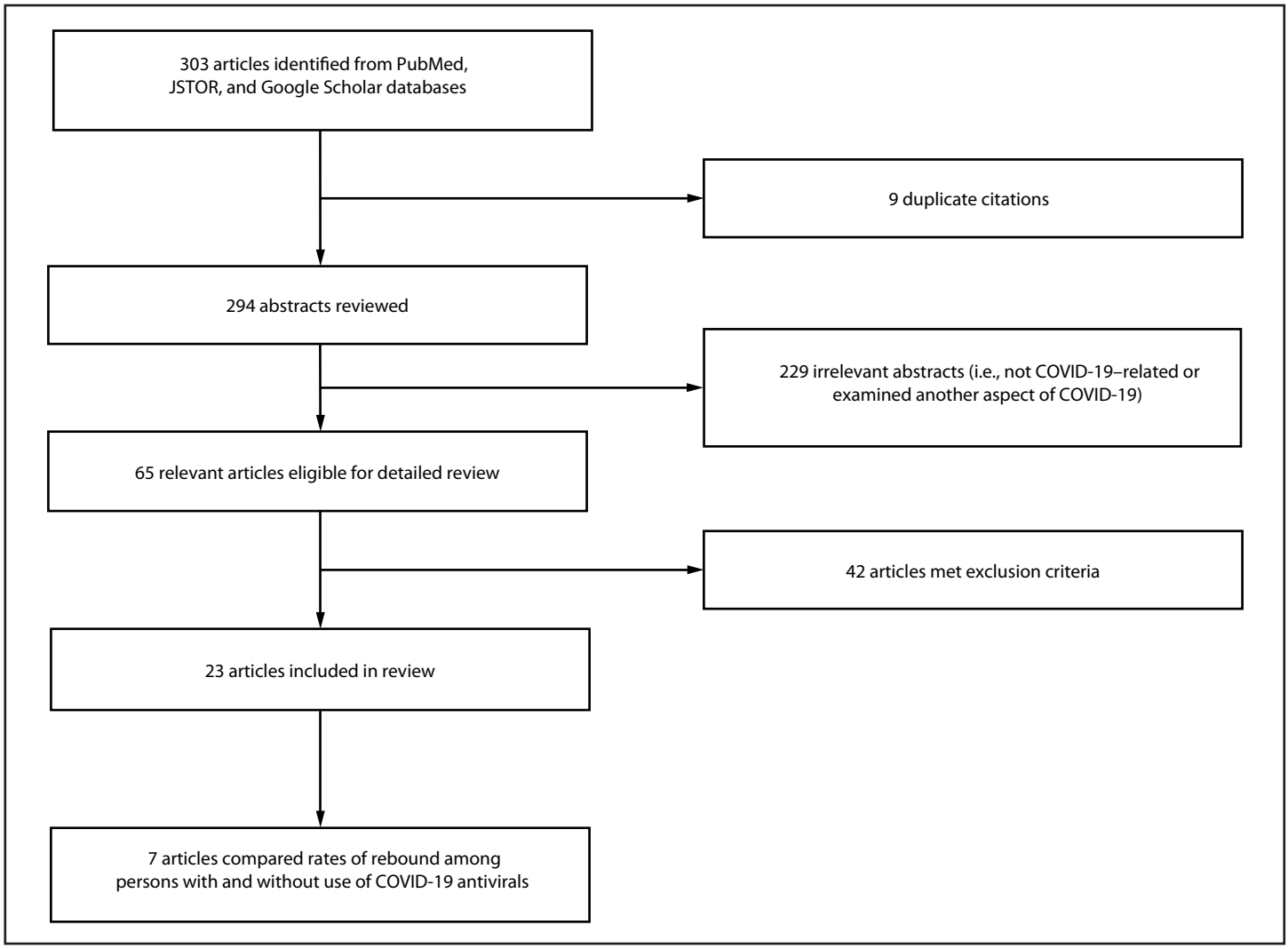
FIGURE 1. Review of SARS-CoV-2 rebound studies based on specific selection criteria*,† — February 1, 2020–November 29, 2023



* Keywords used in search were, "Paxlovid rebound," "SARS-CoV-2 viral rebound," "SARS-CoV-2 rebound," "nirmatrelvir/ritonavir rebound," "molnupiravir rebound," "SARS-CoV-2 infection rebound," "SARS-CoV-2 viral load rebound," "rebound phenomenon," "SARS-CoV-2 viral kinetics,""SARS-CoV-2 virologic rebound," and "SARS-CoV-2 clinical rebound."

† Studies were excluded if they were not related to COVID-19, related to nonrebound aspects of COVID-19, were preprints, editorials, case reports, studies of ancillary medications, or other publications not describing original data or analyses of rebound data.

(Table 1) (Supplementary Table, https://stacks.cdc.gov/view/cdc/137156). Seven studies compared rates of rebound among patients who did and did not receive COVID-19 antiviral treatment (Table 2) (*10*–*16*). Findings from two studies examining infectivity, resistance, and immune response were summarized (*11*,*17*). Individual case data from three studies that used the same definition of viral rebound were examined to estimate days to onset of viral rebound and rebound duration (*18*–*20*). Median days to rebound and resolution of acute and rebound illness were calculated. Pearson's chi-square or Fisher's exact test were used to compare proportions for studies that did not report the test statistic. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[§§]

Review Findings

Studies of Rebound in Patients Who Did and Did Not Receive Antiviral Treatment

SARS-CoV-2 rebound with and without the use of antiviral treatment were described in previous studies (*10*–*16*). The definition of and methods assessing SARS-CoV-2 rebound,

[§§] 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; and 44 U.S.C. Sect. 3501 et seq.

TABLE 1. SARS-CoV-2 rebound literature review* inclusion and exclusion criteria — February 1, 2020–November 29, 2023

Characteristic	Inclusion criteria	Exclusion criteria
Publication type	Peer-reviewed	Preprints Conference abstracts Editorials
Characteristic	Published in English Explicitly stated a focus on "rebound" SARS-CoV-2 infection	Published in any other language Not focused on "rebound" All other pathogens such as influenza
Study type	Randomized control trials Prospective or retrospective cohort studies Case control studies Case series of two or more patients	Case reports of single patients
Population	Adults with SARS-CoV-2 infection	Animal studies
Interventions	Treatment of COVID-19 with oral antivirals No treatment of COVID-19	Treatment with ancillary medications or medications not recommended for COVID-19 treatment such as corticosteroids, ivermectin, and anticoagulation.
Outcomes	Prevalence, hospitalizations, deaths, resistance, recovery, and immune response	Adverse events and side effects

* The CDC library conducted a search for studies published during February 1, 2020–November 29, 2023 using the following terms: "Paxlovid rebound," "SARS-CoV-2 viral rebound," "SARS-CoV-2 rebound," "nirmatrelvir/ritonavir rebound," "molnupiravir rebound," "SARS-CoV-2 infection rebound," "SARS-CoV-2 viral load rebound," "rebound phenomenon," "SARS-CoV-2 viral kinetics," "SARS-CoV-2 virologic rebound," and "SARS-CoV-2 clinical rebound."

including frequency and duration of specimen collection, varied among studies (Table 2). No hospitalizations or deaths were reported among outpatients who experienced rebound, because symptoms were mild.

Four retrospective cohort studies found similar frequencies of viral rebound among persons who did and did not receive COVID-19 antiviral treatment (*10*,*12*,*15*–*16*). Three studies found higher frequencies of rebound among treated persons: the first study examined persons with chronic lymphocytic leukemia (*14*); the second examined treated persons who were older (median age = 57 years versus 39 years; p<0.001), received more COVID-19 vaccine doses (4 versus 3; p<0.001), and had higher rates of immunosuppression (32% versus 9%; p<0.001) than did untreated persons (*11*); and the third used propensity score matching to ensure the treated and untreated groups were well matched, but had limited follow-up time (*13*).

A large retrospective, observational study found similar rates of rebound and no statistically significant differences among patients treated with nirmatrelvir/ritonavir (6.6%; 95% CI = 4.1%–10.5%), molnupiravir (4.8%; 95% CI = 3.3%–6.9%) and those who received no treatment (4.5%; 95% CI = 3.9%–5.2%) (Table 2) (*15*). Persons with immunocompromising conditions had higher odds of viral rebound regardless of treatment status: nirmatrelvir/ritonavir (odds ratio [OR] = 7.37; 95% CI = 2.56–21.26), molnupiravir (OR = 3.05; 95% CI = 1.28–7.25), and no treatment (OR = 2.21; 95% CI = 1.50–3.27). Among patients receiving nirmatrelvir/ritonavir, the odds of virologic rebound were higher among those aged 18–65 years compared with those aged >65 years (OR = 3.09; 95% CI = 1.00–9.53), those with high comorbidity prevalence (score >6 on the Charlson Comorbidity Index [OR = 6.02; 95% CI = 2.09–17.38]), and those concomitantly taking corticosteroids (OR = 7.51; 95% CI = 1.67–33.82), whereas the odds were lower among those who were not fully vaccinated (OR = 0.16; 95% CI = 0.04–0.67).

Initial analysis of EPIC-HR trial data showed that viral rebound rates were low and similar between the treated and untreated groups (Table 2) (*10*). In addition, rebound was not associated with low nirmatrelvir/ritonavir levels, hospitalization or death, severe symptom relapse, vaccination or serologic status, or emergent mutations (*8*,*10*).

Infectivity, Resistance, and Immune Response

One observational study demonstrated that duration of shedding of infectious virus was longer among persons with rebound (14 days) compared with those without rebound (3 days), but found no evidence of resistance-associated mutations using genomic sequencing (*11*). Another study of biomarkers among six patients with rebound after treatment with nirmatrelvir/ritonavir demonstrated that a robust immune response was present during rebound, likely reducing risk for disease progression (*17*). This study also found no evidence of resistance.

Onset and Duration of Rebound

Among 22 patients (from three studies) with available virologic data and who received treatment, median time to negative test results was 6 days (IQR = 5–7 days) after initial positive test result (*18*–*20*) (Figure 2). Median time to viral rebound was 9 days (IQR = 9–13 days) after diagnosis, and to resolution was 16 days (IQR = 16–19 days) into the viral illness. Rebound occurred during the course of illness when there was variability in viral load because of host factors (*21*).

Discussion

Current evidence, including randomized controlled trial and observational data, suggests that SARS-CoV-2 rebound occurs initially as a mild illness 3–7 days after resolution of the initial acute illness, occurs in both treated and untreated patients, and is not associated specifically with receiving nirmatrelvir/ritonavir. Moreover, rebound occurs when there is variable,

TABLE 2. Summary of seven SARS-CoV-2 rebound studies among persons who did and did not receive antiviral treatment with nirmatrelvir/ritonavir or molnupiravir — February 1, 2020–November 29, 2023*

Study author, year	Study type	Definition of rebound	Sample size	Treatment	Rebound prevalence, % (no./No.) With treatment	Rebound prevalence, % (no./No.) Without treatment	p-value	Study conclusions and key limitations
Anderson et al., 2022†	RCT	0.5-log increase in viral load on day 10 or day 14 if only one value was available or on days 10 and 14 if both values were available	2,216	N/R	2.3 (23/990)	1.7 (17/980)	0.34	Similar incidence of viral load rebound in N/R and placebo groups Viral load rebound not retrospectively associated with low nirmatrelvir exposure; recurrence of moderate to severe symptoms, or development of nirmatrelvir resistance Limitations: only unvaccinated persons included in study, conducted during pre-Omicron period, viral load determined by PCR, does not translate directly to the presence of infectious virus, and is not perfectly correlated with current or new clinical symptoms
Edelstein et al., 2023§	PC	Def 1: a positive SARS-CoV-2 viral culture result after a previous negative test result Def 2: combination of a nadir viral load below 4.0 $\log_{10}$ copies/mL followed by an increase in viral load that was ≥1.0 $\log_{10}$ copies/mL above the nadir, and two consecutive viral load results of 4.0 $\log_{10}$ copies/mL or higher	127	N/R	21 (15/72)	2 (1/55)	0.001	Viral rebound associated with N/R use Limitations: not RCT; significant differences between those taking N/R and untreated persons (e.g., number of COVID-19 vaccinations, older, and immunosuppression)
Pandit et al., 2023¶	PC	Positive rapid antigen test result after a negative antigen test result and symptom rebound	N/R = 127; control = 43	N/R	14 (18/127)	9 (4/43)	0.41	Rebound after clearance of test result positivity or symptom resolution is higher than previously reported Limitations: not RCT
Smith-Jeffcoat et al., 2023**	Prospective/propensity score matching	Symptom rebound was defined as an increase of at least two symptoms any time after treatment completion or proxy. Viral load rebound was defined as an increase of ≥1 $\log_{10}$ IU/mL (increasing to or above 5.0 $\log_{10}$ IU/mL) any time after treatment	1,234	N/R	Symptom rebound: 32 (41/130) Viral load rebound: 27 (26/130)	Symptom rebound: 20 (47/241) Viral load rebound: 7 (12/241)	0.009 <0.001	Patients completing N/R treatment experienced fewer symptoms and lower viral load but rebound occurred more often compared with untreated persons; providers should prescribe N/R, when indicated, and communicate rebound risk to patients Limitations: not RCT; daily symptoms and viral load were only available for 10 days after enrollment; unmeasured differences between N/R-treated and untreated participants
Tadmor et al., 2023††	RC (EMR)	Positive PCR test result after negative test result	331	N/R	9.0 (8/89)	3.6 (8/219)	0.05	Higher incidence of rebound in patients with CLL treated for SARS-CoV-2 with N/R or molnupiravir compared with nontreated CLL patients or nonleukemia high-risk patients
				molnupiravir	8.7 (2/23)		0.24	Limitations: not RCT
Wong et al., 2023§§	RC	Reduction in Ct value (≥3) on quantitative RT-PCR test between 2 consecutive measurements, with decrease sustained in an immediately subsequent Ct measurement (for those patients with ≥3 Ct measurements)	4,592	N/R	6.6; 95% CI = 4.1–10.5 (6/242)	4.5; 95% CI = 3.9–5.2 (170/3,787)	0.13	Viral rebound rates were similar between patients with and without antiviral treatment
				molnupiravir	4.8; 95% CI = 3.3–6.9 (27/563)		0.75	Viral burden rebound not associated with adverse clinical outcomes Limitations: not RCT

See table footnotes on the next page.

