IN THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

No. 22-2230

KATIE SCZESNY, MARIETTE VITTI, DEBRA HAGEN, AND JAIME RUMFIELD,

Plaintiffs-Appellants

v.

Governor PHILIP MURPHY,

Defendant-Appellee,

On appeal from the United States District Court of New Jersey's denial of a temporary restraining order pursuant to *Fed. R. Civ. P.* 65

JOINT APPENDIX VOLUME III

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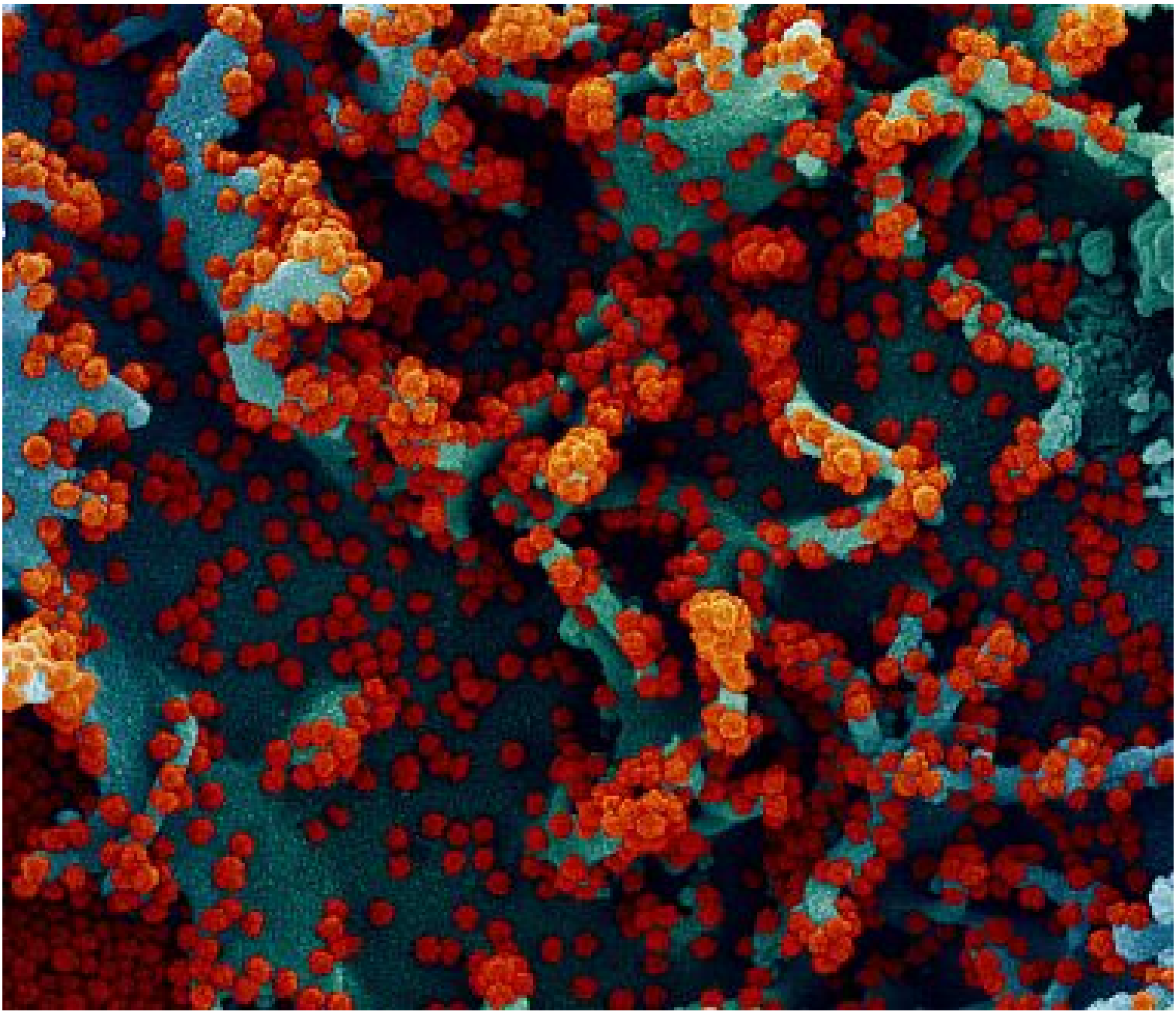
January 26, 2021

Lasting immunity found after recovery from COVID-19

At a Glance

- The immune systems of more than 95% of people who recovered from COVID-19 had durable memories of the virus up to eight months after infection.
- The results provide hope that people receiving SARS-CoV-2 vaccines will develop similar lasting immune memories after vaccination.



Colorized scanning electron micrograph of a cell, isolated from a patient sample, that is heavily infected with SARS-CoV-2 virus particles (red). *NIAID Integrated Research Facility, Fort Detrick, Maryland*

After people recover from infection with a virus, the immune system retains a memory of it. Immune cells and proteins that circulate in the body can recognize and kill the pathogen if it's encountered again, protecting against disease and reducing illness severity.

This long-term immune protection involves several components. Antibodies—proteins that circulate in the blood—recognize foreign substances like viruses and neutralize them. Different types of T cells help recognize and kill pathogens. B cells make new antibodies when the body needs them.

All of these immune-system components have been found in people who recover from SARS-CoV-2, the virus that causes COVID-19. But the details of this immune response and how long it lasts after infection have been unclear. Scattered reports of reinfection with SARS-CoV-2 have raised concerns that the immune response to the virus might not be durable.

To better understand immune memory of SARS-CoV-2, researchers led by Drs. Daniela Weiskopf, Alessandro Sette, and Shane Crotty from the La Jolla Institute for Immunology analyzed immune cells and antibodies from almost 200 people who had been exposed to SARS-CoV-2

and recovered.

Time since infection ranged from six days after symptom onset to eight months later. More than 40 participants had been recovered for more than six months before the study began. About 50 people provided blood samples at more than one time after infection.

The research was funded in part by NIH's National Institute of Allergy and Infectious Diseases (NIAID) and National Cancer Institute (NCI). Results were published on January 6, 2021, in *Science*.

The researchers found durable immune responses in the majority of people studied. Antibodies against the spike protein of SARS-CoV-2, which the virus uses to get inside cells, were found in 98% of participants one month after symptom onset. As seen in previous studies, the number of antibodies ranged widely between individuals. But, promisingly, their levels remained fairly stable over time, declining only modestly at 6 to 8 months after infection.

Virus-specific B cells increased over time. People had more memory B cells six months after symptom onset than at one month afterwards. Although the number of these cells appeared to reach a plateau after a few months, levels didn't decline over the period studied.

Levels of T cells for the virus also remained high after infection. Six months after symptom onset, 92% of participants had CD4+ T cells that recognized the virus. These cells help coordinate the immune response. About half the participants had CD8+ T cells, which kill cells that are infected by the virus.

As with antibodies, the numbers of different immune cell types varied substantially between individuals. Neither gender nor differences in disease severity could account for this variability. However, 95% of the people had at least 3 out of 5 immune-system components that could recognize SARS-CoV-2 up to 8 months after infection.

"Several months ago, our studies showed that natural infection induced a strong response, and this study now shows that the responses last," Weiskopf says. "We are hopeful that a similar pattern of responses lasting over time will also emerge for the vaccine-induced responses."

—by Sharon Reynolds

Related Links

- Experimental Coronavirus Vaccine Highly Effective (https://www.nih.gov/news-events/nih-research-matters/experimental-coronavirus-vaccine-highly-effective)
- Antibodies and T Cells Protect Against SARS-CoV-2 (https://www.nih.gov/news-events/nih-research-matters/antibodies-t-cells-protect-against-sars-cov-2)
- Immune Cells for Common Cold May Recognize SARS-CoV-2 (https://www.nih.gov/news-events/nih-research-matters/immune-cells-common-cold-may-recognize-sars-cov-2)
- Potent Neutralizing Antibodies Target New Regions of Coronavirus Spike (https://www.nih.gov/news-events/nih-research-matters/potent-neutralizing-antibodies-target-new-regions-coronavirus-spike)
- Potent Antibodies Found in People Recovered from COVID-19 (https://www.nih.gov/news-events/nih-research-matters/potent-antibodies-found-people-recovered-covid-19)
- Novel Coronavirus Structure Reveals Targets for Vaccines and Treatments (https://www.nih.gov/news-events/nih-research-matters/novel-coronavirus-structure-reveals-targets-vaccines-treatments)
- Coronavirus (COVID-19) (https://covid19.nih.gov/)
- Coronavirus Prevention Network (https://www.coronaviruspreventionnetwork.org/)

- Coronavirus (COVID-19) (https://www.coronavirus.gov/)

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Infection fatality rate of COVID-19 inferred from seroprevalence data

John P A Ioannidis[a]

Objective To estimate the infection fatality rate of coronavirus disease 2019 (COVID-19) from seroprevalence data.
Methods I searched PubMed and preprint servers for COVID-19 seroprevalence studies with a sample size ≥ 500 as of 9 September 2020. I also retrieved additional results of national studies from preliminary press releases and reports. I assessed the studies for design features and seroprevalence estimates. I estimated the infection fatality rate for each study by dividing the cumulative number of COVID-19 deaths by the number of people estimated to be infected in each region. I corrected for the number of immunoglobin (Ig) types tested (IgG, IgM, IgA).
Findings I included 61 studies (74 estimates) and eight preliminary national estimates. Seroprevalence estimates ranged from 0.02% to 53.40%. Infection fatality rates ranged from 0.00% to 1.63%, corrected values from 0.00% to 1.54%. Across 51 locations, the median COVID-19 infection fatality rate was 0.27% (corrected 0.23%): the rate was 0.09% in locations with COVID-19 population mortality rates less than the global average (< 118 deaths/million), 0.20% in locations with 118–500 COVID-19 deaths/million people and 0.57% in locations with > 500 COVID-19 deaths/million people. In people younger than 70 years, infection fatality rates ranged from 0.00% to 0.31% with crude and corrected medians of 0.05%.
Conclusion The infection fatality rate of COVID-19 can vary substantially across different locations and this may reflect differences in population age structure and case-mix of infected and deceased patients and other factors. The inferred infection fatality rates tended to be much lower than estimates made earlier in the pandemic.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

The infection fatality rate, the probability of dying for a person who is infected, is one of the most important features of the coronavirus disease 2019 (COVID-19) pandemic. The expected total mortality burden of COVID-19 is directly related to the infection fatality rate. Moreover, justification for various non-pharmacological public health interventions depends on the infection fatality rate. Some stringent interventions that potentially also result in more noticeable collateral harms[1] may be considered appropriate, if the infection fatality rate is high. Conversely, the same measures may fall short of acceptable risk–benefit thresholds, if the infection fatality rate is low.