TABLE 2. (*Continued*) Summary of seven SARS-CoV-2 rebound studies among persons who did and did not receive antiviral treatment with nirmatrelvir/ritonavir or molnupiravir — February 1, 2020–November 29, 2023*

Study author, year	Study type	Definition of rebound	Sample size	Treatment	Rebound prevalence, % (no./No.) With treatment	Rebound prevalence, % (no./No.) Without treatment	p-value	Study conclusions and key limitations
Wong et al., 2022¶¶	RC	Def 1: Ct >40, decreased to ≤40	12,629	N/R	Def 1: N/R: 1.0	Def 1: 0.6	Def 1: 0.56	Low incidences of viral rebound in molnupiravir users, N/R users, and antiviral nonusers among patients with COVID-19
		Def 2: Ct >36, decreased to ≤36			Def 2: N/R: 4.6	Def 2: 4.4	Def 2: 0.95	Viral rebound is not associated with higher mortality in antiviral users
		Def 1: Ct>40, decreased to ≤40		molnupiravir	Def 1: molnupiravir: 0.8	Def 1: 0.6	Def 1: 0.56	
		Def 2: Ct >36, decreased to ≤36			Def 2: molnupiravir: 4.6	Def 2: 4.4	Def 2: 0.95	Limitations: not RCT

Abbreviations: CLL = chronic lymphocytic leukemia; Ct = cycle threshold; Def = definition; EMR = electronic medical records; N/R = nirmatrelvir/ritonavir; PC = prospective cohort; RC = retrospective cohort; RCT = randomized controlled trial; RT-PCR = real-time polymerase chain reaction.

* From PubMed, JSTOR, and Google Scholar databases, 303 publications published during February 1, 2020–November 29, 2023, were identified; nine duplicate citations were removed. Among the 294 abstracts reviewed, 229 irrelevant abstracts were removed (i.e., not COVID-19–related or examined another aspect of COVID-19). Among the 65 relevant publications determined to be eligible for detailed review, 42 publications were removed because they did not meet inclusion criteria (i.e., preprints, editorials, case reports, or studies of ancillary medications). Overall, 23 publications were included in the review including these seven publications that compared rates of rebound among persons with and without use of COVID-19 antivirals.

† https://doi.org/10.1056/NEJMc2205944

§ https://doi.org/10.7326/M23-1756

¶ https://doi.org/10.1093/cid/ciad102

** https://doi.org/10.1093/cid/ciad696

†† https://doi.org/10.1080/10428194.2023.2183732

§§ https://doi.org/10.1016/S1473-3099(22)00873-8

¶¶ https://doi.org/10.1001/jamanetworkopen.2022.45086

host-mounted immune response to infection during the course of illness. Finally, no hospitalizations or deaths were reported among outpatients who experienced rebound.

Some observational studies demonstrated a higher frequency of rebound among treated persons (10%–14%) (*11*,*14*,*22*) than reported by the randomized controlled trial, EPIC-HR (*8*,*10*) (Supplementary Table, https://stacks.cdc.gov/view/cdc/137156). Viral rebound might occur in persons on antiviral treatment because they are at high risk for severe disease and might have host factors, such as immunosuppression, that contribute to the natural variability in viral dynamics (*21*). Risk factors for rebound appear to be similar to risk for severe disease, but further studies are needed to understand whether persons with certain characteristics or underlying medical conditions are predisposed to experiencing rebound. Another important consideration is that persons receiving antiviral treatment might be at higher risk for experiencing rebound given the viral suppression related to use of treatment early in the disease course and resumption of viral replication after completion of treatment because of delayed viral clearance. This elevated risk could be due to early discontinuation of antiviral treatment or the need for longer courses of treatment among certain persons, such as those who are immunocompromised (*14*). Two ongoing clinical trials of nirmatrelvir/ritonavir will further characterize the frequency of rebound after different durations of nirmatrelvir/ritonavir treatment among immunocompromised subjects¶¶ and the potential benefit of nirmatrelvir/ritonavir retreatment among subjects with posttreatment rebound.***

Rebound does not likely represent reinfection or resistance to treatment (*12*); however, further studies are needed to confirm this finding. The FDA analysis identified potential treatment-associated mutations that were not clinically relevant among two treated patients because rebound symptoms resolved without hospitalization (*8*). It is important to ensure that use of antivirals does not accelerate viral evolution and result in resistant mutations, such as through counseling patients to complete antiviral treatment and monitoring for resistance using molecular analyses. Two studies demonstrated shedding of infectious virus during rebound (*8*,*11*). Comparisons of genomic strains present in both acute and rebound episodes and viral culture to determine infectiousness are important to understanding the clinical implications of rebound. In addition, a large assessment of innate and adaptive immunity and monitoring biomarkers of inflammation and cytokine storm would contribute to understanding of the underlying pathophysiology of recurrence.

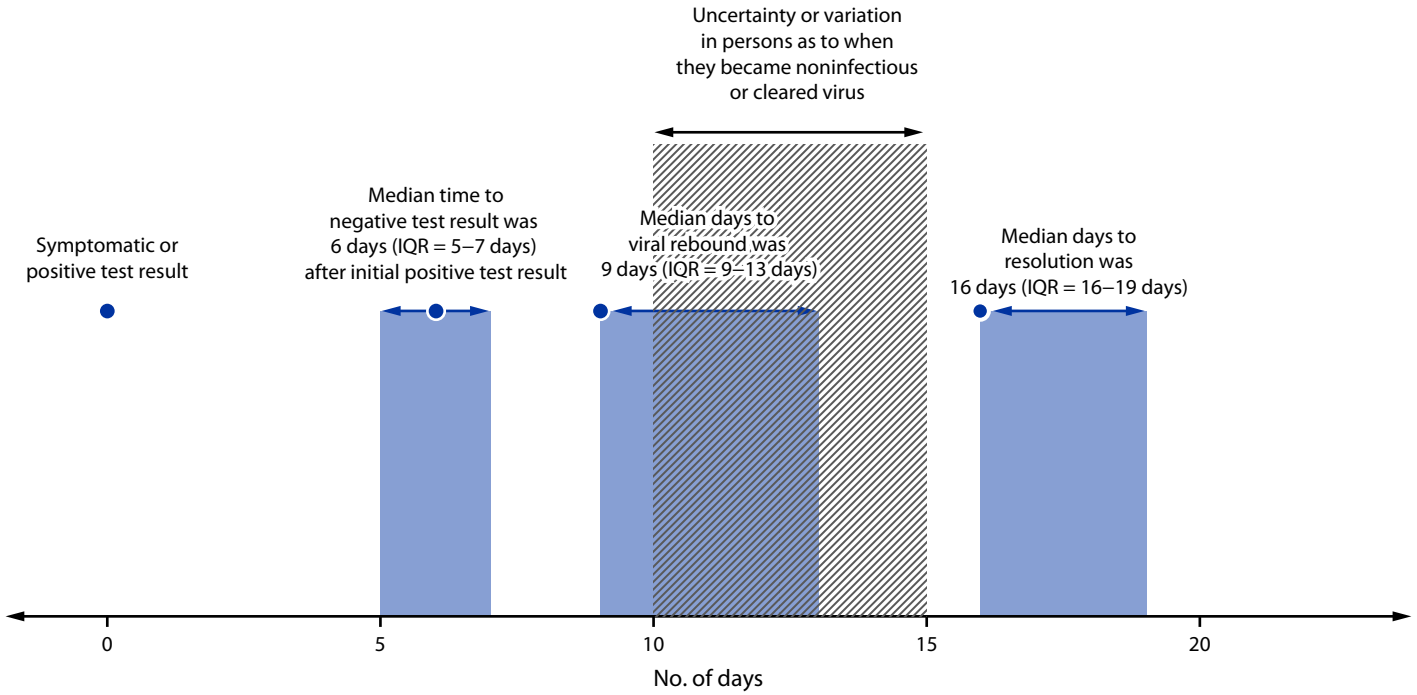
Limitations

The findings in this report are subject to at least five limitations. First, standardized definitions for symptom, viral, and clinical rebound were not used across studies. Using standard definitions to accurately reflect outcomes could improve interpretability and comparisons of data across studies and settings.

¶¶ https://clinicaltrials.gov/ct2/show/NCT05438602

*** https://clinicaltrials.gov/study/NCT05567952?cond=post-treatment%20rebound%20COVID-19&rank=1

FIGURE 2. Timing of viral rebound and resolution during SARS-CoV-2 infection among 22 patients*,† — February 1, 2020–November 29, 2023



* Median time to negative test result was defined as day of first negative viral test result (polymerase chain reaction or antigen) after initial positive test result. Viral rebound was defined as the first positive viral test result (polymerase chain reaction or antigen) after a negative test result. Resolution was defined as first negative viral test result after day 1 of viral rebound.

† Timing and duration of viral rebound generated using data from 22 patients in three studies that used a virologic definition of rebound and had complete data: https://doi.org/10.1093/cid/ciac512, https://doi.org/10.1056/NEJMc2206449, and https://doi.org/10.1016/j.jinf.2022.06.011.

Most studies examined symptom or viral rebound. A definition that requires reemergence of virus after complete resolution of illness, which takes 7–10 days for a healthy adult, and a negative viral test result after resolution of initial symptoms would allow for examination of clinical implications of rebound or recrudescence, such as a dysregulated immune response (*23*). Second, publications about recurrences and viral kinetics might have been missed given the narrow search. Third, a major limitation of observational studies is the difficulty in verifying whether antiviral treatment courses were completed and whether vaccination status and previous infection were documented accurately. Fourth, few studies correlated symptoms with viral load, which makes the significance of recurrence of mild symptoms difficult to understand because symptoms are subjective and might not represent viral reactivation. Finally, ascertainment bias is also possible given that persons receiving antiviral treatment are closely followed, and more likely to report recurrent symptoms, which would explain the early case reports being associated with nirmatrelvir/ritonavir, the most commonly used oral antiviral in the United States.

Summary

What is already known about this topic?

Early recommended antiviral treatment prevents hospitalizations and deaths among patients with mild-to-moderate COVID-19 who are at risk for severe disease.

What is added by this report?

CDC examined SARS-CoV-2 rebound studies among patients who did and did not receive antiviral treatment. No consistent association between treatment and rebound was identified. The prevalence of rebound varied, depending upon host factors and the definition of rebound. Rebound symptoms were mild. No hospitalizations or deaths occurred from viral rebound.

What are the implications for public health practice?

This review suggests that per National Institutes of Health COVID-19 Treatment Guidelines, rebound should not deter providers from prescribing lifesaving antiviral treatments when indicated to prevent morbidity and mortality from COVID-19.

Implications for Public Health Practice

Viral rebound can occur in persons who do and do not receive antiviral treatment and might reflect viral fluctuation that is part of the natural disease process early in the course of illness. Risk for experiencing rebound could be related to many

factors, such as immunosuppression, delayed viral clearance, and overall immune response. The current literature review, along with a recently published randomized trial (*8*), suggests the substantial benefit of antiviral treatment among persons at risk for severe disease outweighs the risk for rebound, because rebound resolves quickly and is not associated with an increase in severity of recurring signs and symptoms. Increased education and awareness among practitioners and patients about rebound not increasing risk for hospitalization or death might increase use of COVID-19 treatment. According to NIH COVID-19 Treatment Guidelines, rebound should not deter providers from prescribing life-saving antiviral treatments when indicated to prevent morbidity and mortality from COVID-19 (*1*).

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Evaluation of SARS-CoV-2 RNA Rebound After Nirmatrelvir/Ritonavir Treatment in Randomized, Double-Blind, Placebo-Controlled Trials — United States and International Sites, 2021–2022

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Abstract

Rebound of SARS-CoV-2 shedding or COVID-19 signs and symptoms has been described after treatment with nirmatrelvir/ritonavir (Paxlovid). The direct association of nirmatrelvir/ritonavir to COVID-19 rebound remains unclear because most reports are based on individual cases or nonrandomized studies. Viral RNA shedding data from two phase 2/3, randomized, double-blind, placebo-controlled clinical trials of nirmatrelvir/ritonavir (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients [EPIC-HR] and Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients [EPIC-SR]) were analyzed to investigate the role of nirmatrelvir/ritonavir treatment in COVID-19 rebound. Rates of rebound of SARS-CoV-2 RNA shedding, identified based on an increase in nasopharyngeal viral RNA levels from day 5 (end-of-treatment) to day 10 or day 14, were similar between nirmatrelvir/ritonavir and placebo recipients. Among subjects with a virologic response through day 5, viral RNA rebound occurred in 6.4%–8.4% of nirmatrelvir/ritonavir recipients and 5.9%–6.5% of placebo recipients across EPIC-HR and the 2021/pre-Omicron and 2022/Omicron enrollment periods of EPIC-SR. Viral RNA rebound after nirmatrelvir/ritonavir treatment was not associated with COVID-19–related hospitalization or death. Data from randomized trials demonstrated that SARS-CoV-2 rebound can occur with or without antiviral treatment, supporting the Food and Drug Administration's determination of safety and efficacy of nirmatrelvir/ritonavir in eligible patients at high risk for severe COVID-19.

Introduction

Nirmatrelvir/ritonavir (Paxlovid)* is a COVID-19 oral antiviral treatment consisting of nirmatrelvir, a SARS-CoV-2 main protease (M^{pro} or 3C-like protease [$3CL^{pro}$]) inhibitor, and ritonavir, a pharmacokinetic enhancer. Several reports have described patients who have experienced a rebound in SARS-CoV-2 detection or COVID-19 signs and symptoms after treatment with nirmatrelvir/ritonavir, or without antiviral treatment (*1*–*8*). Identifying the direct contribution of nirmatrelvir/ritonavir to the rebound phenomenon has been challenging. Other than limited analyses from the pharmaceutical sponsor of nirmatrelvir/ritonavir based on the Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients (EPIC-HR) trial (*9*), conducted before SARS-CoV-2 Omicron emergence, reports of COVID-19 rebound are primarily based on individual cases and nonrandomized cohort studies. The lack of clarity and persistent concerns about COVID-19 rebound have reportedly contributed to reduced nirmatrelvir/ritonavir use (*10*). This analysis used data submitted to the Food and Drug Administration (FDA) to investigate the frequency of rebound in SARS-CoV-2 RNA shedding among outpatients with COVID-19 treated with nirmatrelvir/ritonavir or placebo in two randomized, double-blind clinical trials.

Methods

Data Sources

The authors conducted retrospective analyses of viral RNA shedding levels in nasopharyngeal samples from phase 2/3 clinical trials EPIC-HR and Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients (EPIC-SR).† Both were double-blind trials in which adult outpatients with mild-to-moderate COVID-19 were randomized 1:1 to receive 5 days of nirmatrelvir (300 mg)/ritonavir (100 mg) or placebo, twice daily. EPIC-HR enrolled participants in 2021, before the emergence of SARS-CoV-2 Omicron, and included adults who were unvaccinated against COVID-19 and at high risk for progression to severe disease. EPIC-SR originally enrolled two groups of participants in 2021, before Omicron emergence: 1) adults with high risk of SARS-CoV-2 exposure who had completed a primary vaccination series, and 2) unvaccinated adults without risk factors for severe disease. EPIC-SR reopened in 2022 when SARS-CoV-2 Omicron (primarily

* Nirmatrelvir/ritonavir (Paxlovid) first became available in the United States for the treatment of mild-to-moderate COVID-19 through Emergency Use Authorization from the Food and Drug Administration (FDA) on December 22, 2021, (https://www.fda.gov/media/155049/download) and was approved by FDA on May 25, 2023, for the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization or death. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/217188Orig1s000ltr.pdf

† Data from clinical trials EPIC-HR and EPIC-SR were submitted to FDA by the applicant (Pfizer) in support of the review and approval of New Drug Application (NDA) 217188 (Paxlovid). Analyses of viral RNA and symptom rebound for this report were conducted for all randomized subjects in these trials who took ≥1 dose of nirmatrelvir/ritonavir or placebo and were randomized ≤5 days of symptom onset. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/217188Orig1s000IntegratedR.pdf

BA.2-related) predominated, and adults without risk factors for severe disease who had not received a COVID-19 vaccine during the preceding 12 months were enrolled.

Viral RNA levels were measured in nasopharyngeal swab samples collected by health care providers at prespecified study visits on days 1 (baseline), 3, 5 (end-of-treatment), 10, and 14 (Table 1).[§] Viral RNA data from EPIC-HR used in these analyses overlap with those described in the 2022 study of nirmatrelvir/ritonavir and viral RNA rebound (*9*), although analysis definitions differed.

Data Analyses

Subjects with posttreatment viral RNA rebound were identified based on an increase in viral RNA levels from day 5 to day 10 or day 14 (Table 1). In a subanalysis to account for on-treatment virologic responses and assess more directly the impact of removing nirmatrelvir/ritonavir antiviral pressure after an initial viral RNA decline, rebound rates were compared between nirmatrelvir/ritonavir and placebo recipients who had a virologic response on day 5. To compare rebound rates in the treatment and posttreatment periods, viral RNA rebound rates during the treatment period between day 3 and day 5, among subjects with a virologic response on day 3, were determined. A viral RNA level ≥5 $\log_{10}$ copies/mL was considered potentially predictive of positive cell culture viral infectivity.[¶]

Exploratory statistical analyses were conducted using two-sided Fisher's exact tests to provide nominal p-values, without multiplicity adjustments; $p<0.05$ was considered statistically significant. Analyses were conducted using JMP (version 16; SAS Institute). This study was reviewed by the FDA Institutional Review Board and deemed not to constitute research involving human subjects as defined in 45 CFR part 46.

[§] Viral RNA levels in nasopharyngeal samples were measured in a central laboratory (University of Washington) using the Abbott RealTime Quantitative SARS-CoV-2 assay, which had a lower limit of quantification (LLOQ) and limit of detection of 2 $\log_{10}$ copies/mL. For analysis purposes, SARS-CoV-2 RNA results that were detected, but <LLOQ, were imputed as 1.7 $\log_{10}$ copies/mL, and the results that were "Not Detected" were imputed as zero $\log_{10}$ copies/mL. In limited cases (4%–6% of visits), samples were not explicitly reported as nasopharyngeal swabs (e.g., nasal swabs).

[¶] Analysis of selected samples from EPIC-HR for cell culture infectious SARS-CoV-2 demonstrated a trend of positive infectivity for samples with viral RNA ≥5 $\log_{10}$ copies/mL (per FDA Integrated Review of NDA 217188). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/217188Orig1s000IntegratedR.pdf

TABLE 1. Definitions used to analyze SARS-CoV-2 RNA rebound in the Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients and Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients clinical trials — United States and international sites, 2021–2022

Analysis	Rationale	Parameters
Visit timepoints	SARS-CoV-2 RNA ($\log_{10}$ copies/mL) results from all protocol-specified study visits considered Visit windows based on protocol statistical analysis plans, one result per visit window	Day 1/Baseline (visit window: day −2 to 1), day 3 (day 2 to 4), day 5/End-of-treatment (day 4 to 6), day 10 (day 7 to 11), and day 14 (day 12 to 17) Results collected on day 4 assigned day 3 or day 5 based on planned study visit Day 1/Baseline = start of nirmatrelvir/ritonavir or placebo dosing
Posttreatment viral RNA rebound overall	Sensitive parameters to identify subjects with any evidence of an increase in SARS-CoV-2 RNA level in the posttreatment period	Day 10 rebound: day 5 RNA <LLOQ and day 10 RNA ≥LLOQ, or day 5 RNA ≥LLOQ and day 10 RNA ≥0.5 $\log_{10}$ copies/mL increase from day 5 Day 14 rebound: day 5 RNA <LLOQ and day 14 RNA ≥LLOQ, or day 5 RNA ≥LLOQ and day 14 RNA ≥0.5 $\log_{10}$ copies/mL increase from day 5 Day 10 or day 14 rebound: met either (or both) of the definitions above
Posttreatment viral RNA rebound among day 5 virologic responders	Subanalysis of posttreatment viral RNA rebound overall To account for greater impact of nirmatrelvir/ritonavir on viral RNA levels during treatment, and compare rebound rates between nirmatrelvir/ritonavir and placebo recipients with similar virologic responses through day 5	Day 5 virologic response: day 5 RNA <LLOQ, or ≥1 $\log_{10}$ copies/mL RNA decrease from baseline to day 5 and Day 10 or day 14 rebound (defined above)
Posttreatment viral RNA rebound with potentially infectious virus	Identification of posttreatment rebound with high viral RNA level at time of rebound potentially associated with cell culture infectivity	Day 10 or day 14 ≥5 $\log_{10}$ copies/mL rebound: day 10 or day 14 rebound (defined above), and day 10 or day 14 viral RNA ≥5 $\log_{10}$ copies/mL
Viral RNA rebound during treatment period	To identify nirmatrelvir/ritonavir or placebo recipients with a viral RNA response followed by rebound during the treatment period To compare rates of rebound in the treatment and posttreatment periods	Day 3 virologic response: day 3 RNA <LLOQ, or ≥1 $\log_{10}$ copies/mL RNA decrease from baseline to day 3 and Day 3 to day 5 rebound: day 3 RNA <LLOQ and day 5 RNA ≥LLOQ, or day 3 RNA ≥LLOQ and day 5 RNA ≥0.5 $\log_{10}$ copies/mL increase from day 3
Cross-sectional viral RNA levels	To identify subjects with low viral RNA levels, or with high viral RNA levels potentially associated with cell culture infectivity, at individual timepoints irrespective of rebound	Viral RNA <LLOQ at indicated visit Viral RNA ≥5 $\log_{10}$ copies/mL at indicated visit

Abbreviation: LLOQ = lower limit of quantification.

Results

SARS-CoV-2 RNA Rebound Rates

Demographic characteristics and predominant SARS-CoV-2 variants were similar between nirmatrelvir/ritonavir and placebo recipients within clinical trial EPIC-HR and within the 2021/pre-Omicron and 2022/Omicron periods of EPIC-SR (Supplementary Table, https://stacks.cdc.gov/view/cdc/136166). In EPIC-HR, overall rates of posttreatment viral RNA rebound on day 10 or day 14 were numerically higher in nirmatrelvir/ritonavir recipients than in placebo recipients, with most cases of observed rebound occurring at day 10 (Table 2). At either posttreatment timepoint (i.e., day 10 or day 14), viral RNA rebound rates in nirmatrelvir/ritonavir and placebo recipients were 8.3% (77 of 925) and 5.7% (53 of 922), respectively (p = 0.036). When the analysis was restricted to subjects with a virologic response on day 5, the difference between day 10 or day 14 rebound rates among nirmatrelvir/ritonavir and placebo recipients narrowed, and the rates were no longer significantly different (8.1% [69 of 849] and 6.5% [50 of 772], respectively; p = 0.22). In EPIC-SR, viral RNA rebound rates by either analysis approach were not significantly different between nirmatrelvir/ritonavir and placebo recipients across both enrollment periods.

TABLE 2. SARS-CoV-2 RNA rebound and responses in Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients and Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients clinical trials, by enrollment period — United States and international sites, 2021–2022

Responses	% (no./No.) Nirmatrelvir/ Ritonavir	Placebo	p-value*
EPIC-HR, total no.†	**1,038**	**1,053**	—
Posttreatment viral RNA rebound			
Day 10	6.6 (57/865)	4.7 (40/856)	0.095
Day 14	2.6 (23/884)	1.9 (17/893)	0.34
Day 10 or day 14	8.3 (77/925)	5.7 (53/922)	0.036
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	2.8 (26/925)	1.7 (16/922)	0.16
Among day 5 virologic responders			
Day 10 or day 14	8.1 (69/849)	6.5 (50/772)	0.22
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	2.6 (22/849)	1.9 (15/772)	0.41
Viral RNA rebound during treatment period			
Days 3–5§	11.3 (77/680)	12.5 (74/594)	0.54
Viral RNA <LLOQ			
Day 3	35.1 (340/970)	32.8 (321/980)	0.29
Day 5/End-of-treatment	47.8 (447/936)	44.1 (415/942)	0.12
Day 10	76.1 (702/922)	68.9 (622/903)	<0.001
Day 14	88.6 (835/942)	86.0 (815/948)	0.084
Viral RNA ≥5 $\log_{10}$ copies/mL			
Day 3	29.1 (282/970)	38.9 (381/980)	<0.001
Day 5/End-of-treatment	10.3 (96/936)	23.9 (225/942)	<0.001
Day 10	3.7 (34/922)	5.3 (48/903)	0.11
Day 14	1.0 (9/942)	1.5 (14/948)	0.40
EPIC-SR 2021/pre-Omicron period, total no.	**540**	**528**	—
Posttreatment viral RNA rebound			
Day 10	5.9 (28/477)	5.4 (25/467)	0.78
Day 14	2.4 (12/492)	1.5 (7/472)	0.36
Day 10 or day 14	6.6 (33/502)	6.2 (30/486)	0.90
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	3.4 (17/502)	1.9 (9/486)	0.16
Among day 5 virologic responders			
Day 10 or day 14	6.4 (31/482)	6.4 (27/421)	1.0
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	3.3 (16/482)	1.7 (7/421)	0.14
Viral RNA <LLOQ			
Day 3	31.5 (164/520)	30.3 (154/509)	0.69
Day 5/End-of-treatment	49.3 (251/509)	40.4 (199/492)	0.005
Day 10	77.3 (382/494)	72.1 (352/488)	0.066
Day 14	89.2 (456/511)	85.7 (425/496)	0.11
Viral RNA ≥5 $\log_{10}$ copies/mL			
Day 3	29.0 (151/520)	39.7 (202/509)	<0.001
Day 5/End-of-treatment	9.0 (46/509)	22.2 (109/492)	<0.001
Day 10	3.4 (17/494)	3.9 (19/488)	0.74
Day 14	1.8 (9/511)	1.4 (7/496)	0.80
EPIC-SR 2022/Omicron period, total no.	**114**	**106**	—
Posttreatment viral RNA rebound			
Day 10	6.0 (6/100)	4.0 (4/100)	0.75
Day 14	3.8 (4/105)	2.0 (2/102)	0.68
Day 10 or day 14	8.6 (9/105)	5.8 (6/103)	0.59
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	1.9 (2/105)	1.9 (2/103)	1.0
Among day 5 virologic responders			
Day 10 or day 14	8.4 (8/95)	5.9 (5/85)	0.57
Day 10 or day 14 ≥5 $\log_{10}$ copies/mL	1.1 (1/95)	2.4 (2/85)	0.60
Viral RNA <LLOQ			
Day 3	32.4 (35/108)	19.0 (20/105)	0.029
Day 5/End-of-treatment	56.6 (60/106)	36.5 (38/104)	0.004
Day 10	86.4 (89/103)	77.5 (79/102)	0.11
Day 14	91.7 (99/108)	90.4 (94/104)	0.81
Viral RNA ≥5 $\log_{10}$ copies/mL			
Day 3	38.0 (41/108)	52.4 (55/105)	0.04
Day 5/End-of-treatment	9.4 (10/106)	20.2 (21/104)	0.03
Day 10	1.9 (2/103)	2.9 (3/102)	0.68
Day 14	0.9 (1/108)	— (0/104)	1.0

Abbreviations: EPIC-HR = Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients; EPIC-SR = Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients; LLOQ = lower limit of quantification.

* Nominal p-values shown based on two-sided Fisher's exact test, unadjusted for multiplicity.

† Total number of randomized subjects who took ≥1 dose of study intervention and had initial onset of COVID-19 signs and symptoms within 5 days of randomization. Denominators for viral RNA rebound and response rates are based on the number of subjects with data at the relevant visit timepoints.

§ Assessed in subjects with a virologic response on day 3.

For both trials, when considering a higher threshold for viral RNA rebound (requiring a day 10 or day 14 viral RNA ≥5 $\log_{10}$ copies/mL, associated with cell culture infectivity) viral RNA rebound rates remained similar for nirmatrelvir/ritonavir and placebo recipients. Further, no consistent differences in viral RNA patterns were observed between nirmatrelvir/ritonavir and placebo recipients with viral RNA rebound (Supplementary Figure, https://stacks.cdc.gov/view/cdc/136167). In the analysis of EPIC-HR data, viral RNA rebound during the treatment period was frequently observed, with rates numerically higher than posttreatment rebound rates (Table 2).

Hospitalization, Immunosuppression, and Antiviral Resistance Among Study Subjects

Viral RNA rebound was generally not associated with COVID-19–related hospitalization or death from any cause through day 28. Among subjects in EPIC-HR with viral RNA rebound, 1.3% (one of 77) of nirmatrelvir/ritonavir recipients and 5.7% (three of 53) of placebo recipients had a COVID-19–related hospitalization, without death, comparable with overall hospitalization rates in the trial.** In EPIC-SR, three subjects (one nirmatrelvir/ritonavir and two placebo recipients; 2021/pre-Omicron period) had viral RNA rebound and a COVID-19–related hospitalization. Analyses of viral RNA levels showed no consistent temporal relationship between viral RNA rebound and hospitalization (Figure). Viral RNA rebound was not associated with immunosuppression; however, only 13 subjects in EPIC-HR were immunosuppressed, including six nirmatrelvir/ritonavir recipients (none with rebound) and seven placebo recipients (one with rebound).

Among 59 nirmatrelvir/ritonavir recipients in EPIC-HR with viral RNA rebound for whom viral sequencing data were available, two (3%) had a treatment-emergent, nirmatrelvir resistance–associated substitution detected in M^{pro} on day 10 (Figure). Neither subject was immunosuppressed at baseline or hospitalized because of COVID-19.