Early data from China suggested a 3.4% case fatality rate[2] and that asymptomatic infections were uncommon,[3] thus the case fatality rate and infection fatality rate would be about the same. Mathematical models have suggested that 40–81% of the world population could be infected,[4,5] and have lowered the infection fatality rate to 1.0% or 0.9%.[5,6] Since March 2020, many studies have estimated the spread of the virus causing COVID-19 – severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – in various locations by evaluating seroprevalence. I used the prevalence data from these studies to infer estimates of the COVID-19 infection fatality rate.

Methods

Seroprevalence studies

The input data for calculations of infection fatality rate were studies on the seroprevalence of COVID-19 done in the general population, or in samples that might approximately represent the general population (e.g. with proper reweighting), that had been published in peer-reviewed journals or as preprints (irrespective of language) as of 9 September 2020. I considered only studies with at least 500 assessed samples because smaller data sets would result in large uncertainty for any calculations based on these data. I included studies that made seroprevalence assessments at different time intervals if at least one time interval assessment had a sample size of at least 500 participants. If there were different eligible time intervals, I selected the one with the highest seroprevalence, since seroprevalence may decrease over time as antibody titres decrease. I excluded studies with data collected for more than a month that could not be broken into at least one eligible time interval less than one month duration because it would not be possible to estimate a point seroprevalence reliably. Studies were eligible regardless of the exact age range of participants included, but I excluded studies with only children.

I also examined results from national studies from preliminary press releases and reports whenever a country had no other data presented in published papers or preprints. This inclusion allowed these countries to be represented, but information was less complete than information in published papers or preprints and thus requires caution.

I included studies on blood donors, although they may underestimate seroprevalence and overestimate infection fatality rate because of the healthy volunteer effect. I excluded studies on health-care workers, since this group is at a potentially high exposure risk, which may result in seroprevalence estimates much higher than the general population and thus an improbably low infection fatality rate. Similarly, I also excluded studies on communities (e.g. shelters or religious or other shared-living communities). Studies were eligible regardless of whether they aimed to evaluate seroprevalence in large or small regions, provided that the population of reference in the region was at least 5000 people.

I searched PubMed® (LitCOVID), and medRxiv, bioRxiv and Research Square using the terms "seroprevalence" OR "antibodies" with continuous updates. I made the first search in early May and did monthly updates, with the last update

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on 9 September 2020. I contacted field experts to retrieve any important studies that may have been missed.

From each study, I extracted information on location, recruitment and sampling strategy, dates of sample collection, sample size, types of antibody measured (immunoglobulin G (IgG), IgM and IgA), the estimated crude seroprevalence (positive samples divided by all samples tested), adjusted seroprevalence and the factors that the authors considered for adjustment.

Inferred infection fatality rate

If a study did not cover an entire country, I collected information on the population of the relevant location from the paper or recent census data so as to approximate as much as possible the relevant catchment area (e.g. region(s) or county(ies)). Some studies targeted specific age groups (e.g. excluding elderly people and/or excluding children) and some estimated numbers of people infected in the population based on specific age groups. For consistency, I used the entire population (all ages) and, separately, the population 0–70 years to estimate numbers of infected people. I assumed that the seroprevalence would be similar in different age groups, but I also recorded any significant differences in seroprevalence across age strata so as to examine the validity of this assumption.

I calculated the number of infected people by multiplying the relevant population size and the adjusted estimate of seroprevalence. If a study did not give an adjusted seroprevalence estimate, I used the unadjusted seroprevalence instead. When seroprevalence estimates with different adjustments were available, I selected the analysis with largest adjustment. The factors adjusted for included COVID-19 test performance, sampling design, and other factors such as age, sex, clustering effects or socioeconomic factors. I did not adjust for specificity in test performance when positive antibody results were already validated by a different method.

For the number of COVID-19 deaths, I chose the number of deaths accumulated until the date 1 week after the midpoint of the study period (or the date closest to this that had available data) – unless the authors of the study had strong arguments to choose some other time point or approach. The 1-week lag accounts for different delays in developing antibodies versus dying from infection. The number of deaths is an approximation because it is not known when exactly each patient who died was infected. The 1-week cut-off after the study midpoint may underestimate deaths in places where patients are in hospital for a long time before death, and may overestimate deaths in places where patients die soon because of poor or even inappropriate care. Whether or not the health system became overloaded may also affect the number of deaths. Moreover, because of imperfect diagnostic documentation, COVID-19 deaths may have been both overcounted and undercounted in different locations and at different time points.

I calculated the inferred infection fatality rate by dividing the number of deaths by the number of infected people for the entire population, and separately for people younger than 70 years. I took the proportion of COVID-19 deaths that occurred in people younger than 70 years from situational reports for the respective locations that I retrieved at the time I identified the seroprevalence studies. I also calculated a corrected infection fatality rate to try and account for the fact that only one or two types of antibodies (among IgG, IgM, IgA) might have been used. I corrected seroprevalence upwards (and inferred infection fatality rate downwards) by one tenth of its value if a study did not measure IgM and similarly if IgA was not measured. This correction is reasonable based on some early evidence,[7] although there is uncertainty about the exact correction factor.

Data synthesis

The estimates of the infection fatality rate across all locations showed great heterogeneity with I^2 exceeding 99.9%; thus, a meta-analysis would be inappropriate to report across all locations. Quantitative synthesis with meta-analysis across all locations would also be misleading since locations with high COVID-19 seroprevalence would tend to carry more weight than locations with low seroprevalence. Furthermore, locations with more studies (typically those that have attracted more attention because of high death tolls and thus high infection fatality rates) would be represented multiple times in the calculations. In addition, poorly conducted studies with fewer adjustments would get more weight because of spuriously narrower confidence intervals than more rigorous studies with more careful adjustments which allow for more uncertainty. Finally, with a highly skewed distribution of the infection fatality rate and with large between-study heterogeneity, typical random effects models would produce an incorrectly high summary infection fatality rate that approximates the mean of the study-specific estimates (also strongly influenced by high-mortality locations where more studies have been done); for such a skewed distribution, the median is more appropriate.

Therefore, in a first step, I grouped estimates of the infection fatality rate from studies in the same country (or for the United States of America, the same state) together and calculated a single infection fatality rate for that location, weighting the study-specific infection fatality rates by the sample size of each study. This approach avoided inappropriately giving more weight to studies with higher seroprevalence estimates and those with seemingly narrower confidence intervals because of poor or no adjustments, while still giving more weight to larger studies. Then, I used the single summary estimate for each location to calculate the median of the distribution of location-specific infection fatality rate estimates. Finally, I explored whether the location-specific infection fatality rates were associated with the COVID-19 mortality rate in the population (COVID-19 deaths per million people) in each location as of 12 September 2020; this analysis allowed me to assess whether estimates of the infection fatality rate tended to be higher in locations with a higher burden of death from COVID-19.

Results

Seroprevalence studies

I retrieved 61 studies with 74 eligible estimates published either in the peer-reviewed literature or as preprints as of 9 September 2020.[8–68] Furthermore, I considered another eight preliminary national estimates.[69–76] This search yielded a total of 82 eligible estimates (Fig. 1).

The studies varied substantially in sampling and recruitment designs (Table 1; available at: http://www.who.int/bulletin/volumes/99/1/20-265892). Of the 61 studies, 24 studies[8,10,16,17,20,22,25,33,34,36,37,42,46–49,52–54,57,61,63,65,68]

explicitly aimed for random sampling from the general population. In principle, random sampling is a stronger design. However, even then, people who cannot be reached (e.g. by email or telephone or even by visiting them at a house location) will not be recruited, and these vulnerable populations are likely to be missed. Moreover, several such studies[8,10,16,37,42] focused on geographical locations with high numbers of deaths, higher than other locations in the same city or country, and this emphasis would tend to select eventually for a higher infection fatality rate on average.

Eleven studies assessed blood donors,[12,15,18,24,28,31,41,44,45,55,60] which might underestimate COVID-19 seroprevalence in the general population. For example, 200 blood donors in Oise, France showed 3.00% seroprevalence, while the seroprevalence was 25.87% (171/661) in pupils, siblings, parents, teachers and staff at a high school with a cluster of cases in the same area; the true population seroprevalence may be between these two values.[13]

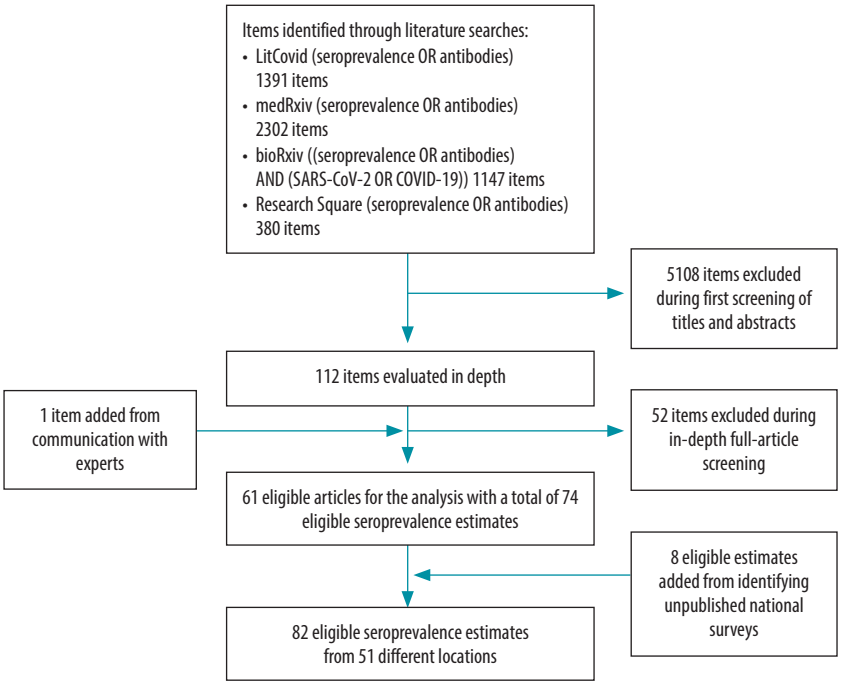
For other studies, healthy volunteer bias[19] may underestimate seroprevalence, attracting people with symptoms[26] may overestimate seroprevalence, and studies of employees,[14,21,25,32,66] grocery store clients[23] or patient cohorts[11,14,27–30,36,38,40,50,51,56,59,62,64,67] risk sampling bias in an unpredictable direction.