SARS-CoV-2 RNA Levels at Individual Timepoints

Across both trials, for all subjects irrespective of viral RNA rebound by any definition, a similar or higher percentage of nirmatrelvir/ritonavir recipients than placebo recipients had viral RNA below the lower limit of quantification (LLOQ) at all postbaseline visits, indicating nirmatrelvir/ritonavir treatment was not associated with delayed viral clearance overall (Table 2). Likewise, a similar or lower percentage of nirmatrelvir/ritonavir recipients than placebo recipients had viral RNA ≥5 $\log_{10}$ copies/mL at all postbaseline visits.

Discussion

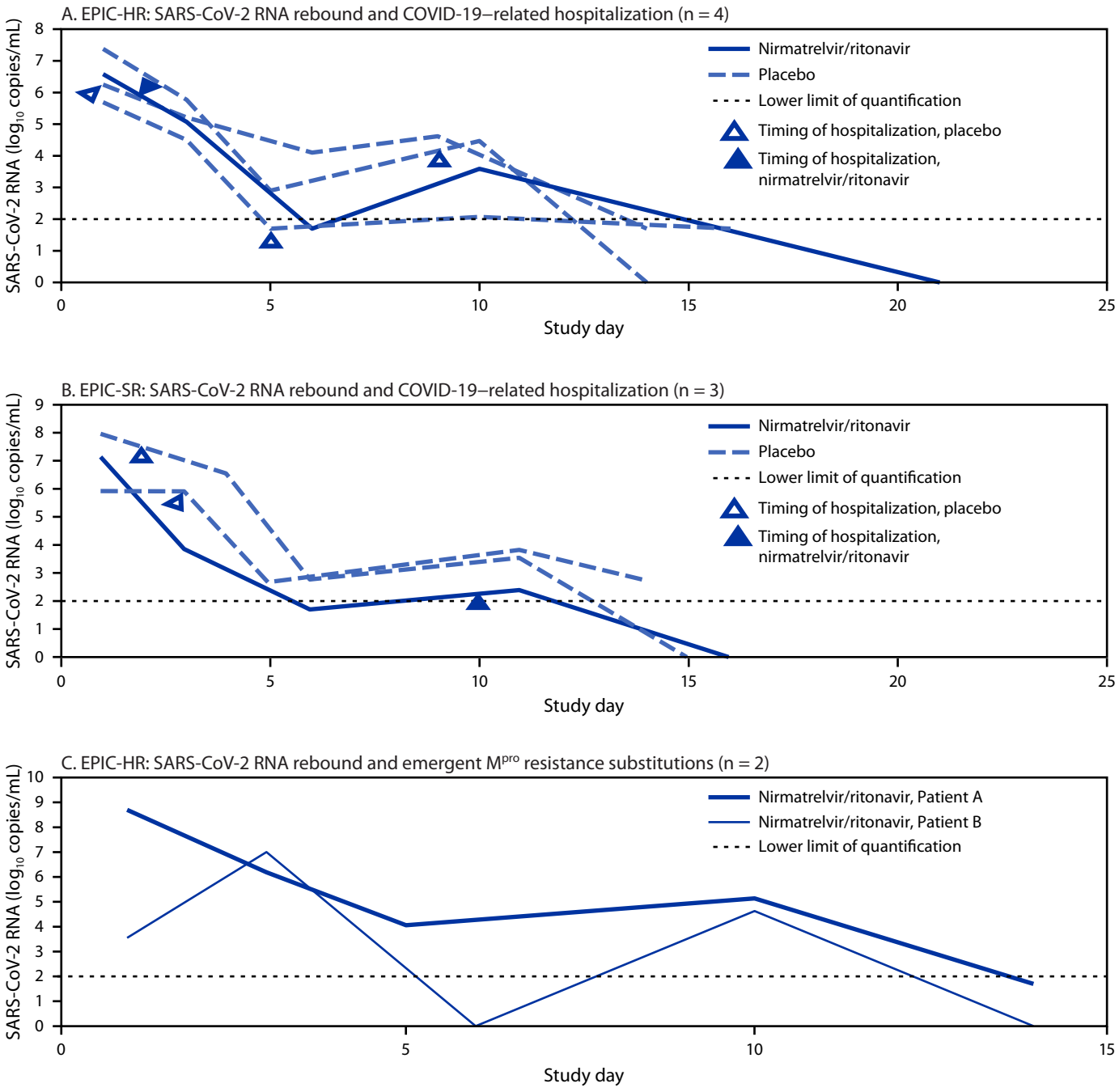
Analyses of nasopharyngeal SARS-CoV-2 RNA levels from two randomized, double-blind, placebo-controlled trials that collectively enrolled approximately 3,000 subjects did not identify a consistent association between virologic rebound and nirmatrelvir/ritonavir treatment. One analysis from EPIC-HR indicated a statistically significantly higher rate of viral RNA rebound overall in nirmatrelvir/ritonavir recipients compared with that in placebo recipients (8.3% versus 5.7%, respectively; $p = 0.036$), but this analysis did not account for differences in viral RNA declines while on treatment. Other analyses from EPIC-HR and EPIC-SR did not show significant differences but did show modestly (nonsignificant) higher viral RNA rebound rates in nirmatrelvir/ritonavir recipients. Collectively, these data indicate that viral RNA rebound might be more common with nirmatrelvir/ritonavir treatment. However, viral RNA rebound was not restricted to nirmatrelvir/ritonavir recipients, and rebound rates were generally similar to those in placebo recipients across all analyses. Further, regardless of virologic rebound, nirmatrelvir/ritonavir treatment did not appear to contribute to delayed viral clearance overall, as nirmatrelvir/ritonavir recipients were more likely than were placebo recipients to have viral RNA levels below the LLOQ at all study visits. Viral RNA rebound during the treatment period between day 3 and day 5 was frequently observed, indicating that viral RNA rebound after treatment cannot definitively be attributed to virologic relapse caused by drug clearance and loss of antiviral activity. Rather, at least some cases of posttreatment rebound likely reflect natural variability in virus production, periods of shedding of viral components related to host factors, or technical variability in sampling via topical swab, any of which might also explain the occurrence of rebound in placebo recipients. Although nirmatrelvir drug resistance was not typically associated with viral RNA rebound, consistent with previous studies, two nirmatrelvir/ritonavir-treated subjects in EPIC-HR had virus with nirmatrelvir resistance-associated substitutions at the time of rebound. Genomic databases should continue to be monitored for the emergence or spread of nirmatrelvir-resistant SARS-CoV-2 variants.

Limitations

The findings in this report are subject to at least four limitations. First, rebound rates are highly dependent on analysis definitions and the types, frequency, and timing of sample collection. The described analyses used sensitive parameters

** In the EPIC-HR modified intent-to-treat-2 population, which included all randomized subjects who took ≥1 dose of study intervention and were dosed ≤5 days of symptom onset, 1.0% (10 of 1,038) of nirmatrelvir/ritonavir recipients and 6.2% (65 of 1,053) of placebo recipients experienced COVID-19–related hospitalization through day 28 (per FDA Integrated Review of NDA 217188). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/217188Orig1s000IntegratedR.pdf

FIGURE. SARS-CoV-2 RNA shedding levels for subjects with viral RNA rebound who experienced COVID-19–related hospitalization any time through day 28 in the Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients (A) and Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients (B) clinical trials, and two subjects with evidence of treatment-emergent nirmatrelvir resistance–associated substitutions detected in the viral main protease gene (C)* — United States and international sites, 2021–2022



Abbreviations: EPIC-HR = Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients; EPIC-SR = Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients; M^{pro} = viral main protease gene.
* On study day 10, 23.9% of patient A's M^{pro} sequence reads had a T304I substitution, and 23.6% of patient B's M^{pro} sequence reads had an E166V substitution.

Summary

What is already known about this topic?

Nirmatrelvir/ritonavir (Paxlovid) is recommended for treatment of mild-to-moderate COVID-19 in adults at high risk for progression to severe COVID-19. Rebound in SARS-CoV-2 shedding or COVID-19 signs and symptoms has been described after nirmatrelvir/ritonavir treatment, although the drug's direct contribution to rebound remains unclear.

What is added by this report?

Similar SARS-CoV-2 RNA rebound rates were observed in nirmatrelvir/ritonavir and placebo recipients in two randomized, double-blind, clinical trials. Virologic rebound after nirmatrelvir/ritonavir treatment was not associated with COVID-19–related hospitalization or death.

What are the implications for public health practice?

SARS-CoV-2 RNA rebound can occur with or without nirmatrelvir/ritonavir treatment, supporting the Food and Drug Administration's determination of safety and efficacy of nirmatrelvir/ritonavir in eligible patients at high risk for severe COVID-19.

(within limitations of available sampling timepoints) to identify viral RNA rebound, and unlike a previous analysis from EPIC-HR (*9*), rebound only at a single posttreatment timepoint was sufficient to identify subjects as having viral RNA rebound. However, some rebound events were likely missed between study visits or after day 14. Given that viral RNA rebound rates in nirmatrelvir/ritonavir and placebo recipients were similar and progressively declined on days 3–5, 10, and 14 (and further considering the short half-life of nirmatrelvir), a significant association between nirmatrelvir/ritonavir and rebound only when considering intermediate timepoints or only after day 14 is considered unlikely, although this possibility cannot be excluded. Second, EPIC-HR included only 13 subjects with immunosuppression, in whom posttreatment COVID-19 rebound might be more common or clinically significant. Third, subjects at high risk infected with SARS-CoV-2 Omicron or subsequent sublineages were not represented because of the availability of nirmatrelvir/ritonavir through Emergency Use Authorization after Omicron emergence. Nevertheless, the analyses identified both nirmatrelvir/ritonavir and placebo recipients with viral RNA rebound within the EPIC-SR 2022/Omicron population. Finally, analyses focused on objective virologic measures and severe disease outcomes as reflected by COVID-19–related hospitalization or death, and available data did not permit a detailed investigation into less severe disease signs and symptoms.

Implications for Public Health Practice

Data from randomized, double-blind clinical trials demonstrated similar rates of SARS-CoV-2 RNA rebound in nirmatrelvir/ritonavir and placebo recipients. These findings support FDA's determination of safety and efficacy of nirmatrelvir/ritonavir in eligible patients at high risk for severe COVID-19.

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Coverage with Influenza, Respiratory Syncytial Virus, and Updated COVID-19 Vaccines Among Nursing Home Residents — National Healthcare Safety Network, United States, December 2023

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Abstract

Nursing home residents are at risk for becoming infected with and experiencing severe complications from respiratory viruses, including SARS-CoV-2, influenza, and respiratory syncytial virus (RSV). Fall 2023 is the first season during which vaccines are simultaneously available to protect older adults in the United States against all three of these respiratory viruses. Nursing homes are required to report COVID-19 vaccination coverage and can voluntarily report influenza and RSV vaccination coverage among residents to CDC's National Healthcare Safety Network. The purpose of this study was to assess COVID-19, influenza, and RSV vaccination coverage among nursing home residents during the current 2023–24 respiratory virus season. As of December 10, 2023, 33.1% of nursing home residents were up to date with vaccination against COVID-19. Among residents at 20.2% and 19.4% of facilities that elected to report, coverage with influenza and RSV vaccines was 72.0% and 9.8%, respectively. Vaccination varied by U.S. Department of Health and Human Services region, social vulnerability index level, and facility size. There is an urgent need to protect nursing home residents against severe outcomes of respiratory illnesses by continuing efforts to increase vaccination against COVID-19 and influenza and discussing vaccination against RSV with eligible residents during the ongoing 2023–24 respiratory virus season.

Introduction

Nursing home residents are at risk for becoming infected with and experiencing severe complications from respiratory viruses, including SARS-CoV-2 (*1*), influenza (*2*), and respiratory syncytial virus (RSV) (*3*). In 2023, the Food and Drug Administration approved the first two RSV vaccines for adults aged ≥60 years (*4*), making the 2023–24 respiratory virus season the first in which vaccines against SARS-CoV-2, influenza, and RSV are simultaneously available in the United States. CDC recommends that all persons aged ≥6 months receive an updated (2023–2024) COVID-19 vaccine dose* and a 2023–24 seasonal influenza vaccine.† Among adults aged ≥60 years, CDC recommends RSV vaccine on the basis of shared clinical decision-making; residence in a nursing home is an important risk factor for RSV to consider in such decision-making (*4*). Since 2021, the Centers for Medicare & Medicaid Services (CMS) has required nursing homes to report weekly aggregate COVID-19 vaccination coverage among residents to CDC's National Healthcare Safety Network (NHSN).§ Since October 21, 2023, nursing homes can also voluntarily report weekly, aggregate resident influenza and RSV vaccination coverage data to NHSN.¶ The purpose of this study was to assess COVID-19, influenza, and RSV vaccination coverage among nursing home residents during the ongoing 2023–24 respiratory virus season.

Methods

Data Collection

Nursing homes report COVID-19, influenza, and RSV vaccination coverage among residents who occupied a bed at the facility ≥1 day during the week of data collection. For each vaccine, nursing homes also report the number of residents who 1) received the most recently recommended vaccine, 2) had a medical contraindication to the vaccine, 3) declined the vaccine, or 4) had other or unknown vaccination status. NHSN defined up-to-date COVID-19 vaccination as the receipt of a 2023–2024 updated COVID-19 vaccine.**

Data Analysis

Data reported from CMS-certified nursing homes for the week of December 10, 2023, (or the preceding week if data for December 10, 2023, were not available) were used for analysis.†† Because reporting of influenza and RSV vaccination

* https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html
† https://www.cdc.gov/flu/prevent/vaccinations.htm

§ https://www.federalregister.gov/documents/2021/05/13/2021-10122/medicare-and-medicaid-programs-covid-19-vaccine-requirements-for-long-term-care-ltc-facilities-and
¶ https://www.cdc.gov/nhsn/pdfs/covid19/ltcf/vax-rpv-protocol-ltc-residents-oct-2023-508.pdf
** NHSN defines up-to-date vaccination for surveillance purposes at the start of each quarter. https://www.cdc.gov/nhsn/pdfs/hps/covidvax/UpToDateGuidance-508.pdf
†† Facilities were included if they were actively enrolled in the NHSN Long-Term Care Component and had ever reported nonzero vaccination denominator data. Facilities were excluded from the coverage estimates if they reported zero residents or did not report data for either the week of December 10, 2023, or the week of December 3, 2023 (467 facilities were excluded for COVID-19; 12,067 were excluded for influenza; and 12,174 were excluded for RSV).

coverage is voluntary, representativeness of facilities reporting these data was assessed by comparing important facility and county characteristics among reporting facilities and all facilities. Coverage estimates (percentage of residents vaccinated) for COVID-19, influenza, and RSV vaccine and 95% CIs were calculated using Poisson regression models. Residents reported to have a medical contraindication to a vaccine were subtracted from the corresponding denominator. For each vaccine, coverage was stratified by U.S. Department of Health and Human Services (HHS) region,[§§] county-level social vulnerability index (SVI) tertile,[¶¶] and facility size tertile.[***] All analyses were conducted using SAS (version 9.4; SAS Institute). Nonoverlapping 95% CIs were considered to represent statistically significant differences ($\alpha = 0.05$). This activity was reviewed by CDC, deemed not research, and conducted consistent with applicable federal law and CDC policy.[†††]

Results

Representativeness of Voluntary Influenza and RSV Reporters

Coverage with influenza and RSV as of December 10, 2023, was voluntarily reported by 3,046 (20.2%) and 2,939 (19.4%) of 15,113 CMS-certified nursing homes, respectively. Among these, the distributions of facilities by HHS region, SVI tertile, and facility size were comparable to distributions among all CMS-certified nursing homes enrolled in NHSN (Table).