All the studies tested for IgG antibodies but only about half also assessed IgM and few assessed IgA. Only seven studies assessed all three types of antibodies and/or used pan-Ig antibodies. The ratio of people sampled versus the total population of the region was more than 1:1000 in 20 studies (Table 2; available at: http://www.who.int/bulletin/volumes/99/1/20-265892).

Seroprevalence estimates

Seroprevalence for the infection ranged from 0.02% to 53.40% (58.40% in the slum sub-population in Mumbai; Table 3). Studies varied considerably depending on whether or not they tried to adjust their estimates for test performance, sampling (to get closer to a more representative sample), clustering (e.g. when including household members) and other factors. The adjusted seroprevalence occasionally differed substantially from the unadjusted value. In studies that used samples from multiple locations, between-location heterogeneity was seen (e.g. 0.00–25.00% across 133 Brazilian cities).[25]

Fig. 1. **Flowchart for selection of seroprevalence studies on severe acute respiratory syndrome coronavirus 2, 2020**



COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Inferred infection fatality rate

Inferred infection fatality rate estimates varied from 0.00% to 1.63% (Table 4). Corrected values also varied considerably (0.00–1.54%).

For 15 locations, more than one estimate of the infection fatality rate was available and thus I could compare the infection fatality rate from different studies evaluating the same location. The estimates of infection fatality rate tended to be more homogeneous within each location, while they differed markedly across locations (Fig. 2). Within the same location, infection fatality rate estimates tend to have only small differences, even though it is possible that different areas within the same location may also have real differences in infection fatality rate. France is one exception where differences are large, but both estimates come from population studies of outbreaks from schools and thus may not provide good estimates of population seroprevalence and may lead to an underestimated infection fatality rate.

I used summary estimates weighted for sample size to generate a single estimate for each location. Data were available for 51 different locations (including the inferred infection fatality rates from the eight preliminary additional national estimates in Table 5).

The median infection fatality rate across all 51 locations was 0.27% (corrected 0.23%). Most data came from locations with high death tolls from COVID-19 and 32 of the locations had a population mortality rate (COVID-19 deaths per million population) higher than the global average (118 deaths from COVID-19 per million as of 12 September 2020;[79] Fig. 3). Uncorrected estimates of the infection fatality rate of COVID-19 ranged from 0.01% to 0.67% (median 0.10%) across the 19 locations with a population mortality rate for COVID-19 lower than the global average, from 0.07% to 0.73% (median 0.20%) across 17 locations with population mortality rate higher than the global average but lower than 500 COVID-19 deaths per million, and from 0.20% to 1.63% (median 0.71%) across 15 locations with more than 500 COVID-19 deaths per million. The corrected estimates of the median infection fatality rate were

Table 3. **Estimated prevalence of COVID-19 and estimated number of people infected, 2020**

Country (location)	Seroprevalence, %			Estimated no. of people infected
	Crude	Adjusted		
		Value	Adjustments	
Argentina (Barrio Padre Mugica)[47]	ND	53.4	Age, sex, household, non-response	26 691
Belgium[38]	5.7	6.0	Sampling, age, sex, province	695 377
Brazil (133 cities)[25]	1.39	1.62 overall (0–25.0 across the 133 cities)	Test, design	1 209 435[a]
Brazil (Espirito Santo)[34]	2.1	ND	NA	84 391
Brazil (Maranhao)[68]	37	40.4	Clustering, stratification, non-response	2 877 454
Brazil (Rio de Janeiro), blood donors[41]	6	4.7	Age, sex, test	811 452
Brazil (Rio Grande do Sul)[17]	0.222	0.222[b]	Sampling	25 283
Brazil (Sao Paulo)[42]	5.2	4.7	Sampling design	14 017
Canada (British Columbia)[50]	0.45	0.55	Age	27 890
Chile (Vitacura)[43]	11.2	ND	NA	9 500
China, blood donors[55]				
Wuhan	3.87	ND	NA	433 827
Shenzhen	0.06	ND	NA	7 818
Shijiazhuang	0.02	ND	NA	2 206
China (Wuhan)[14]	10	ND	NA	1 108 000
China (Wuhan)[32]	8.36	ND	NA	926 288
Entire period	3.53	2.80	Age, sex, test	–
China (Guangzhou), blood donors[60]	0.09	ND	NA	104 783
China (several regions)[40]				
Hubei (not Wuhan)	3.6	ND	NA	1 718 110
Chongqing	3.8	ND	NA	11 956 109
Sichuan	0.6	ND	NA	487 847
Guangdong	2.2	ND	NA	2 522 010
Croatia[26]	1.27[c]	ND	NA	51 765
Denmark, blood donors[12]	2	1.9	Test	109 665
Denmark (Faroe Islands)[52]	0.6	0.7	Test	365
France (Crepy-en-Valois)[39]	10.4	ND	NA	620 105
France (Oise)[13]	25.9	ND	NA	1 548 000
Germany (Gangelt)[16]	15	20.0	Test, cluster, symptoms	2 519
Germany (Frankfurt)[21]	0.6	ND	NA	16 086
Greece[62]	0.42 (April)	0.49[d]	Age, sex, region	51 023
Hungary[57]	0.67	0.68	Design, age, sex, district	65 671
Iceland[58]	2.3 (quarantined), 0.3 (unknown exposure)	0.9	Including those positive by RT-PCR	3 177
India (Mumbai)[61]				534 750
Slum areas	54.1	58.4	Test, age, sex	–
Non-slum areas	16.1	17.3	Test, age, sex	–
India (Srinagar)[67]	3.8	3.6	Age, sex	54 000
Islamic Republic of Iran (Guilan)[8]	22	33.0	Test, sampling	770 000
Italy (Apulia), blood donors[31]	0.99	ND	NA	39 887
Japan (Kobe)[11]	3.3	2.7	Age, sex	40 999
Japan (Tokyo)[29]	3.83	ND	NA	532 450
Japan (Utsunomiya City)[48]	0.4	1.23	Age, sex, distance to clinic, district, cohabitants	6 378
Kenya, blood donors[44]	5.6	5.2	Age, sex, region, test	2 783 453
Luxembourg[20]	1.9	2.1	Age, sex, district	12 684
Netherlands, blood donors[15]	2.7	ND	NA	461 622
Netherlands (Rotterdam)[64]	3	ND	NA	512 910
Pakistan (Karachi)[49]	16.3	11.9	Age, sex	1 987 300
East	20.0	15.1	Age, sex	–
Malir	12.7	8.7	Age, sex	–
Pakistan (urban)[66]	17.5	ND	NA	13 825 000
Qatar[51]	30.4	ND	NA	851 200

(*continues. . .*)

(. . .*continued*)

Country (location)	Seroprevalence, %			Estimated no. of people infected
	Crude	Adjusted		
		Value	Adjustments	
Entire period	24.0	ND	NA	–
Republic of Korea[59]	0.07	ND	NA	1 867
Spain[36]	ND	5.0[e]	Sampling, age, sex, income	2 347 000
Spain (Barcelona)[30]	14.3	ND	NA	1 081 938
Switzerland (Geneva)[10]	10.6	10.9	Test, age, sex	54 500
Switzerland[28]				
Zurich[f]	Unclear	1.3	Multivariate Gaussian conditioning	19 773
Zurich and Lucerne[g]	Unclear	1.6	Multivariate Gaussian conditioning	30 888
United Kingdom (England)[65]	5.6	6.0	Test, sampling	3 360 000
United Kingdom (Scotland) blood donors[18]	1.2	ND	NA	64 800
USA (10 states)[35]				
Washington, Puget Sound	1.3	1.1	Age, sex, test	48 291
Utah	2.4	2.2	Age, sex, test	71 550
New York, New York City	5.7	6.9	Age, sex, test	641 778
Missouri	2.9	2.7	Age, sex, test	161 936
Florida, south	2.2	1.9	Age, sex, test	117 389
Connecticut	4.9	4.9	Age, sex, test	176 012
Louisiana	ND	5.8	Age, sex, test	267 033
California, San Francisco Bay	ND	1	Age, sex, test	64 626
Pennsylvania, Philadelphia	ND	3.2	Age, sex, test	156 633
Minnesota, Minneapolis	ND	2.4	Age, sex, test	90 651
USA (California, Bay Area) blood donors[24]	0.4	0.1	Test and confirmation	7 753
USA (California, Los Angeles)[22]	4.06	4.65	Test, sex, race and ethnicity, income	367 000
USA (California, San Francisco), in census tract 022 901[33]	4.3	6.1	Age, sex, race and ethnicity, test	316
USA (California, Santa Clara)[19]	1.5	2.6	Test, sampling, cluster	51 000
USA (Idaho, Boise)[9]	1.79	ND	NA	8620
USA (Georgia, DeKalb and Fulton counties)[53]	2.7	2.5	Age, sex, race and ethnicity	45 167
USA (Idaho, Blaine County)[46]	22.4	23.4	Test, age, sex, household	5 403
USA (Indiana)[54]	2.3 (IgG and RT-PCR)[h]	2.8	Age, race, Hispanic ethnicity	187 802
USA (Louisiana, Baton Rouge)[63]	6	6.6	Census, race, parish, including RT-PCR positives	46 147
USA (Louisiana, Orleans and Jefferson Parish)[37]	6.9 (IgG and RT-PCR)[h]	6.9 for IgG	Census weighting, demographics	56 578
USA (New York)[23]	12.5	14.0	Test, sex, age race and ethnicity, region	2 723 000
USA, New York[66]				
Columbia University Medical Center, New York City	5	ND	NA	463 044
CareMount central laboratory, five New York state counties	1.8	ND	NA	183 404
USA (New York, Brooklyn)[27]	47	ND	NA	1 203 154
USA (Rhode Island), blood donors[45]	3.9	ND	NA	41 384

COVID-19: coronavirus disease 2019; NA: not applicable; ND: no data available; RT-PCR: real-time polymerase chain reaction; test: test performance.