Updated (2023–2024) COVID-19 Vaccination Coverage

COVID-19 vaccination coverage was reported by 14,646 (96.9%) nursing homes for the week of December 10, 2023. A total of 33.1% of nursing home residents were up to date with COVID-19 vaccination, ranging from 22.5% in HHS Region 6 to 42.4% and 42.9% in HHS regions 2 and 8, respectively. Up-to-date vaccination against COVID-19 varied by SVI tertile, with highest coverage (38.5%) in the least socially vulnerable counties and lowest coverage (29.1%) in the most vulnerable counties. Updated COVID-19 vaccination was higher in small facilities (37.3%) than in medium (32.3%) and large facilities (32.2%).

Influenza Vaccination Coverage

Among the 20.2% of facilities that voluntarily reported influenza vaccination for the week of December 10, 2023, 72.0% of residents had received an influenza vaccine. Coverage ranged from 64.3% and 64.8% in HHS regions 10 and 4, respectively, to 79.9% in HHS Region 8. Influenza vaccination coverage was highest in the least socially vulnerable counties (73.7%) and lowest in the most socially vulnerable counties (70.9%). Influenza vaccination was higher in small facilities (77.4%) than in medium (72.2%) and large facilities (69.8%).

RSV Vaccination Coverage

Among the 19.4% of nursing homes that voluntarily reported RSV vaccination data for the week of December 10, 2023, 9.8% of residents had received an RSV vaccine. Coverage ranged from 5.9% and 7.1% in HHS regions 4 and 2, respectively, to 15.5% and 24.8% in HHS regions 7 and 8, respectively. RSV vaccination coverage was highest in the least socially vulnerable counties (10.7%) and lowest in the most socially vulnerable counties (8.7%); coverage was highest in small facilities (15.3%) and lowest in large facilities (8.0%).

Overall Vaccination Coverage by Region

For all three vaccines, coverage was highest overall in HHS Region 8. Specifically, North Dakota and South Dakota consistently reported high coverage with all three vaccines (Figure).

Discussion

Although vaccination against SARS-CoV-2, influenza, and RSV reduces severe disease from these respiratory viruses in populations at high risk,[§§§] coverage with each of the three vaccines, especially updated (2023–2024) COVID-19 and RSV vaccines, was low among nursing home residents. Compared with COVID-19 vaccination coverage among adults aged ≥65 years and RSV vaccination coverage among adults aged ≥60 years reported by the National Immunization Survey (NIS) Adult COVID-19 Module (37.4% and 17.0%, respectively), COVID-19 and RSV vaccination coverage reported to NHSN was lower among nursing home residents (33.1% and 9.8%, respectively). In contrast, influenza vaccination coverage among nursing home residents (72.0%) was slightly higher than that among the general adult population aged ≥65 years (69.3%) (*5*). Although data from NHSN and NIS cannot be directly compared because of different methodology and populations, these directional differences deserve further exploration.

Vaccine fatigue, defined as inaction toward vaccine information or instruction attributable to "perceived burden and burnout" (*6*), inaccurate health information, and vaccine

[§§] https://www.hhs.gov/about/agencies/iea/regional-offices/index.html

[¶¶] SVI considers socioeconomic status, household characteristics, race, ethnicity, housing type, and transportation. Counties in a lower SVI tertile are less socially vulnerable than are those in an upper SVI tertile. SVI categories were based on the tertile distribution of the SVI of the counties where the facilities are located (low: ≤0.38; medium: >0.38 to <0.66; and high: ≥0.66). Fifty-five facilities were excluded because they were located in counties that did not have an SVI score assigned. https://www.atsdr.cdc.gov/placeandhealth/svi/index.html

[***] Facility size category was based on the tertile distribution of the total number of residents per facility (small: ≤58 residents; medium: 59–94 residents; and large: ≥95 residents).

[†††] 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/respiratory-viruses/tools-resources/health-care-providers.html

TABLE. Estimates* of coverage with influenza, respiratory syncytial virus, and updated COVID-19 vaccination among nursing home residents — National Healthcare Safety Network, United States, December 2023†

Characteristic	Total no. of facilities § (column %)	Updated (2023–2024) COVID-19 vaccine			Influenza vaccine			RSV vaccine		
		Facilities reporting, no. (row %)	Total no. of residents	Coverage, % (95% CI)	Facilities reporting, no. (row %)	Total no. of residents	Coverage, % (95% CI)	Facilities reporting, no. (row %)	Total no. of residents	Coverage, % (95% CI)
Total	**15,113 (100.0)**	**14,646 (96.9)**	**1,240,163**	**33.1 (33.0–33.2)**	**3,046 (20.2)**	**247,280**	**72.0 (71.6–72.3)**	**2,939 (19.4)**	**238,449**	**9.8 (9.6–9.9)**
HHS region¶										
1	**826 (5.5)**	807 (5.5)	**75,349**	38.3 (37.8–38.7)	166 (5.4)	**13,421**	77.4 (75.9–78.9)	160 (5.4)	**13,055**	8.2 (7.7–8.7)
2	**969 (6.4)**	943 (6.4)	**136,743**	42.4 (42.0–42.7)	256 (8.4)	**33,738**	74.8 (73.8–75.7)	244 (8.3)	**31,891**	7.1 (6.9–7.4)
3	**1,383 (9.2)**	1,346 (9.2)	**135,526**	36.1 (35.8–36.4)	260 (8.5)	**24,557**	74.3 (73.2–75.4)	249 (8.5)	**23,593**	10.0 (9.6–10.4)
4	**2,682 (17.7)**	2,613 (17.8)	**241,100**	27.5 (27.3–27.7)	612 (20.1)	**55,566**	64.8 (64.2–65.5)	591 (20.1)	**53,802**	5.9 (5.7–6.1)
5	**3,285 (21.7)**	3,188 (21.8)	**240,295**	34.7 (34.5–35.0)	482 (15.8)	**34,473**	72.0 (71.1–72.9)	461 (15.7)	**33,141**	12.7 (12.3–13.1)
6	**2,050 (13.6)**	1,998 (13.6)	**148,859**	22.5 (22.3–22.8)	336 (11.0)	**23,244**	74.3 (73.2–75.4)	328 (11.2)	**22,483**	9.2 (8.8–9.6)
7	**1,430 (9.5)**	1,372 (9.4)	**81,667**	38.9 (38.4–39.3)	295 (9.7)	**16,292**	77.4 (76.1–78.8)	291 (9.9)	**15,994**	15.5 (14.9–16.1)
8	**592 (3.9)**	559 (3.8)	**34,722**	42.9 (42.2–43.6)	125 (4.1)	**7,235**	79.9 (77.9–82.0)	120 (4.1)	**7,039**	24.8 (23.7–26.0)
9	**1,469 (9.7)**	1,401 (9.6)	**119,888**	29.5 (29.2–29.8)	417 (13.7)	**33,181**	72.3 (71.4–73.2)	400 (13.6)	**31,932**	10.1 (9.8–10.5)
10	**427 (2.8)**	419 (2.9)	**26,014**	34.7 (34.0–35.4)	97 (3.2)	**5,573**	64.3 (62.2–66.4)	95 (3.2)	**5,519**	11.7 (10.9–12.7)
SVI**										
Low	**5,022 (33.4)**	4,882 (33.3)	**379,417**	38.5 (38.3–38.7)	963 (31.6)	**73,512**	73.7 (73.0–74.3)	930 (31.6)	**70,759**	10.7 (10.5–11.0)
Medium	**5,052 (33.6)**	4,890 (33.4)	**434,613**	32.3 (32.1–32.5)	968 (31.8)	**83,342**	71.6 (71.0–72.2)	932 (31.7)	**80,244**	10.0 (9.7–10.2)
High	**4,984 (33.1)**	4,823 (32.9)	**422,627**	29.1 (28.9–29.2)	1,098 (36.0)	**89,609**	70.9 (70.4–71.5)	1,060 (36.1)	**86,629**	8.7 (8.5–8.9)
Facility size††										
Small	**5,072 (33.6)**	4,810 (32.8)	**197,427**	37.3 (37.0–37.5)	1,156 (38.0)	**46,674**	77.4 (76.6–78.2)	1,116 (38.0)	**45,063**	15.3 (15.0–15.7)
Medium	**5,098 (33.7)**	4,996 (34.1)	**382,940**	32.3 (32.1–32.5)	985 (32.3)	**75,460**	72.2 (71.6–72.8)	953 (32.4)	**73,006**	9.3 (9.1–9.5)
Large	**4,943 (32.7)**	4,840 (33.0)	**659,796**	32.2 (32.1–32.4)	905 (29.7)	**125,146**	69.8 (69.3–70.2)	870 (29.6)	**120,380**	8.0 (7.8–8.1)

Abbreviations: HHS = U.S. Department of Health and Human Services; RSV = respiratory syncytial virus; SVI = social vulnerability index.

* Estimates of coverage (percentage of residents vaccinated) with influenza, RSV, and updated (2023–2024) COVID vaccines and 95% CIs were calculated using Poisson regression models. Residents who reported having a medical contraindication to each vaccine were subtracted from the corresponding denominator. Nonoverlapping 95% CIs were considered to represent statistically significant differences (α = 0.05).

† Data reported from nursing homes certified by the Centers for Medicare & Medicaid Services for the week of December 10, 2023 (or the preceding week if data for December 10, 2023, were not available) were used for analysis.

§ Facilities were included if they were actively enrolled in the National Healthcare Safety Network Long-Term Care Component and had ever reported nonzero vaccination denominator data. Facilities were excluded from the coverage estimates if they reported zero residents or did not report data for either the week of December 10, 2023, or the week of December 3, 2023 (467 facilities were excluded for COVID-19; 12,067 were excluded for influenza; and 12,174 were excluded for RSV).

¶ https://www.hhs.gov/about/agencies/iea/regional-offices/index.html

** SVI categories are based on the tertile distribution of the SVI of the counties where the facilities are located (low: ≤0.38; medium: >0.38–<0.66; and high: ≥0.66). Fifty-five facilities are located in counties that have no assigned SVI score (COVID-19: 51 facilities; influenza: 17 facilities; and RSV: 17 facilities). https://www.atsdr.cdc.gov/placeandhealth/svi/index.html

†† Facility size category is based on the tertile distribution of the total number of residents per facility (small: ≤58 residents; medium: 59–94 residents; and large: ≥95 residents).

hesitancy (*7*) contribute to lack of vaccine demand, especially in areas with a high SVI (*8*). For all three vaccines, coverage among nursing home residents was lowest in the most socially vulnerable counties. Lower coverage in areas with higher social vulnerability might be related to challenges to vaccine access and cost and payment barriers associated with COVID-19 vaccine commercialization.¶¶¶

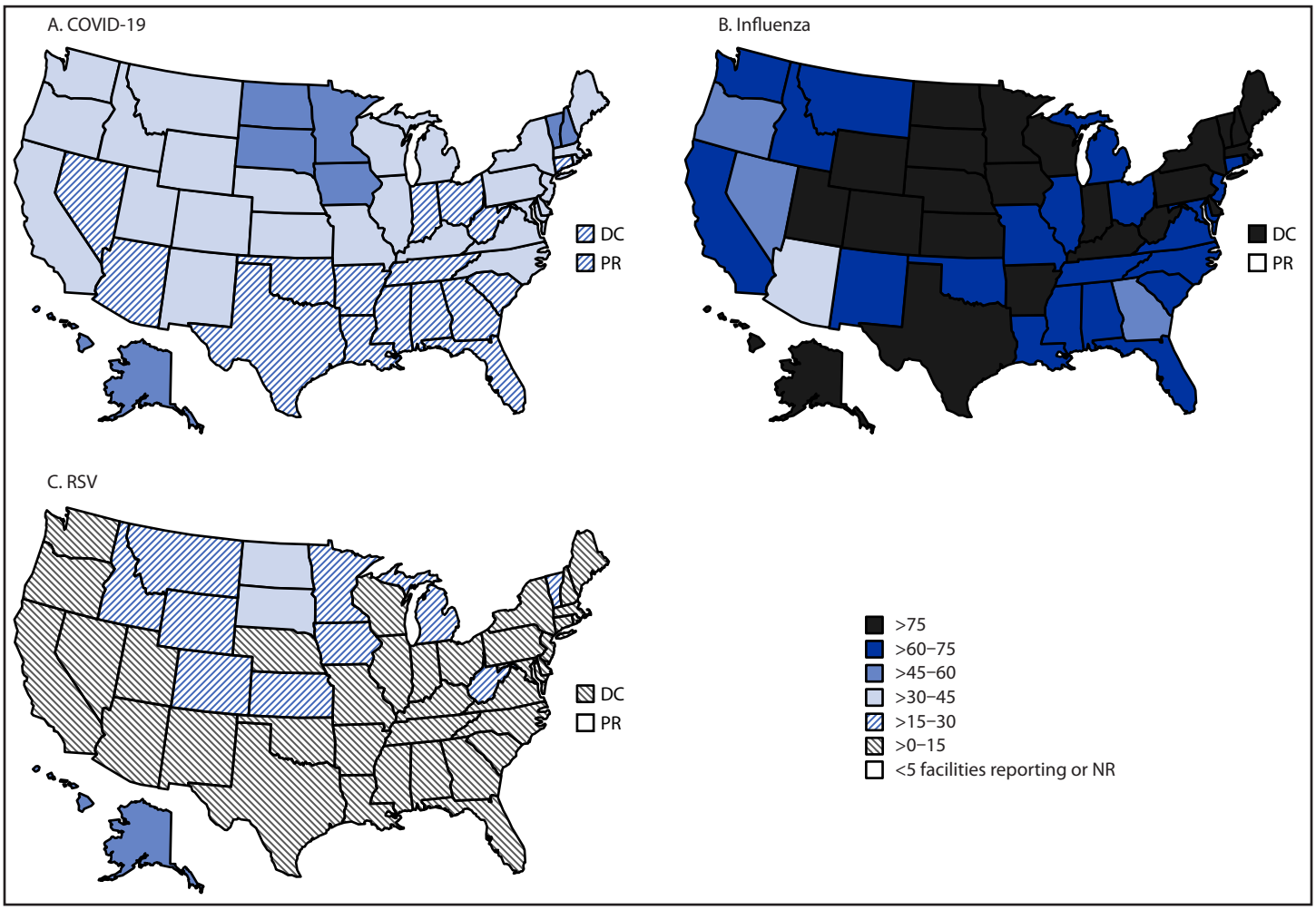
The low RSV vaccination coverage relative to the other two vaccines might be driven by the relative recency of the recommendation, vaccine fatigue associated with the introduction of a fourth respiratory vaccine (in addition to influenza, COVID-19, and pneumococcal), implementation challenges with adding new vaccines, and the recommendation being 2024 shared clinical decision-making between a patient (or patient's guardian) and a health care provider (*4*). Facilities have had limited time to train providers to implement a shared clinical decision-making recommendation and develop processes and policies to support RSV vaccine administration. Nursing home staff members might also be less familiar with the risk for RSV outbreaks and severe disease among residents (*9*). Increasing awareness of RSV as a cause of disease among nursing home residents might facilitate increased coverage.

In addition, these data highlight the success that can be achieved through surveillance and coordinated public health efforts to address barriers. During the 2023–24 season, influenza vaccination coverage among nursing home residents was significantly higher than updated (2023–2024) COVID-19 vaccination and RSV vaccination coverage. Annual influenza vaccination has been universally recommended since the 2010–11 influenza season,**** and CMS requires nursing homes to educate residents about and offer both influenza and COVID-19 vaccination. Notably, coverage with all three vaccines was highest in small nursing homes, suggesting that medical directors and other providers at these small facilities

¶¶¶ https://www.healthaffairs.org/content/forefront/commercialization-covid-19-vaccines-raises-equity-concerns

**** https://www.cdc.gov/flu/professionals/vaccination/vax-summary.htm

FIGURE. Estimates* of coverage with updated (2023–2024) COVID-19 vaccination (A), influenza vaccination (B), and RSV vaccination (C) among nursing home residents, by U.S. jurisdiction — National Healthcare Safety Network, United States, December 2023†



Abbreviations: DC = District of Columbia; NR = not reported; PR = Puerto Rico; RSV = respiratory syncytial virus.

* Estimates of coverage (percentage of residents vaccinated) with influenza, RSV, and updated (2023–2024) COVID-19 vaccines were calculated using Poisson regression models. Residents who reported having a medical contraindication to each vaccine were subtracted from the corresponding denominator.

† Data reported from nursing homes certified by the Centers for Medicare & Medicaid Services for the week of December 10, 2023, (or the preceding week if data for December 10, 2023, were not available) were used for analysis. Facilities were excluded from the coverage estimates if they reported zero residents or did not report data for either the week of December 10, 2023, or the week of December 3, 2023 (467 facilities were excluded for COVID-19; 12,067 were excluded for influenza; and 12,174 were excluded for RSV).

with lower patient-to-provider ratios might be best able to build trust with residents and families and mitigate barriers to vaccination coverage. HHS Region 8, driven largely by North Dakota and South Dakota, achieved relatively high coverage among nursing home residents with all three vaccinations because of robust relationships and frequent, persistent, clear communication among nursing homes, health care systems, state and local health departments, and pharmacies;†††† similar strategies might have the potential to improve vaccination coverage in other states. CDC is also engaged in efforts to increase vaccination coverage, including sharing NHSN surveillance data with state and local health departments and CMS Quality Innovation Networks-Quality Improvement Organizations to guide targeted outreach and educational efforts in nursing homes with lower vaccination coverage, contacting facilities with high coverage to learn about and promote successful strategies employed, working with national organizations that represent nursing homes to help educate staff members and residents, responding to barriers by developing a Healthcare Provider Toolkit to facilitate vaccination and conduct

†††† https://www.washingtonpost.com/opinions/2023/12/05/covid-vaccine-nursing-homes-dakota/; https://www.washingtonpost.com/opinions/2023/12/07/lessons-nursing-home-covid-vaccine/?utm_campaign=wp_follow_leana_s.+wen&utm_medium=email&utm_source=newsletter&wpisrc=nl-leanas.+wen

webinars with partners,[§§§§] collaborating with CMS leaders to communicate reported billing barriers, and collaborating with CMS Quality Innovation Networks-Quality Improvement Organizations to increase vaccine confidence and demand.

Limitations

The findings in this report are subject to at least three limitations. First, although it is mandatory for facilities to report COVID-19 vaccination coverage to NHSN, reporting of influenza and RSV vaccination coverage is optional, and the proportion of facilities reporting was low. Facilities that elected to report these data might be more likely to offer influenza or RSV vaccines. However, similarities in distribution of a small number of important facility demographics suggest that facilities voluntarily reporting these data might be representative of all facilities. Second, this analysis was conducted using aggregate, facility-level data reported to NHSN; therefore, vaccination coverage could not be directly examined by person-level covariates such as age, race, and ethnicity. Further, this limitation means that RSV vaccination coverage was calculated among all residents, not just the approximately 91% of residents aged ≥60 years (*10*). It is likely that RSV vaccination coverage among residents aged ≥60 years was higher than the overall coverage. Finally, NHSN does not collect data on the outcome of shared clinical decision-making discussions or reasons for declining vaccination.

Implications for Public Health Practice

There is an urgent need to protect nursing home residents against severe outcomes of respiratory illnesses through continuing effective strategies to increase updated COVID-19 vaccination and influenza vaccination coverage and discussing RSV vaccination as an option among nursing home residents during the ongoing 2023–24 respiratory virus season. Health care providers should counsel residents that immunizations are the most effective way to prevent severe outcomes from COVID-19, influenza, and RSV and offer recommended immunizations.[¶¶¶¶] It is important for nursing homes to collaborate with state and local health departments, federal agencies, and partners to address low vaccination coverage. Because vaccination coverage varied by vaccine type, region, SVI, and facility size, ongoing surveillance of vaccination coverage among nursing home residents remains essential to help guide timely efforts to increase vaccination in this population at high risk and address inequities.

Summary

What is already known about this topic?

Nursing home residents are vulnerable to infection with and complications from SARS-CoV-2, influenza, and respiratory syncytial virus (RSV). Vaccination reduces severe illness and death from these vaccine-preventable respiratory diseases.

What is added by this report?

As of December 10, 2023, 33% of nursing home residents were up to date with COVID-19 vaccination. Among residents at 20% and 19% of facilities that elected to report influenza and RSV vaccination coverage, respectively, 72% had received influenza vaccination, and 10% had received RSV vaccination.

What are the implications for public health practice?

There is an urgent need to protect nursing home residents against severe outcomes of respiratory illnesses by increasing vaccination against COVID-19 and influenza and discussing RSV vaccination with eligible residents.

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[§§§§] CDC developed a toolkit for health care providers to prepare their patients for the fall and winter virus season (https://www.cdc.gov/respiratory-viruses/tools-resources/health-care-providers.html). This toolkit includes a guide for talking with patients about fall and winter viruses (https://www.cdc.gov/respiratory-viruses/tools-resources/downloads/HCP-conversation-guide-508.pdf), tips to prepare practices and patients for the fall and winter viruses season (https://www.cdc.gov/respiratory-viruses/tools-resources/downloads/6-tips-prepare-fall-winter-virus-season.pdf), an overview of immunization recommendations for the 2023–24 respiratory disease season (https://www.cdc.gov/respiratory-viruses/tools-resources/downloads/respiratory-disease-at-a-glance-508.pdf), and print materials for patients (https://www.cdc.gov/respiratory-viruses/tools-resources/downloads/protect-health-your-everything-infographic.pdf; https://www.cdc.gov/respiratory-viruses/tools-resources/downloads/protect-health-your-everything-poster-11x17.pdf).

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Influenza, Updated COVID-19, and Respiratory Syncytial Virus Vaccination Coverage Among Adults — United States, Fall 2023

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Abstract

During the 2023–24 respiratory virus season, the Advisory Committee on Immunization Practices recommends influenza and COVID-19 vaccines for all persons aged ≥6 months, and respiratory syncytial virus (RSV) vaccine is recommended for persons aged ≥60 years (using shared clinical decision-making), and for pregnant persons. Data from the National Immunization Survey-Adult COVID Module, a random-digit–dialed cellular telephone survey of U.S. adults aged ≥18 years, are used to monitor influenza, COVID-19, and RSV vaccination coverage. By December 9, 2023, an estimated 42.2% and 18.3% of adults aged ≥18 years reported receiving an influenza and updated 2023–2024 COVID-19 vaccine, respectively; 17.0% of adults aged ≥60 years had received RSV vaccine. Coverage varied by demographic characteristics. Overall, approximately 27% and 41% of adults aged ≥18 years and 53% of adults aged ≥60 years reported that they definitely or probably will be vaccinated or were unsure whether they would be vaccinated against influenza, COVID-19, and RSV, respectively. Strong provider recommendations for and offers of vaccination could increase influenza, COVID-19, and RSV vaccination coverage. Immunization programs and vaccination partners are encouraged to use these data to understand vaccination patterns and attitudes toward vaccination in their jurisdictions to guide planning, implementation, strengthening, and evaluation of vaccination activities.

Introduction

Influenza, SARS-CoV-2, and respiratory syncytial virus (RSV) typically circulate in the United States during the fall through early spring each year, causing epidemics of respiratory illness, although patterns of influenza and RSV transmission shifted during the COVID-19 pandemic (*1*–*3*). Certain groups, including older adults (those aged ≥65 years), persons with chronic conditions, and racial and ethnic minority populations, have experienced disproportionate influenza-, COVID-19–, and RSV-associated morbidity and mortality (*1*–*4*). Since 2010, the Advisory Committee on Immunization Practices (ACIP) has recommended routine annual influenza vaccination for all persons aged ≥6 months who do not have contraindications (*1*). On September 12, 2023, ACIP recommended updated 2023–2024 COVID-19 vaccination for all persons aged ≥6 months to help protect against currently circulating SARS-CoV-2 variants (*2*). In June 2023, ACIP recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making, which is the first time a vaccine for prevention of RSV-associated respiratory disease has been recommended* (*3*). CDC monitors coverage with these vaccines and makes these data available during the respiratory season for use in planning vaccination activities.

Methods

Data Collection

The National Immunization Survey-Adult COVID Module (NIS-ACM) is a random-digit–dialed cellular telephone survey of adults aged ≥18 years in all 50 states, the District of Columbia, and selected local areas and U.S. territories. Data are weighted to represent the noninstitutionalized U.S. population.† The survey includes questions about receipt of COVID-19, influenza, and RSV vaccines, vaccination intent, sociodemographic characteristics, and behavioral and social drivers of COVID-19 vaccination. Respondents are asked if they have received a COVID-19 or RSV vaccine or have received an influenza vaccine since July 1, 2023, and for affirmative responses, the month and year of vaccination.§ Those reporting receipt of any COVID-19 vaccine since September 14,

* On September 22, 2023, ACIP and CDC recommended maternal Pfizer RSVpreF vaccination for pregnant persons as a one-time dose at 32–36 weeks' gestation using seasonal administration (i.e., September–January in most of the continental United States) for prevention of RSV-associated lower respiratory tract infection among infants aged <6 months. Either maternal RSVpreF vaccination during pregnancy at 32–36 weeks' gestation or nirsevimab (a human recombinant monoclonal antibody) immunization for infants aged <8 months who are born during or are entering their first RSV season is recommended, but administration of both products is not needed for most infants. (http://dx.doi.org/10.15585/mmwr.mm7241e1). Information about RSV vaccination during pregnancy and nirsevimab receipt among infants is not included in this report.

† Data were weighted to represent the noninstitutionalized U.S. population aged ≥18 years using population control totals for age group, sex, metropolitan statistical area status, education, Hispanic origin, and race. https://www.cdc.gov/vaccines/imz-managers/nis/about.html

§ Respondents reporting receipt of an influenza vaccine since July 1, 2023, are asked the month and year of first vaccination since July 1, 2023. Respondents reporting receipt of ≥1 dose of any COVID-19 vaccine are asked the month and year of most recent COVID-19 vaccination; if the reported month of vaccination is September 2023, they are further asked if they received a COVID-19 vaccine since September 14, 2023. Those reporting receiving any COVID-19 vaccine since September 14, 2023, are considered vaccinated with the updated 2023–2024 COVID-19 vaccine. Respondents reporting receipt of RSV vaccine are asked the month and year that they received the RSV vaccine.

2023, are considered to be vaccinated with the updated 2023–2024 COVID-19 vaccine, because this was the only COVID-19 vaccine authorized in the United States after that date.

Data Analysis

Data collected during September 24–December 9, 2023, are included in this analysis.[¶] Estimates of coverage (percentage of the population vaccinated) with influenza, COVID-19, and RSV vaccines were calculated for weekly data collection periods using a nondecreasing composite estimation procedure that uses data from completed interviews from the current week combined with data from all previous weeks (*5*). Estimates for vaccination intent are based on interviews conducted each respective week and are adjusted to the cumulative vaccination coverage estimate for that week. Influenza and COVID-19 vaccination coverage is estimated among adults aged ≥18 years, and RSV vaccination coverage estimates are restricted to respondents aged ≥60 years. Differences among estimates were determined using t-tests with $p<0.05$ considered statistically significant. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[**]

[¶] Respondents were excluded from the analysis if they did not answer the question or questions about receipt of vaccine or intent to be vaccinated, and for RSV, if they did not report age. Number of excluded respondents was 365 for influenza vaccination coverage assessment, 595 for COVID-19 vaccination coverage assessment, and 3,890 for RSV vaccination coverage assessment. Sample sizes for data collected through December 9, 2023, and included in this analysis were 168,899 for influenza vaccination assessment, 168,669 for COVID-19 vaccination assessment, and 62,816 for RSV vaccination assessment.