[a] The authors calculated 760 000 to be infected in the 90 cities that had 200–250 samples tested, but many of the other 43 cities with < 200 samples may be equally or even better represented since they tended to be smaller than the 90 cities (mean population 356 213 versus 659 326).

[b] An estimate is also provided adjusting for test performance, but the assumed specificity of 99.0% seems inappropriately low, since as part of the validation process the authors found that several of the test-positive individuals had household members who were also infected, thus the estimated specificity was deemed by the authors to be at least 99.95%.

[c] 1.20% in workers in Split without mobility restrictions, 3.37% in workers in Knin without mobility restrictions, 1.57% for all workers without mobility restrictions; Split and Knin tended to have somewhat higher death rates than nationwide Croatia, but residence of workers is not given, so the entire population of the country is used in the calculations.

[d] An estimate is also provided adjusting for test performance resulting in adjusted seroprevalence of 0.23%, but this seems inappropriately low, since the authors report that all positive results were further validated by ELISA (enzyme-linked immunosorbent assay).

[e] 5.0% with point of care test, 4.6% with immunoassay, 3.7% with both tests positive, 6.2% with at least one test positive.

[f] Patients during 1–15 April.

[g] Blood donors in May.

[h] The study counts in prevalence also those who were currently/recently infected as determined by a positive RT-PCR.

Notes: Of the studies where seroprevalence was evaluated at multiple consecutive time points, the seroprevalence estimate was the highest in the most recent time interval with few exceptions, for example: in the Switzerland (Geneva) study,[10] the highest value was seen 2 weeks before the last time interval; in the Switzerland (Zurich) study,[28] the highest value was seen in the period 1–15 April for patients at the university hospital and in May for blood donors; and in the China (Wuhan) study,[32] the highest value was seen about 3 weeks before the last time interval.

Table 4. **Deaths from COVID-19 and inferred infection fatality rates, overall and in people younger than 70 years, by location, 2020**

Location	No. of site-specific cumulative deaths from COVID-19 (to date)[a]	Inferred infection fatality rate, % (corrected)	% of site-specific cumulative deaths from COVID-19 in people < 70 years[a]	Infection fatality rate in people < 70 years, % (corrected)
Argentina (Barrio Padre Mugica)[47]	44 (1 July)	0.16 (0.13)	~70	0.11 (0.09)
Belgium[38]	7594 (30 April)	1.09 (0.87)	10	0.13 (0.10)
Brazil (133 cities)[25]	–[b]	Median 0.30 (0.27)	31 (< 60 years)	0.10 (0.09)
Brazil (Espirito Santo)[34]	363 (21 May)	0.43 (0.39)	31 (Brazil, < 60 years)	0.14 (0.13)
Brazil (Maranhao)[68]	4272 (8 August)	0.15 (0.14)	23	0.04 (0.03)
Brazil (Rio de Janeiro), blood donors[41]	1019 (3 May)	0.12 (0.11)	31 (Brazil, < 60 years)	0.04 (0.04)
Brazil (Rio Grande do Sul)[17]	124 (14 May)	0.49 (0.39)	31 (Brazil, < 60 years)	0.19 (0.15)
Brazil (Sao Paulo)[42]	NA[c] (15 May)	Unknown, but likely > 0.4	31 (Brazil, < 60 years)	Unknown, but likely > 0.1
Canada (British Columbia)[50]	164 (28 May)	0.59 (0.59)	13	0.08 (0.08)
Chile (Vitacura)[43]	NA[c] (18 May)	Unknown, but likely < 0.2	36 (Chile)	Unknown, but likely < 0.1
China, blood donors[55]				
Wuhan	1935 (20 February)	0.45 (0.41)	50	0.24 (0.22)
Shenzhen	1 (5 March)	0.01 (0.01)	About 50 (if similar to Wuhan)	0.01 (0.01)
Shijiazhuang	1 (27 February)	0.05 (0.04)	About 50 (if similar to Wuhan)	0.03 (0.02)
China (Wuhan)[14]	3869 (2 May)	0.35 (0.31)	50	0.19 (0.15)
China (Wuhan)[32]	3869 (13 April)	0.42 (0.38)	50	0.23 (0.21)
China (Guangzhou), blood donors[60]	8 (5 April)	0.00 (0.00)	About 50 (if similar to Wuhan)	0.00 (0.00)
China (several regions)[40]				
Hubei (not Wuhan)	643 (12 April)	0.04 (0.03)	About 50 (if similar to Wuhan)	0.02 (0.02)
Chongqing	6 (12 April)	0.00 (0.00)	About 50 (if similar to Wuhan)	0.00 (0.00)
Guangdong	8 (12 April)	0.00 (0.00)	About 50 (if similar to Wuhan)	0.00 (0.00)
Sichuan	3 (12 April)	0.00 (0.00)	About 50 (if similar to Wuhan)	0.00 (0.00)
Croatia[26]	79 (3 May)	0.15 (0.14)	13	0.02 (0.02)
Denmark, blood donors[12]	370 (21 April)	0.34 (0.27)	12	0.05 (0.04)
Faroe Islands[52]	0 (5 May)	0.00 (0.00)	0	0.00 (0.00)
France (Crepy-en-Valois)[39]	2325 (5 May)[d]	0.37 (0.30)	7 (France, < 65 years)	0.04 (0.03)
France (Oise)[13]	932 (7 April)[d]	0.06 (0.05)	7 (France, < 65 years)	0.01 (0.01)
Germany (Gangelt)[16]	7 (15 April)	0.28 (0.25)	0	0.00 (0.00)
Germany (Frankfurt)[21]	42[e] (17 April)	0.26 (0.21)	14 (Germany)	0.04 (0.03)
Greece[62]	121 (22 April)	0.24 (0.19)	30	0.09 (0.07)
Hungary[57]	442 (15 May)	0.67 (0.54)	No data	No data
Iceland[58]	10 (1 June)	0.30 (0.30)	30	0.10 (0.10)
India (Mumbai)[61]	495 (13–20 July)	0.09 (0.07)	50 (< 60 years, India)	0.04 (0.03)
India (Srinagar)[67]	35 (15 July)[f]	0.06 (0.05)	50 (< 60 years, India)	0.03 (0.03)
Islamic Republic of Iran (Guilan)[8]	617 (23 April)	0.08 (0.07)	No data	No data
Italy (Apulia), blood donors[31]	530 (22 May)	1.33 (1.20)	15 (Italy)	0.24 (0.22)
Japan (Kobe)[11]	10 (mid-April)	0.02 (0.02)	21 (Japan)	0.01 (0.01)
Japan (Tokyo)[29]	189 (11 May)	0.04 (0.03)	21 (Japan)	0.01 (0.01)
Japan (Utsunomiya City)[48]	0 (14 June)	0.00 (0.00)	0	0.00 (0.00)
Kenya, blood donors[44]	64 (31 May)	0.00 (0.00)	58 (< 60 years)	0.00 (0.00)
Luxembourg[20]	92 (2 May)	0.73 (0.58)	9	0.07 (0.06)
Netherlands, blood donors[15]	3134 (15 April)	0.68 (0.68)	11	0.09 (0.09)
Netherlands (Rotterdam)[64]	3134 (15 April)	0.65 (0.52)	11	0.08 (0.06)
Pakistan (Karachi)[49]	~1500 (9 July)[g]	0.08 (0.07)	~70	0.06 (0.05)
Pakistan (urban)[66]	5266 (13 July)[h]	0.04 (0.04)	~70	0.03 (0.03)
Qatar[51]	93 (19 June)	0.01 (0.01)	74	0.01 (0.01)
Republic of Korea[59]	2 (3 June)[i]	0.10 (0.09)	0	0.00 (0.00)
Spain[36]	26 920 (11 May)	1.15 (0.92)	13	0.18 (0.14)
Spain (Barcelona)[30]	5137 (2 May)	0.48 (0.48)	13 (Spain)	0.07 (0.07)
Switzerland (Geneva)[10]	243 (30 April)	0.45 (0.36)	8	0.04 (0.03)

(*continues. . .*)