Results

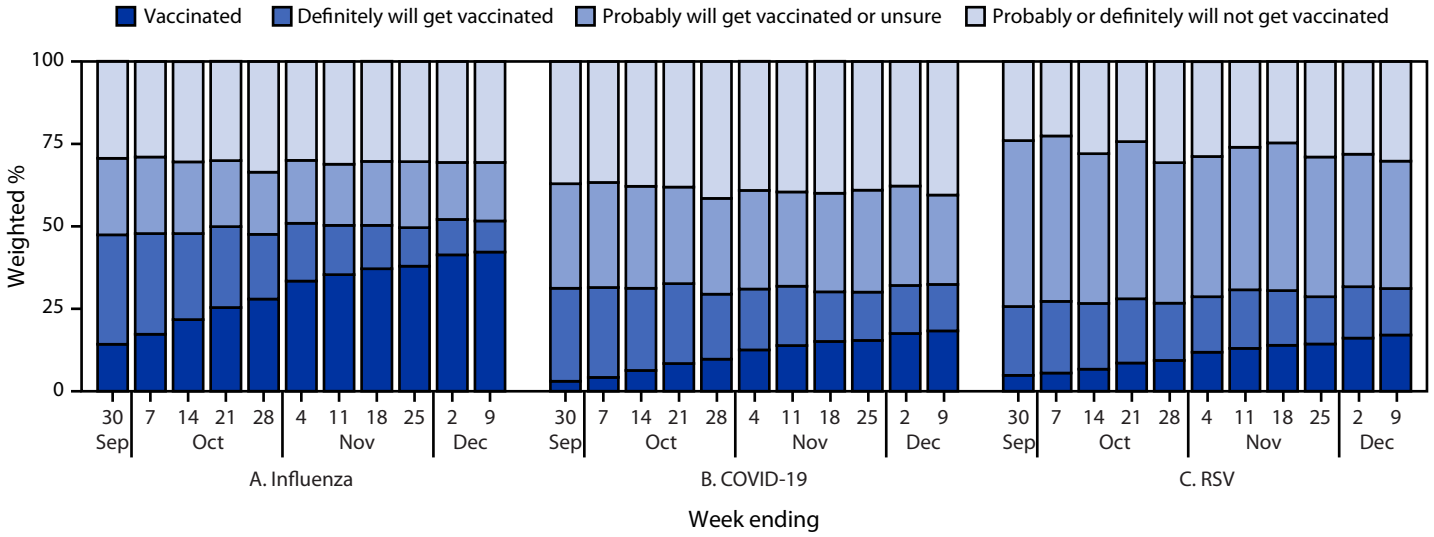
Overall Vaccination Coverage and Intent

As of December 9, 2023, estimated influenza and updated COVID-19 vaccination coverage among adults aged ≥18 years was 42.2% and 18.3%, respectively; estimated RSV vaccination coverage among all adults aged ≥60 years was 17.0% and among those with chronic health conditions[††] was 21.4% (Figure 1) (Supplementary Table, https://stacks.cdc.gov/view/cdc/136452). From September 24 through December 9, the percentage of adults who reported being unvaccinated, but who definitely will get vaccinated, decreased over time as vaccination coverage increased, from 33.2% to 9.4% for influenza and from 28.2% to 14.1% for COVID-19 vaccines. The decrease was less for RSV vaccine (from 20.9% to 14.1%). Throughout the study period, the proportion of adults who were unvaccinated

[**] 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.

[††] Includes persons who reported any of the following chronic conditions: chronic lung disease, diabetes, heart conditions, kidney disease, liver disease, or weakened immune system.

FIGURE 1. Weekly influenza (A), updated COVID-19 (B), and respiratory syncytial virus (C) vaccination status* and vaccination intent† among adults§ — National Immunization Survey-Adult COVID Module, United States, September 24–December 9, 2023



Abbreviation: RSV = respiratory syncytial virus.

* Estimates of vaccination coverage were calculated for December 3–9, 2023 using a nondecreasing composite estimation procedure that uses data from all completed interviews during September 24–December 9, 2023: influenza (168,899), COVID-19 (168,669), and RSV (62,816).

† Estimates for vaccination intent are based on interviews conducted during December 3–9, 2023, and were adjusted to the cumulative vaccination coverage estimate for that week: influenza (14,562), COVID-19 (14,539), and RSV (5,258). Estimates for vaccination intent are not shown for groups with sample size <30.

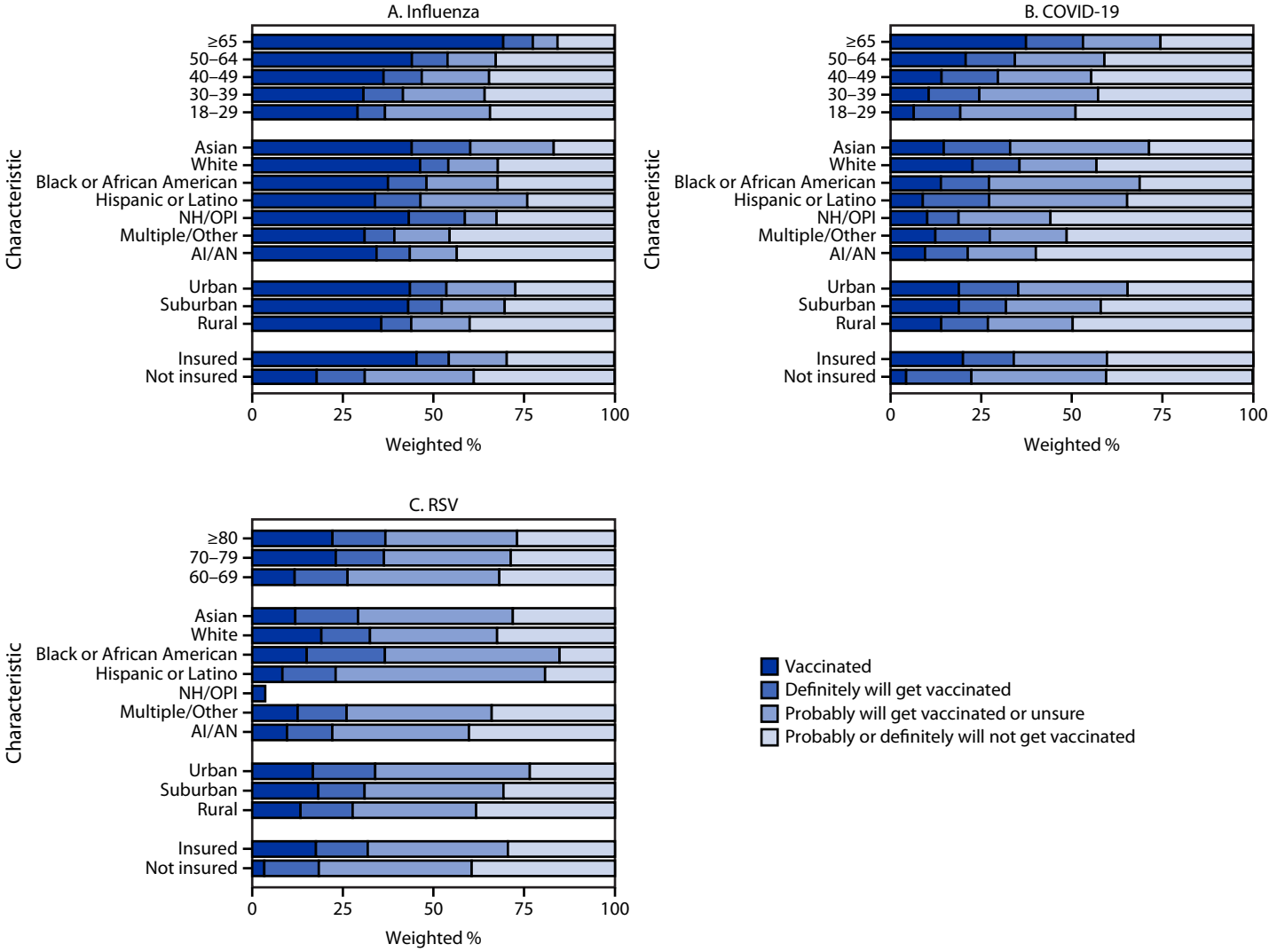
§ Estimates for influenza and COVID-19 vaccination coverage and vaccination intent are among adults aged ≥18 years. Estimates for RSV vaccination coverage and intent are among adults aged ≥60 years.

and reported they probably or definitely would not get vaccinated was lowest for RSV, whereas the proportion who were unvaccinated and reported they probably would get vaccinated or were unsure was highest for RSV.

Vaccination Coverage and Intent by Demographic Characteristics and Jurisdiction

Coverage with all vaccines was lowest among uninsured persons. Coverage and intent to be vaccinated increased with age and were higher among adults living in urban and suburban areas compared with those living in rural areas (Figure 2). Influenza vaccination coverage was higher among non-Hispanic White (White) and non-Hispanic Asian (Asian) adults than among most other racial and ethnic groups. However, the percentage of persons reporting that they probably or definitely will not get an influenza vaccination was similar among White adults (32.2%) and Black or African American (Black) adults (32.2%) and was lower among Hispanic or Latino (Hispanic)

FIGURE 2. Influenza (A), updated COVID-19 (B), and respiratory syncytial virus (C) vaccination status* and vaccination intent† among adults§ by demographic characteristics¶ — National Immunization Survey-Adult COVID Module, United States, December 3–9, 2023



Abbreviations: AI/AN = American Indian or Alaska Native; NH/OPI = Native Hawaiian or other Pacific Islander; RSV = respiratory syncytial virus.

* Estimates of vaccination coverage were calculated for December 3–9, 2023 using a nondecreasing composite estimation procedure that uses data from all completed interviews from September 24–December 9, 2023: influenza (168,899), COVID-19 (168,669), and RSV (62,816).

† Estimates for vaccination intent are based on interviews conducted during December 3–9, 2023, and were adjusted to the cumulative vaccination coverage estimate for that week: influenza (14,562), COVID-19 (14,539), and RSV (5,258). Estimates for vaccination intent are not shown for groups with sample size <30.

§ Estimates presented for influenza and COVID-19 vaccination coverage and vaccination intent are among adults aged ≥18 years. Estimates for RSV vaccination and intent are among adults aged ≥60 years.

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

adults (24.0%). Updated COVID-19 and RSV vaccination coverage was higher among White adults than among most other racial and ethnic groups. However, a higher percentage of White adults reported that they probably or definitely will not receive a COVID-19 vaccine (43.2%) than did Black (31.3%) and Hispanic (34.7%) adults. Similarly, a higher percentage of White adults reported that they probably or definitely will not receive an RSV vaccine (32.5%) than did Black (15.3%) and Hispanic (19.3%) adults. Coverage with all vaccines varied by jurisdiction, ranging from 15.6% to 54.8% for influenza vaccine, from 2.4% to 35.6% for updated COVID-19 vaccine, and from 1.9% to 32.4% for RSV vaccine (Table).

Discussion

As of December 9, 2023, self-reported coverage with influenza, updated COVID-19, and RSV vaccines among U.S. adults was low, particularly for updated COVID-19 and RSV vaccines. RSV vaccination coverage was low even among persons with chronic conditions who are at highest risk for severe RSV disease and might benefit from vaccination. As of mid-November, influenza vaccination coverage was approximately 2.5 percentage points lower than it was at the same time during the 2022–23 influenza season (*6*). Approximately 41% of all adults and 53% of adults aged ≥60 years were unvaccinated but reported that they definitely or probably plan to receive or are unsure about receiving updated COVID-19 and RSV vaccines, respectively, suggesting they are open to vaccination. A health care provider recommendation for and offer of vaccination are strongly associated with vaccination (*7*). A previous report found that unvaccinated adults who were open to receiving a bivalent COVID-19 vaccine had not yet done so mainly because of concerns about side effects, being too busy, or just had not gotten around to getting vaccinated (*8*). Making vaccination available in provider offices, pharmacies, workplaces, and other convenient locations at convenient times, along with a strong provider recommendation for vaccination, could increase vaccination coverage, particularly for RSV, which is recommended on the basis of shared clinical decision-making between a patient and provider (*3*).

Despite disparities in vaccination coverage by race and ethnicity, when responses indicating the person is open to vaccination are included, the potential vaccination coverage that could be achieved for Hispanic, Black, and Asian adults is similar to or higher than that for White adults. Programmatic measures that helped reduce disparities in coverage with the primary series of COVID-19 vaccine, such as making vaccines available free of charge, use of trusted messengers, and bringing vaccines into communities through nontraditional settings (e.g., local libraries and local businesses such as barber shops and restaurants)[§§] (*4*,*9*), might increase equitable access to vaccination and decrease disparities for these currently recommended vaccines.

CDC is partnering with community-based organizations, health care providers, and other trusted messengers to build vaccine confidence and awareness, including through the Partnering for Vaccine Equity program.[¶¶] CDC is also working to expand COVID-19 vaccine access to all through the Bridge Access Program, which provides COVID-19 vaccines for adults without health insurance and adults whose insurance does not cover all COVID-19 vaccine costs. Public health safety net and pharmacy locations offering influenza and COVID-19 vaccines, including COVID-19 vaccines through the Bridge Access Program, are available at https://www.vaccines.gov. Communication campaigns,[***] such as the "Wild to Mild" and "Get My Flu Shot" influenza vaccine campaign and the "Everything" broad respiratory virus communication initiative, include various materials and resources to promote vaccination, including to persons who are disproportionately affected by disease. Finally, CDC has developed health care provider toolkits to empower providers with knowledge to confidently recommend vaccination.[†††]

CDC makes vaccination coverage estimates rapidly available during the respiratory virus season.[§§§,¶¶¶] In addition to data from the NIS-ACM, vaccination data are available from multiple sources and include coverage among children, pregnant persons, Medicare beneficiaries, and national projected vaccination in pharmacies and medical offices. Jurisdiction-level estimates of COVID-19 vaccination coverage and intent stratified by demographic factors, behavioral and social drivers of vaccination, and barriers to vaccination are available.[****] CDC's COVID-19 Vaccination Geographic Information System Mapping Tool, designed with feedback from several local health departments, provides web maps where jurisdiction-level data including demographic characteristics and social determinants of health can be displayed along with vaccine confidence and vaccination coverage.[††††] End-of-season influenza vaccination coverage estimates for children and adults since the 2010–11 influenza season, nationally and by state, are available on FluVaxView.[§§§§]

[§§] https://www.cdc.gov/vaccines/health-equity/field-stories.html

[¶¶] https://www.cdc.gov/vaccines/health-equity/

[***] https://www.cdc.gov/flu/resource-center/toolkit/index.htm

[†††] https://www.cdc.gov/respiratory-viruses/tools-resources/health-care-providers.html; https://www.cdc.gov/vaccines/covid-19/; https://www.cdc.gov/vaccines/vpd/rsv/hcp/older-adults.html; https://www.cdc.gov/flu/professionals/vaccination/prepare-practice-tools.htm

[§§§] https://www.cdc.gov/respiratory-viruses/data-research/dashboard/snapshot.html (Accessed December 15, 2023).

[¶¶¶] https://www.cdc.gov/vaccines/imz-managers/coverage/respvaxview/index.html

[****] Data on updated 2023–2024 COVID-19 vaccine will be added January 24, 2024. https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html

[††††] https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/covid19-vaccination-mapping-tool.html

[§§§§] https://www.cdc.gov/flu/fluvaxview/coverage-by-season.htm

TABLE. Coverage with influenza, updated COVID-19, and respiratory syncytial virus vaccines among adults,* by jurisdiction — National Immunization Survey-Adult COVID Module, United States, September 24–December 9, 2023

Jurisdiction	Influenza		COVID-19		RSV	
	Cumulative unweighted no.	% Vaccinated (95% CI)†	Cumulative unweighted no.	% Vaccinated (95% CI)†	Cumulative unweighted no.	% Vaccinated (95% CI)†
Alabama	4,015	39.1 (35.4–42.8)	4,010	11.4 (9.3–13.4)	1,740	12.1 (8.4–15.7)
Alaska	2,079	39.7 (35.3–44.2)	2,075	16.0 (13.0–19.0)	734	21.3 (16.1–26.6)
Arizona	5,023	41.0 (37.5–44.5)	5,017	17.7 (15.4–20.1)	2,129	22.0 (17.4–26.6)
Arkansas	2,599	42.2 (37.0–47.3)	2,591	14.5 (11.1–17.8)	1,037	14.7 (9.7–19.8)
California	4,232	44.9 (40.6–49.2)	4,227	20.0 (16.8–23.1)	1,300	16.4 (10.5–22.3)
Colorado	3,686	49.1 (45.0–53.3)	3,680	25.7 (22.3–29.2)	1,308	32.4 (25.9–39.0)
Connecticut	1,235	47.0 (39.2–54.8)	1,233	23.6 (16.1–31.0)	212	24.1 (11.1–37.1)
Delaware	2,530	51.2 (43.9–58.6)	2,527	23.1 (17.7–28.6)	1,194	17.2 (12.6–21.8)
District of Columbia	4,307	52.9 (49.2–56.5)	4,304	35.6 (32.2–38.9)	1,291	20.7 (16.3–25.2)
Florida	2,045	36.0 (30.0–41.9)	2,043	10.9 (7.8–14.1)	733	20.7 (13.0–28.4)
Georgia	1,132	33.3 (25.3–41.3)	1,132	11.2 (5.1–17.3)	222	9.4 (5.2–13.7)
Hawaii	3,323	46.1 (42.0–50.1)	3,319	20.1 (17.2–22.9)	1,421	19.2 (14.9–23.5)
Idaho	1,474	34.8 (29.7–39.9)	1,472	16.5 (12.9–20.2)	502	21.0 (13.9–28.2)
Illinois	7,190	48.0 (44.9–51.2)	7,175	24.6 (22.0–27.2)	2,662	20.3 (16.7–23.8)
Indiana	2,678	39.5 (35.7–43.3)	2,671	16.8 (13.9–19.6)	1,003	14.5 (11.2–17.9)
Iowa	1,510	46.1 (38.3–53.9)	1,509	26.8 (18.7–34.9)	583	22.9 (7.3–38.5)
Kansas	2,875	44.7 (39.6–49.7)	2,871	20.0 (16.1–23.8)	960	22.4 (15.0–29.8)
Kentucky	2,290	39.6 (32.6–46.7)	2,287	14.8 (8.8–20.7)	804	22.9 (7.7–38.2)
Louisiana	3,719	36.8 (33.0–40.5)	3,713	10.1 (8.0–12.1)	1,542	13.8 (10.4–17.2)
Maine	4,291	49.2 (42.6–55.9)	4,287	28.8 (22.7–34.8)	1,949	18.0 (11.7–24.4)
Maryland	2,263	46.7 (41.2–52.2)	2,261	24.7 (17.7–31.7)	471	29.3 (17.2–41.3)
Massachusetts	4,696	50.7 (47.5–54.0)	4,689	28.4 (25.8–31.0)	1,764	23.9 (18.7–29.1)
Michigan	1,080	43.6 (35.4–51.7)	1,079	18.1 (12.2–23.9)	226	13.8 (5.2–22.4)
Minnesota	3,154	48.0 (44.6–51.4)	3,149	31.5 (28.4–34.5)	1,316	19.3 (15.2–23.4)
Mississippi	2,663	32.2 (27.9–36.5)	2,663	7.3 (4.9–9.8)	1,106	10.8 (6.0–15.6)
Missouri	1,211	43.3 (34.9–51.7)	1,213	21.1 (14.4–27.7)	315	14.1 (2.8–25.3)
Montana	3,301	39.4 (34.8–44.0)	3,292	20.9 (16.9–24.8)	1,510	17.1 (12.0–22.2)
Nebraska	1,990	47.9 (40.7–55.2)	1,986	18.7 (12.5–24.9)	715	20.7 (10.4–31.0)
Nevada	4,243	34.6 (31.7–37.4)	4,234	14.9 (12.9–16.9)	1,678	19.7 (15.9–23.5)
New Hampshire	4,620	51.0 (47.4–54.7)	4,619	27.6 (24.6–30.7)	2,276	17.6 (14.6–20.7)
New Jersey	3,780	45.7 (41.6–49.9)	3,770	19.1 (16.2–22.0)	1,350	14.6 (9.3–19.8)
New Mexico	4,041	44.5 (40.9–48.1)	4,034	19.8 (17.3–22.2)	1,596	23.3 (19.3–27.3)
New York	5,101	43.0 (39.7–46.2)	5,093	16.3 (14.3–18.4)	1,419	10.8 (8.2–13.5)
North Carolina	4,240	43.9 (40.3–47.4)	4,234	18.3 (15.6–21.0)	1,618	16.0 (12.4–19.6)
North Dakota	1,880	43.9 (39.5–48.2)	1,877	17.7 (14.6–20.8)	684	16.8 (10.4–23.2)
Ohio	1,148	44.1 (36.5–51.7)	1,148	17.5 (12.2–22.7)	206	19.9 (9.3–30.5)
Oklahoma	4,872	39.8 (36.7–42.9)	4,866	13.6 (11.7–15.5)	1,938	17.3 (13.9–20.8)
Oregon	3,080	40.8 (37.1–44.5)	3,078	25.0 (21.6–28.5)	1,200	20.3 (15.8–24.7)
Pennsylvania	8,446	43.4 (40.8–46.0)	8,432	19.8 (17.8–21.7)	3,217	14.4 (10.3–18.6)
Puerto Rico	4,742	28.3 (25.8–30.8)	4,735	5.3 (4.2–6.4)	1,911	4.1 (2.3–6.0)
Rhode Island	894	44.4 (36.6–52.2)	895	27.0 (19.1–35.0)	138	10.9 (2.0–19.7)
South Carolina	2,951	42.5 (36.6–48.3)	2,955	16.7 (11.9–21.4)	1,285	10.1 (7.3–12.9)
South Dakota	3,794	49.4 (45.5–53.3)	3,790	20.0 (17.4–22.6)	1,711	15.5 (12.2–18.9)
Tennessee	855	35.6 (27.7–43.4)	853	11.4 (5.8–17.0)	183	8.8 (2.4–15.3)
Texas	9,153	40.1 (34.9–45.4)	9,136	15.2 (11.0–19.4)	2,964	14.6 (10.2–19.0)
U.S. Virgin Islands	1,782	15.6 (12.5–18.6)	1,784	2.4 (1.5–3.3)	876	1.9 (0.9–2.9)
Utah	854	41.2 (33.7–48.7)	852	15.0 (9.7–20.3)	175	19.9 (4.4–35.4)
Vermont	831	54.8 (44.9–64.8)	831	32.0 (24.9–39.0)	164	21.8 (10.5–33.0)
Virginia	5,900	47.5 (45.0–50.1)	5,890	22.4 (20.5–24.3)	2,034	18.5 (15.5–21.5)
Washington	1,445	41.5 (35.0–48.0)	1,440	21.7 (15.9–27.6)	278	20.2 (12.0–28.4)
West Virginia	1,886	44.8 (35.9–53.7)	1,888	16.4 (9.6–23.2)	771	7.7 (5.5–10.0)
Wisconsin	2,690	46.4 (41.8–51.0)	2,684	23.7 (20.1–27.3)	1,054	14.3 (10.3–18.2)
Wyoming	3,080	35.6 (32.3–38.8)	3,076	14.9 (12.7–17.0)	1,341	16.6 (12.8–20.5)
Range across jurisdictions	—	**15.6–54.8**	—	**2.4–35.6**	—	**1.9–32.4**

Abbreviation: RSV = respiratory syncytial virus.

* Estimates presented for influenza and COVID-19 vaccination are among adults aged ≥18 years. Estimates for RSV vaccination are among adults aged ≥60 years. Estimates of vaccination coverage were calculated for December 3–9, 2023 using a nondecreasing composite estimation procedure, which uses data collected from all completed interviews during September 24–December 9, 2023: influenza (168,899), COVID-19 (168,669), and RSV (62,816).

† Weighted percentage.

Summary

What is already known about this topic?

The Advisory Committee on Immunization Practices recommends that all adults receive influenza and COVID-19 vaccines, and those aged ≥60 years may receive respiratory syncytial virus (RSV) vaccine during the 2023–24 respiratory virus season.

What is added by this report?

By December 9, 2023, an estimated 42.2% and 18.3% of adults aged ≥18 years had received influenza and updated 2023–2024 COVID-19 vaccine, respectively; 17.0% of adults aged ≥60 years had received RSV vaccine. Many adults who had not received the vaccines reported being open to vaccination.

What are the implications for public health practice?

Strong provider recommendations for and offers of vaccination could increase influenza, COVID-19, and RSV vaccination coverage. Immunization programs and vaccination partners might benefit from using these within-season data to understand vaccination patterns in their jurisdictions to strengthen vaccination activities.

Limitations

The findings in this report are subject to at least three limitations. First, response rates for NIS-ACM were relatively low (<25%). Data were weighted to mitigate possible bias resulting from incomplete sample frame (i.e., exclusion of households with no phone service or only landline telephones) or nonresponse, but some selection bias might persist. Second, all responses were self-reported; vaccination receipt, and month and year of receipt of most recent dose might be subject to recall or social desirability bias. Nonresponse and social desirability bias could result in overestimation of coverage. Third, the survey sampled noninstitutionalized U.S. adults; therefore, adults who were incarcerated or who live in long-term care facilities[¶¶¶¶] might not be represented in the sample.

Implications for Public Health Practice

Although influenza, updated COVID-19, and RSV vaccination has slowed for the 2023–24 respiratory season, vaccination is recommended to continue while viruses are circulating (*1*–*3*), and many unvaccinated persons continue to report intent to be vaccinated. Health care provider recommendations for and offers of vaccination are important to increasing vaccination coverage (*7*). Immunization programs and vaccination partners are encouraged to use CDC developed dashboards and tools, as well as other data sources available to them, such as immunization information systems, to identify undervaccinated populations and better understand vaccination patterns, attitudes and behaviors, and systemic barriers to vaccination in their jurisdiction to help tailor vaccination activities to improve coverage and health equity.

[¶¶¶¶] https://www.cdc.gov/mmwr/volumes/72/wr/mm7251a3.htm?s_cid=mm7251a3_w

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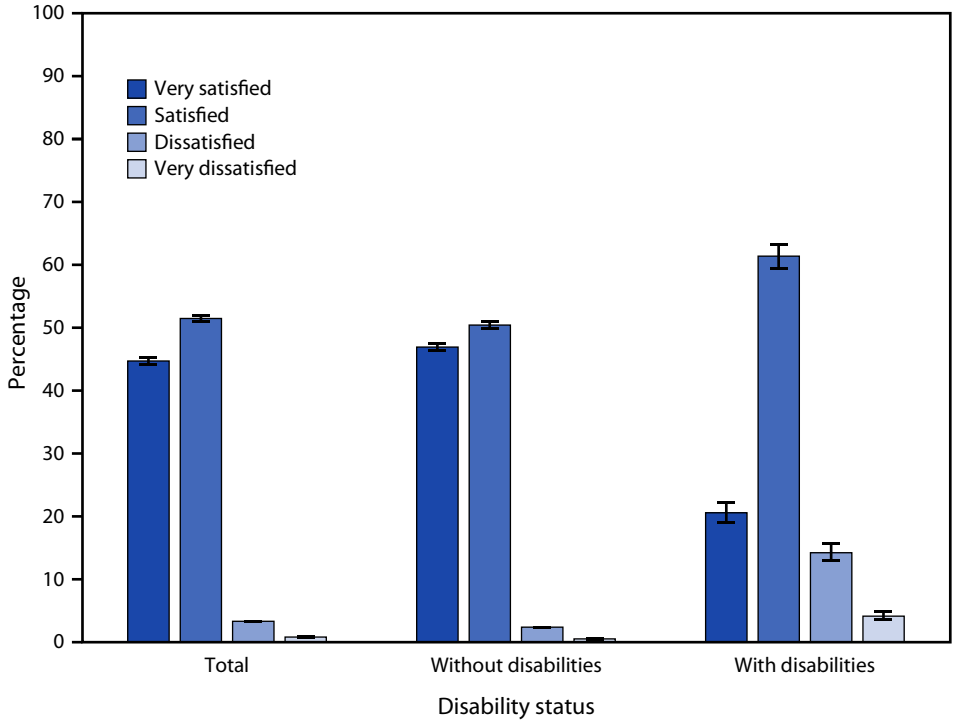
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentage* of Adults Aged ≥18 Years Who Reported Their Level of Satisfaction with Life,† by Disability Status§ — National Health Interview Survey,¶ United States, 2022



* Age-adjusted percentages are based on the 2000 U.S. Census Bureau standard population, using age groups 18–44, 45–54, 55–64, 65–74, and ≥75 years, with 95% CIs indicated by error bars.

† Based on responses to the survey question, "In general, how satisfied are you with your life? Would you say very satisfied, satisfied, dissatisfied, or very dissatisfied?"

§ Disability was defined by the reported level of difficulty to questions about six domains of functioning: "Do you have any difficulty… seeing, even if wearing glasses; hearing, even if wearing hearing aids; walking or climbing stairs; communicating, for example understanding or being understood; remembering or concentrating; and administering self-care, such as washing all over or dressing." Response categories were "no difficulty," "some difficulty," "a lot of difficulty," or "cannot do at all." Adults who responded "a lot of difficulty" or "cannot do at all" to at least one domain were classified with disability.

¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2022, 44.6% of adults aged ≥18 years reported they were very satisfied with their life, 51.3% reported they were satisfied, 3.3% reported they were dissatisfied, and 0.8% reported they were very dissatisfied. Adults without disabilities were more likely to be very satisfied (46.8%) or satisfied (50.3%) with their life than dissatisfied (2.4%) or very dissatisfied (0.5%). Adults with disabilities were more likely to be satisfied with their life (61.2%) compared with very satisfied (20.5%), dissatisfied (14.2%), or very dissatisfied (4.1%). Adults without disabilities were more likely than adults with disabilities to be very satisfied with their life. Conversely, adults with disabilities were more likely than adults without disabilities to be satisfied, dissatisfied, or very dissatisfied.

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/ncbddd/disabilityandhealth/index.html

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