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Location	No. of site-specific cumulative deaths from COVID-19 (to date)[a]	Inferred infection fatality rate, % (corrected)	% of site-specific cumulative deaths from COVID-19 in people < 70 years[a]	Infection fatality rate in people < 70 years, % (corrected)
Switzerland (Zurich)[28]	107 (15 April, Zurich), 147 (22 May, Zurich and Lucerne)	0.51 (0.41)	8 (Switzerland)	0.05 (0.04)
England[65]	38 854 (9 July)	1.16 (0.93)	20	0.27 (0.22)
Scotland, blood donors[18]	47 (1 April)	0.07 (0.06)	9 (< 65 years)	0.01 (0.01)
USA (10 states)[35]				
Washington, Puget Sound	207 (4 April)	0.43 (0.43)	10 (state, < 60 years)	0.05 (0.05)
Utah	58 (4 May)	0.08 (0.08)	28 (< 65 years)	0.03 (0.03)
New York	4146 (4 April)	0.65 (0.65)	34 (state)	0.25 (0.25)
Missouri	329 (30 April)	0.20 (0.20)	23	0.05 (0.05)
Florida, south	295 (15 April)	0.25 (0.25)	28 (state)	0.08 (0.08)
Connecticut	2718 (6 May)	1.54 (1.54)	18	0.31 (0.31)
Louisiana	806 (11 April)	0.30 (0.30)	32	0.10 (0.10)
California, San Francisco Bay	321 (1 May)	0.50 (0.50)	25	0.14 (0.14)
Pennsylvania, Philadelphia	697 (26 April)	0.45 (0.45)	21 (state)	0.10 (0.10)
Minnesota, Minneapolis	436 (13 May)	0.48 (0.48)	20 (state)	0.10 (0.10)
USA (California, Bay Area)[24]	12 (22 March)	0.15 (0.12)	25	0.04 (0.03)
USA (California, Los Angeles)[22]	724 (19 April)	0.20 (0.18)	24 (< 65 years)	0.06 (0.05)
USA (California, San Francisco)[33]	0 (4 May)	0.00 (0.00)	0	0.00 (0.00)
USA (California, Santa Clara)[19]	94 (22 April)	0.18 (0.17)	35	0.07 (0.06)
USA (Idaho, Boise)[9]	14 (24 April)	0.16 (0.13)	14 (Idaho)	0.02 (0.02)
USA (Georgia)[53]	198 (7 May)	0.44 (0.44)	30	0.15 (0.15)
USA (Idaho, Blaine County)[46]	5 (19 May)	0.10 (0.08)	14 (Idaho)	0.02 (0.01)
USA (Indiana)[54]	1099 (30 April)	0.58 (0.46)	24	0.16 (0.13)
USA (Louisiana, Baton Rouge)[63]	420 (30 July)	0.91 (0.73)	32 (Louisiana)	0.32 (0.25)
USA (Louisiana, Orleans and Jefferson Parish)[37]	925 (16 May)	1.63 (1.31)	32	0.57 (0.46)
USA (New York)[23]	18 610 (30 April)[j]	0.68 (0.54)[j]	34	0.26 (0.23)
USA (New York Columbia University Medical Center, New York City and CareMount central laboratory, five New York state counties)[56]	965 (28 March, New York state)	0.15 (0.14)	34	0.06 (0.05)
USA (New York, Brooklyn)[27]	4894 (19 May)[j]	0.41 (0.33)[j]	34 (New York state)	0.15 (0.14)
USA (Rhode Island), blood donors[45]	430 (11 May)	1.04 (0.83)	17	0.20 (0.16)

COVID-19: coronavirus disease 2019; NA: not available.

[a] Whenever the number or proportion of COVID-19 deaths at age < 70 years was not provided in the paper, I retrieved the proportion of these deaths from situation reports of the relevant location. If I could not find this information for the specific location, I used a larger geographic area. For Brazil, the closest information that I found was from a news report.[77] For Croatia, I retrieved data on age for 45/103 deaths through Wikipedia.[78] Geographical location in parentheses specifies the population

[b] Data are provided by the authors for deaths per 100 000 population in each city along with inferred infection fatality rate in each city, with wide differences across cities; the infection fatality rate shown here is the median across the 36 cities with 200–250 samples and at least one positive sample (the interquartile range for the uncorrected infection fatality rate is 0.20–0.60% and across all cities is 0–2.4%, but with very wide uncertainty in each city). A higher infection fatality rate is alluded to in the preprint, but the preprint also shows a scatter diagram for survey-based seroprevalence versus reported deaths per population with a regression slope that agrees with an infection fatality rate of 0.3%.

[c] Information on deaths was not available for the specific locations. In the Sao Paulo study, the authors selected six districts of Sao Paulo most affected by COVID-19; they do not name the districts and the number of deaths as of mid-May is not available, but using data for death rates across all Sao Paulo would give an infection fatality rate of > 0.4% overall. In the Vitacura study, similarly one can infer from the wider Santiago metropolitan area that the infection fatality rate in the Vitacura area would probably be < 0.2% overall.

[d] For France, government situation reports provide the number of deaths per region only for in-hospital deaths; therefore, I multiplied the number of in-hospital deaths by a factor equal to: total number of deaths/in-hospital deaths for all of France.

[e] Estimated from number of deaths in Hesse province on 17 April × proportion of deaths in the nine districts with key enrolment (enrolment ratio > 1:10 000) in the study among all deaths in Hesse province.

[f] I calculated the approximate number of deaths assuming the same case fatality ratio in the Srinagar district as in the Jammu and Kashmir state where it is located.

[g] For Karachi, it is assumed that about 30% of COVID-19 deaths in Pakistan are in Karachi (since about 30% of the cases are there).

[h] The number of deaths across all Pakistan; I assumed that this number is a good approximation of deaths in urban areas (most deaths occur in urban areas and there is some potential underreporting).

[i] I calculated the approximate number of deaths from the number of cases in the study areas in south-western Seoul, assuming a similar case fatality as in Seoul overall.

[j] Confirmed COVID-19 deaths; inclusion of probable COVID-19 deaths would increase the infection fatality rate estimates by about a quarter.

Note: Cumulative deaths are sourced from the specific study or from situation report on the same location unless otherwise stated.

0.09%, 0.20% and 0.57%, respectively, for the three location groups.

For people younger than 70 years old, the infection fatality rate of COVID-19 across 40 locations with available data ranged from 0.00% to 0.31% (median 0.05%); the corrected values were similar.

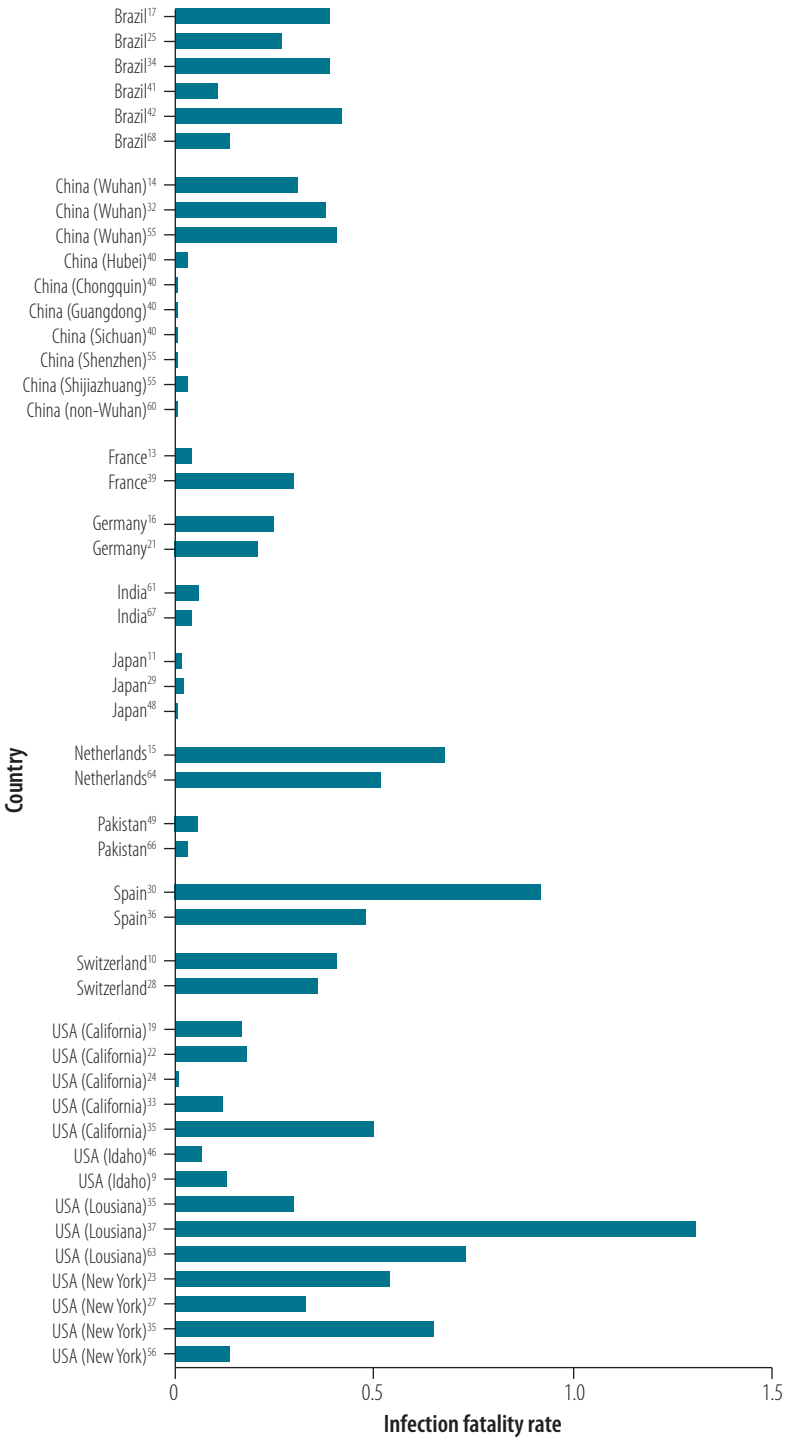
Discussion

The infection fatality rate is not a fixed physical constant and it can vary substantially across locations, depending on the population structure, the case-mix of infected and deceased individuals and other, local factors. The studies analysed here represent 82 different estimates of the infection fatality rate of COVID-19, but they are not fully representative of all countries and locations around the world. Most of the studies are from locations with overall COVID-19 mortality rates that are higher than the global average. The inferred median infection fatality rate in locations with a COVID-19 mortality rate lower than the global average is low (0.09%). If one could sample equally from all locations globally, the median infection fatality rate might even be substantially lower than the 0.23% observed in my analysis.

COVID-19 has a very steep age gradient for risk of death.[80] Moreover, in European countries that have had large numbers of cases and deaths[81], and in the USA[82], many, and in some cases most, deaths occurred in nursing homes. Locations with many nursing home deaths may have high estimates of the infection fatality rate, but the infection fatality rate would still be low among non-elderly, non-debilitated people.

Within China, the much higher infection fatality rate estimates in Wuhan compared with other areas of the country may reflect widespread nosocomial infections,[83] as well as unfamiliarity with how to manage the infection as the first location that had to deal with COVID-19. The very many deaths in nursing homes, nosocomial infections and overwhelmed hospitals may also explain the high number of fatalities in specific locations in Italy[84] and New York and neighbouring states.[23,27,35,56] Poor decisions (e.g. sending COVID-19 patients to nursing homes), poor management (e.g. unnecessary mechanical ventilation and hydroxychloroquine) may also have contributed to worse outcomes.

Fig. 2. **Estimates of infection fatality rates for COVID-19 in locations that had two or more estimates, 2020**



COVID-19: coronavirus disease 2019.
Notes: Locations are defined at the level of countries, except for the United States of America where they are defined at the level of states and China is separated into Wuhan and non-Wuhan areas. Corrected infection fatality rate estimates are shown (correcting for what types of antibodies were assayed).

High levels of congestion (e.g. in busy public transport systems) may also have exposed many people to high infectious loads and, thus, perhaps more severe disease. A more aggressive viral clade has also been speculated.[85] The infection fatality rate may be very high among disadvantaged populations and in settings with a combination of factors predisposing to higher fatalities.[37]

Very low infection fatality rates seem common in Asian coun-

Table 5. **Infection fatality rates for COVID-19 inferred from preliminary nationwide seroprevalence data, 2020**

Country	Sample size	Date	Reported seroprevalence (%)	Population, no.	Deaths, no. (date)	Inferred infection fatality rate (corrected), %
Afghanistan[75]	9 500 (NR)	NR	31.5	39 021 453	1 300 (8 May)	0.01 (0.01)
Czechia[71]	26 549 (IgG)	23 April–1 May	0.4	10 710 000	252 (4 May)	0.59 (0.47)
Finland[69]	674 (IgG)	20–26 April[a]	2.52	5 541 000	211 (30 April)	0.15 (0.12)
Georgia[76]	1 068 (NR)	18–27 May	1	3 988 264	12 (30 May)	0.03 (0.03)[b]
Israel[72]	1 709 (NR)	May	2–3	9 198 000	299 (10 June)	0.13 (0.10)[c]
Russian Federation[74]	650 000 (NR)	NR	14	145 941 776	5 859 (7 June)	0.03 (0.03)
Slovenia[73]	1 368 (NR)	April	3.1	2 079 000	92 (1 May)	0.14 (0.11)
Sweden[70]	1 200 (IgG)	18–24 May	6.3	10 101 000	4 501 (28 May)	0.71 (0.57)

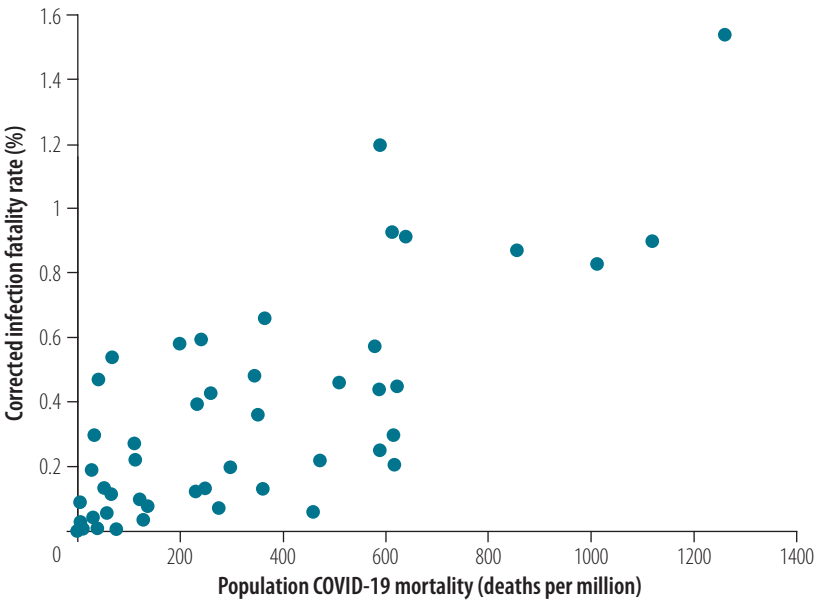
COVID-19: coronavirus disease 2019; Ig: immunoglobin; NR: not reported.
[a] The seroprevalence was slightly lower in subsequent weeks.
[b] The survey was done in Tbilisi, the capital city with a population 1.1 million. I could not retrieve the count of deaths in Tbilisi, but if more deaths happened in Tbilisi, then the infection fatality rate may be higher, but still < 0.1%.
[c] Assuming a seroprevalence of 2.5%.
Notes: These are countries for which no eligible studies were retrieved in the literature search. The results of these studies have been announced to the press and/or in preliminary reports, but are not yet peer reviewed and published.

tries.[8,11,29,48,49,51,59,61,67] A younger population in these countries (excluding Japan), previous immunity from exposure to other coronaviruses, genetic differences, hygiene etiquette, lower infectious load and other unknown factors may explain these low rates. The infection fatality rate is low also in low-income countries in both Asia and Africa,[44,49,66,67] perhaps reflecting the young age structure. However, comorbidities, poverty, frailty (e.g. malnutrition) and congested urban living circumstances may have an adverse effect on risk and thus increase infection fatality rate.

Antibody titres may decline with time[10,28,32,86,87] and this would give falsely low prevalence estimates. I considered the maximum seroprevalence estimate when multiple repeated measurements at different time points were available, but even then some of this decline cannot be fully accounted for. With four exceptions,[10,28,32,51] the maximum seroprevalence value was at the latest time point.

Positive controls for the antibody assays used were typically symptomatic patients with positive polymerase chain reaction tests. Symptomatic patients may be more likely to develop antibodies.[87–91] Since seroprevalence studies specifically try to reveal undiagnosed asymptomatic and mildly symptomatic infections, a lower sensitivity for these mild infections could lead to substantial underestimates of the number of

Fig. 3. **Corrected estimates of COVID-19 infection fatality rate in each location plotted against COVID-19 cumulative deaths per million as of September 12 2020 in that location**



COVID-19: coronavirus disease 2019.
Notes: Locations are defined at the level of countries, except for the United Kingdom of Great Britain and Northern Ireland where they are defined by jurisdiction, United States of America (USA) are defined at the level of states and China is separated into Wuhan and non-Wuhan areas. Included locations are: Afghanistan; Argentina; Belgium; Brazil; Canada; Chile; China (non-Wuhan and Wuhan); Croatia; Czechia; Denmark; Faroe Islands; Finland; France; Georgia; Germany; Greece; Hungary; Iceland; India; Iran (Islamic Republic of); Israel; Italy; Japan; Kenya; Luxembourg; Netherlands; Pakistan; Qatar; Republic of Korea; Russian Federation; Slovenia; Spain; Sweden; Switzerland; United Kingdom (England, Scotland); and USA (California, Connecticut, Florida, Georgia, Idaho, Indiana, Louisiana, Minnesota, Missouri, New York, Pennsylvania, Rhode Island, Utah, Washington). When several infection fatality rate estimates were available from multiple studies for a location, the sample size-weighted mean is used. One outlier location with very high deaths per million population (1702 for New York) is not shown.

infected people and overestimates of the inferred infection fatality rate.

A main issue with seroprevalence studies is whether they offer a representative picture of the population in the assessed region. A generic problem is that vulnerable people at high risk of infection and/or death may be more difficult to recruit in survey-type studies. COVID-19 infection is particularly widespread and/or lethal in nursing homes, in homeless people, in prisons and in disadvantaged minorities.[92] Most of these populations are very difficult, or even impossible, to reach and sample and they are probably under-represented to various degrees (or even entirely missed) in surveys. This sampling obstacle would result in underestimating the seroprevalence and overestimating infection fatality rate.

In principle, adjusted seroprevalence values may be closer to the true estimate, but the adjustments show that each study alone may have unavoidable uncertainty and fluctuation, depending on the type of analysis chosen. Furthermore, my corrected infection fatality rate estimates try to account for undercounting of infected people when not all three antibodies (IgG, IgM and IgA) were assessed. However, the magnitude of the correction is uncertain and may vary in different circumstances. An unknown proportion of people may have responded to the virus using immune mechanisms (mucosal, innate, cellular) without generating any detectable serum antibodies.[93–97]

A limitation of this analysis is that several studies included have not yet been fully peer-reviewed and some are still ongoing. Moreover, despite efforts made by seroprevalence studies to generate estimates applicable to the general population, representativeness is difficult to ensure, even for the most rigorous studies and despite adjustments made. Estimating a single infection fatality rate value for a whole country or state can be misleading, when there is often huge variation in the population mixing patterns and pockets of high or low mortality. Furthermore, many studies have evaluated people within restricted age ranges, and the age groups that are not included may differ in seroprevalence. Statistically significant, modest differences in seroprevalence across some age groups have been observed in several studies.[10,13,15,23,27,36,38] Lower values have been seen in young children and higher values in adolescents and young adults, but these patterns are inconsistent and not strong enough to suggest that major differences are incurred by extrapolating across age groups.

Acknowledging these limitations, based on the currently available data, one may project that over half a billion people have been infected as of 12 September 2020, far more than the approximately 29 million documented laboratory-confirmed cases. Most locations probably have an infection fatality rate less than 0.20% and with appropriate, precise non-pharmacological measures that selectively try to protect high-risk vulnerable populations and settings, the infection fatality rate may be brought even lower. ■

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Competing interests: I am a co-author (not principal investigator) of one of the seroprevalence studies.

ملخص

معدل وفيات عدوى كوفيد 19 المستدل عليه من بيانات الانتشار المصلي

الغرض تقدير معدل الوفيات الناجمة عن الإصابة بمرض فيروس كورونا 2019 (كوفيد 19) من بيانات الانتشار المصلي.

الطريقة قمت بالبحث في خوادم PubMed وخوادم ما قبل الطباعة عن دراسات الانتشار المصلي لكوفيد 19، بحجم عينة أكبر من أو تساوي 500 بدءاً من 9 سبتمبر/أيلول 2020. كما أنني استرجعت النتائج الإضافية للدراسات الوطنية من البيانات الصحفية والتقارير الأولية. قمت بتقييم دراسات ميزات التصميم وتقديرات الانتشار المصلي. لقد قمت بتقدير معدل الوفيات الناجمة عن الإصابة لكل دراسة عن طريق قسمة العدد الإجمالي للوفيات الناتجة عن جائحة كوفيد 19، على عدد الأشخاص المقدر إصابتهم في كل منطقة. وقمت بتصحيح عدد أنواع الأجسام المضادة التي تم اختبارها (الغلوبين المناعي، IgA ، IgM ، IgG).

النتائج قمت بتضمين 61 دراسة (74 تقديرًا) وثمانية تقديرات وطنية أولية. تراوحت تقديرات الانتشار المصلي من 0.02% إلى 53.40%. تراوحت معدلات وفيات العدوى من 0.00% إلى 1.63%، وتم تصحيح القيم من 0.00% إلى 1.54%. عبر 51 موقعًا، كان متوسط معدل وفيات عدوى كوفيد 19 هو 0.27% (تصحيح بنسبة 0.23%): كان المعدل 0.09% في المواقع التي تقل فيها معدلات وفيات السكان المصابين بكوفيد 19 عن المتوسط العالمي (أكثر من 118 حالة وفاة/مليون نسمة)، و0.20% في المواقع التي يوجد بها من 118 إلى 500 حالة وفاة/مليون نسمة مصابين بكوفيد 19، و0.57% في مواقع بها أكثر من 500 حالة وفاة/مليون نسمة بسبب كوفيد 19. في الأشخاص الذين تقل أعمارهم عن 70 عامًا، تراوحت معدلات وفيات الإصابة بالعدوى من 0.00% إلى 0.31% بمتوسطات مبدئية ومصححة قدرها 0.05%.

الاستنتاج يمكن أن يختلف معدل وفيات الإصابة بفيروس كوفيد 19 بشكل كبير عبر المواقع المختلفة، وقد يعكس هذا الاختلافات في التركيب العمري للسكان، ومزيج الحالات من المرضى المصابين والمتوفين، وعوامل أخرى. تميل معدلات الوفيات المستدل عنها من العدوى إلى أن تكون أقل بكثير من التقديرات التي تم إجراؤها في وقت سابق في الجائحة.

摘要

根据血清阳性率数据推断新型冠状病毒肺炎的感染死亡率

目的 根据血清阳性率数据估计 2019 年冠状病毒病（新型冠状病毒肺炎）的感染死亡率。

方法 在 PubMed 和预印本服务器上查找截至 2020 年 9 月 9 日新型冠状病毒肺炎相关的血清阳性率研究，样本量为 500 个。另外根据初步新闻稿和报告检索了其他全国性研究结果。并评估了与设计特征和血清阳性率估计值相关的研究。通过将新型冠状病毒肺炎累计死亡人数除以每个地区估计感染人数，估算出了每项研究的感染死亡率。然后校正了测试的抗体类型（免疫球蛋白、免疫球蛋白 G、免疫球蛋白 M、免疫球蛋白 A）的数量。

结果 我汇总了 61 项研究（74 个估计值）和 8 个全国性初步估计值。血清阳性率估计值介于 0.02% 至 53.40% 之间。感染死亡率介于 0.00% 至 1.63% 之间，校正值则介于 0.00% 至 1.54% 之间。在 51 个地区中，新型冠状病毒肺炎感染死亡率的中位数为 0.27%（校正值为 0.23%）：在新型冠状病毒肺炎导致的人口死亡率低于全球平均水平（每一百万人口中死亡病例小于 118 例）的地区中，该比率为 0.09%；在每一百万人口中新型冠状病毒肺炎死亡病例介于 118 – 500 例之间的地区，该比率为 0.20%；而在每一百万人口中新型冠状病毒肺炎死亡病例大于 500 例的地区，该比率则为 0.57%。70 岁以下人群的感染死亡率介于 0.00% 至 0.31% 之间，经粗略校正后该比率的中位数为 0.05%。

结论 不同地区的新型冠状病毒肺炎感染死亡率可能存在很大的差异，据此可反映出在人口年龄结构、感染和死亡病例组合以及其他因素方面存在差异。推断的感染死亡率往往比全球性流行病爆发初期的估计值要低得多。

Résumé

Ratio de létalité réel de la COVID-19 déduit à partir des données de séroprévalence

Objectif Estimer le ratio de létalité réel de la maladie à coronavirus 2019 (COVID-19) à partir des données de séroprévalence.

Méthodes J'ai effectué des recherches sur PubMed et sur les serveurs de prépublication afin de trouver des études consacrées à la séroprévalence de la COVID-19, avec des échantillons ≥ 500, au 9 septembre 2020. J'ai également prélevé des résultats supplémentaires dérivés d'études nationales qui figurent dans les versions préliminaires de divers rapports et communiqués de presse. J'ai analysé les études pour y déceler des caractéristiques de conception et des estimations de séroprévalence. Ensuite, j'ai calculé le ratio de létalité réel pour chaque étude en divisant le nombre cumulé de décès dus à la COVID-19 par le nombre d'individus qui auraient été infectés dans chaque région. Enfin, j'ai apporté des corrections en fonction des types d'anticorps testés (immunoglobulines, IgG, IgM, IgA).

Résultats J'ai pris 61 études en compte (74 estimations) et huit estimations nationales préliminaires. Les estimations en matière de séroprévalence étaient comprises entre 0,02% et 53,40%. Les ratios de létalité réels allaient de 0,00% à 1,63%, les valeurs corrigées de 0,00% à 1,54%. Dans les 51 lieux étudiés, la médiane du ratio de létalité réel pour la COVID-19 s'élevait à 0,27% (0,23% après correction): le ratio était de 0,09% dans les endroits où le taux de mortalité dû à la COVID-19 était inférieur à la moyenne mondiale (< 118 décès/million d'habitants), de 0,20% dans les endroits dénombrant 118–500 décès COVID-19/million d'habitants, et de 0,57% là où la COVID-19 était responsable de > 500 décès/million d'habitants. Chez les personnes de moins de 70 ans, les ratios de létalité réels se situaient entre 0,00% et 0,31% avec des médianes brutes et corrigées de 0,05%.

Conclusion Le ratio de létalité réel de la COVID-19 peut considérablement varier d'un endroit à l'autre, ce qui pourrait correspondre aux différences de structure de pyramide des âges au sein de la population, au case-mix entre patients infectés et décédés, ainsi qu'à d'autres facteurs. Les ratios de létalité réels que j'ai pu déduire avaient tendance à être nettement inférieurs aux estimations formulées précédemment durant la pandémie.

Резюме

Показатель летальности при инфицировании COVID-19, определенный на основании данных о сераспространенности

Цель Оценить показатель летальности при инфицировании коронавирусным заболеванием 2019 г. (COVID-19) на основании данных о сераспространенности.

Методы Автор провел поиск на серверах PubMed и серверах предварительной публикации на предмет исследований сераспространенности COVID-19 с размером выборки ≥500 по состоянию на 9 сентября 2020 года. Были также получены дополнительные результаты национальных исследований из предварительных пресс-релизов и отчетов. Автор оценил исследования по элементам дизайна и оценкам сераспространенности. Автор оценил показатель летальности при инфицировании для каждого исследования, разделив общее количество смертей от COVID-19 на количество людей, предположительно инфицированных в каждом регионе. При этом была сделана поправка на количество протестированных типов антител (иммуноглобины, IgG, IgM, IgA).

Результаты В работу вошло 61 исследование (74 прогноза) и восемь предварительных национальных прогнозов. Прогнозы сераспространенности варьировались в диапазоне от 0,02 до 53,40%. Показатели летальности при инфицировании варьировались в диапазоне от 0,00 до 1,63%, скорректированные значения — от 0,00 до 1,54%. В 51 регионе средний показатель летальности при инфицировании COVID-19 составил 0,27% (скорректированный показатель 0,23%): этот показатель составил 0,09% в регионах с уровнем летальности населения от COVID-19 ниже, чем в среднем по миру (<118 смертей на миллион), 0,20% в регионах, в которых зарегистрировано 118–500 случаев смерти от COVID-19 на миллион человек, и 0,57% в регионах, где зарегистрировано более 500 случаев смерти от COVID-19 на миллион человек. У людей младше 70 лет показатель летальности при инфицировании колебался в пределах от 0,00 до

0,31% с приблизительными и скорректированными медианными значениями 0,05%.

Вывод Показатель летальности при инфицировании COVID-19 может существенно различаться в разных регионах, и это может отражать различия в возрастной структуре населения, структуре случаев инфицирования и смерти пациентов, а также в других факторах. Предполагаемые показатели летальности при инфицировании, как правило, были намного ниже, чем прогнозы, сделанные ранее во время пандемии.

Resumen

Tasa de letalidad por la infección de la COVID-19 calculada a partir de los datos de seroprevalencia

Objetivo Estimar la tasa de letalidad por la infección de la enfermedad por coronavirus de 2019 (COVID-19) a partir de los datos de seroprevalencia.

Métodos Se buscaron los estudios de seroprevalencia de la COVID-19 con un tamaño de muestra mayor o igual a 500 a partir del 9 de septiembre de 2020 en PubMed y en los servidores de preimpresión. Además, se recuperaron los resultados adicionales de los estudios nacionales a partir de los comunicados de prensa y de los informes preliminares. Se evaluaron los estudios para determinar las características de diseño y las estimaciones de seroprevalencia. Para calcular la tasa de letalidad por la infección de cada estudio, se dividió la cantidad acumulada de muertes por la COVID-19 por la cantidad de personas que se estima que están infectadas en cada región. Asimismo, se corrigió la cantidad de tipos de anticuerpos probados (inmunoglobulinas, IgG, IgM, IgA).

Resultados Se incluyeron 61 estudios (74 estimaciones) y 8 estimaciones nacionales preliminares. Las estimaciones de seroprevalencia oscilaban entre el 0,02 % y el 53,40 %. Las tasas de letalidad por la infección oscilaron entre el 0,00 % y el 1,63 %, los valores corregidos entre el 0,00 % y el 1,54 %. En 51 lugares, la mediana de la tasa de letalidad por la infección de la COVID-19 fue del 0,27 % (corregida en un 0,23 %): la tasa fue del 0,09 % en lugares donde las tasas de letalidad de la población con la COVID-19 eran inferiores al promedio mundial (menos de 118 muertes/millón), del 0,20 % en lugares con 118-500 muertes a causa de la COVID-19/millón de personas y del 0,57 % en lugares con más de 500 muertes a causa de la COVID-19/millón de personas. En personas menores de 70 años, las tasas de letalidad por la infección oscilaron entre el 0,00 % y el 0,31 % con medianas brutas y corregidas del 0,05 %.

Conclusión La tasa de letalidad por infección de la COVID-19 puede variar de manera sustancial en diferentes lugares y esto puede reflejar diferencias en la estructura de edad de la población y en la variedad de casos de los pacientes infectados y fallecidos, así como en otros factores. Las tasas de letalidad por infección que se calculan tienden a ser mucho más bajas que las estimaciones realizadas a principios de la pandemia.

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Table 1. **Eligible seroprevalence studies on COVID-19 published or deposited as preprints as of 9 September 2020: dates, sampling and recruitment**

Author	Country (location)	Dates	Sampling and recruitment
Figar et al.[47]	Argentina (Barrio Padre Mugica)	10–26 June	Probabilistic sampling of a slum neighbourhood, sampling from people 14 years or older across households
Herzog et al.[38]	Belgium	30 March–5 April and 20–26 April	Residual sera from 10 private diagnostic laboratories in Belgium, with fixed numbers per age group, region and periodical sampling, and stratified by sex
Hallal et al.[25]	Brazil	15–22 May	Sampling from 133 cities (the main city in each region), selecting 25 census tracts with probability proportionate to size in each sentinel city, and 10 households at random in each tract. Aiming for 250 participants per city
Gomes et al.[34]	Brazil (Espirito Santo)	13–15 May	Cross-section of major municipalities with houses as the sampling units
Da Silva et al.[68]	Brazil (Maranhao)	27 July–8 August	Three-stage cluster sampling stratified by four state regions in the state of Maranhao; the estimates took clustering, stratification and non-response into account
Amorim Filho et al.[41]	Brazil (Rio de Janeiro)	14–27 April (eligible: 24–27 April)	Blood donors without flulike symptoms within 30 days of donation; had close contact with suspected or confirmed COVID-19 cases in the 30 days before donation; or had travelled abroad in the past 30 days
Silveira et al.[17]	Brazil (Rio Grande do Sul)	9–11 May (third round, after 11–13 April, and 25–27 April)	Multistage probability sampling in each of nine cities to select 500 households, from which one member was randomly chosen for testing
Tess et al.[42]	Brazil (Sao Paulo)	4–12 May	Randomly selected adults and their cohabitants sampled from six districts of Sao Paulo City with high numbers of cases
Skowronski et al.[50]	Canada (British Columbia)	15–27 May (after baseline in 5–13 March)	Specimens from patients attending one of about 80 diagnostic service centres of the only outpatient laboratory network in the Lower Mainland
Torres et al.[43]	Chile (Vitacura)	4–19 May	Classroom stratified sample of children and all staff in a community placed on quarantine after school outbreak
Chang et al.[55]	China	January–April weekly: 3–23 February (Wuhan); 24 February–15 March (Shenzhen); 10 February–1 March (Shijiazhuang)	38 144 healthy blood donors in Wuhan, Shenzhen and Shijiazhuang who met the criteria for blood donation during the COVID-19 pandemic in China
Wu et al.[14]	China (Wuhan)	3–15 April	People applying for permission to resume work ($n = 1021$) and hospitalized patients ($n = 381$)
Ling et al.[32]	China (Wuhan)	26 March–28 April	Age 16–64 years, going back to work, with no fever, headache or other symptoms of COVID-19
Xu et al.[60]	China (Guangzhou)	23 March–2 April	Healthy blood donors in Guangzhou
Xu et al.[40]	China (several regions)	30 March–10 April	Voluntary participation by public call for haemodialysis patients ($n = 979$ in Jingzhou, Hubei and $n = 563$ in Guangzhou/Foshan, Guangdong) and outpatients in Chongqing ($n = 993$), and community residents in Chengdu, Sichuan ($n = 9442$), and required testing for factory workers in Guangzhou, Guandong ($n = 442$)
Jerkovic et al.[26]	Croatia	23–28 April	DIV Group factory workers in Split and Sibenik-Knin invited for voluntary testing
Erikstrup et al.[12]	Denmark	6 April–3 May	All Danish blood donors aged 17–69 years giving blood. Blood donors are healthy and must comply with strict eligibility criteria; they must self-defer for two weeks if they develop fever with upper respiratory symptoms
Petersen et al.[52]	Denmark (Faroe Islands)	27 April–1 May	1 500 randomly selected residents invited to participate, samples collected from 1075
Fontanet et al.[39]	France (Crepy-en-Valois)	28–30 April	Pupils, their parents and relatives, and staff of primary schools exposed to SARS-CoV-2 in February and March 2020 in a city north of Paris
Fontanet et al.[13]	France (Oise)	30 March–4 April	Pupils, their parents and siblings, as well as teachers and non-teaching staff of a high-school
Streeck et al.[16]	Germany (Gangelt)	30 March–6 April	600 adults with different surnames in Gangelt were randomly selected; all household members were asked to participate in the study

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Author	Country (location)	Dates	Sampling and recruitment
Kraehling et al.[21]	Germany (Frankfurt)	6–14 April	Employees of Infraserv Höchst, a large industrial site operator in Frankfurt am Main. No exclusion criteria
Bogogiannidou et al.[62]	Greece	March and April (April data used)	Leftover blood samples collected from a nationwide laboratory network, including both private and public hospital laboratories (27 laboratories in total)
Merkely et al.[57]	Hungary	1–16 May	Representative sample (n = 17 787) of the Hungarian population ≥ 14 years living in private households (8 283 810)
Gudbjartsson et al.[58]	Iceland	Several cohorts between April and June[a]	30 576 people in Iceland, including those documented to be infected, those quarantined and people not known to have been exposed
Malani et al.[61]	India (Mumbai)	29 June–19 July	Geographically-spaced community sampling of households, one individual per household was tested in slum and non-slum communities in three wards, one each from the three main zones of Mumbai
Khan et al.[67]	India (Srinagar)	1–15 July	Adults (> 18 years) who visited selected hospitals across the Srinagar District
Shakiba et al.[8]	Islamic Republic of Iran (Guilan)	April (until 21 April)	Population-based cluster random sampling design through telephone call invitation, household-based
Fiore et al.[31]	Italy (Apulia)	1–31 May	Blood donors 18–65 years old free of recent symptoms possibly related to COVID-19, no close contact with confirmed cases, symptom-free in the preceding 14 days, no contact with suspected cases
Doi et al.[11]	Japan (Kobe)	31 March–7 April	Randomly selected patients who visited outpatient clinics and received blood testing for any reason. Patients who visited the emergency department or the designated fever consultation service were excluded
Takita et al.[29]	Japan (Tokyo)	21 April–20 May	Two community clinics in the main railway stations in Tokyo (Navitas Clinic Shinjuku and Tachikawa)
Nawa et al.[48]	Japan (Utsunomiya City)	14 June–5 July	Invitations enclosed with a questionnaire were sent to 2290 people in 1 000 households randomly selected from Utsunomiya City's basic resident registry; 742 completed the study
Uyoga et al.[44]	Kenya	30 April–16 June (~90% of samples in last 30 days)	Residual blood donor serum samples from donors 16–65 years in four sites (Mombasa, Nairobi, Eldoret and Kisumu)
Snoeck et al.[20]	Luxembourg	16 April–5 May	Representative sample (no details how ensured), 1807 of 2000 contacted provided data, were < 79 years and had serology results
Slot et al.[15]	Netherlands	1–15 April	Blood donors. Donors must be completely healthy, but they may have been ill in the past, provided that they recovered at least 2 weeks before
Westerhuis et al.[64]	Netherlands (Rotterdam)	Early March and early April	Left-over plasma samples from patients of nine age categories in Erasmus Medical Center in Rotterdam: 879 samples in early March and 729 in early April)
Nisar et al.[49]	Pakistan (Karachi)	25 June–11 July (after baseline on 15–25 April)	Cross-sectional household surveys in a low- (district Malir) and high-transmission (district East) area of Karachi with households selected using simple random sampling (Malir) and systematic random sampling (East)
Javed et al.[66]	Pakistan (urban Karachi, Lahore, Multan, Peshawar and Quetta)	Up to 6 July	Adult, working population aged 18–65 years, recruited from dense, urban workplaces including factories, businesses, restaurants, media houses, schools, banks, hospitals (health-care providers), and from families of positive cases in cities in Pakistan
Abu Raddad et al.[51]	Qatar	12 May–12 July (highest seroprevalence on 12–31 May)	Convenience sample of residual blood specimens collected for routine clinical screening or clinical management from 32 970 outpatient and inpatient departments for a variety of health conditions (n = 937 in 12–31 May)
Noh et al.[59]	Republic of Korea	25–29 May	Outpatients who visited two hospitals in south-west Seoul which serve six administrative areas
Pollán et al.[36]	Spain	27 April–11 May	35 883 households selected from municipal rolls using two-stage random sampling stratified by province and municipality size, with all residents invited to participate (75.1% of all contacted individuals participated)

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Author	Country (location)	Dates	Sampling and recruitment
Crovetto et al.[30]	Spain (Barcelona)	14 April–5 May	Consecutive pregnant women for first trimester screening or delivery in two hospitals
Stringhini et al.[10]	Switzerland (Geneva)	6 April–9 May (5 consecutive weeks)	Randomly selected previous participants of the Bus Santé study with an email (or telephone contact, if email unavailable); participants were invited to bring all members of their household aged 5 years and older
Emmenegger et al.[28]	Switzerland (Zurich)	Prepandemic until June (patients) and May (blood donors)	Patients at the University Hospital of Zurich and blood donors in Zurich and Lucerne
Ward et al.[65]	United Kingdom (England)	20 June–13 July	Random population sample of 100 000 adults over 18 years
Thompson et al.[18]	United Kingdom (Scotland)	21–23 March	Blood donors. Donors should not have felt unwell in the past 14 days; some other deferrals also applied regarding travel and COVID-19 symptoms
Havers et al.[35]	USA (10 states)	23 March–1 April (Washington, Puget Sound and New York, New York City), 1–8 April (Louisiana), 5–10 April (Florida, south), 13–25 April (Pennsylvania, Philadelphia, metropolitan area), 20–26 April (Missouri), 23–27 April (California, San Francisco Bay Area), 20 April–3 May (Utah), 26 April–3 May (Connecticut), 30 April–12 May (Minnesota, Minneapolis)	Convenience samples using residual sera obtained for routine clinical testing (screening or management) by two commercial laboratory companies
Ng et al.[24]	USA (California, Bay Area)	March	1000 blood donors in diverse Bay Area locations (excluding those with self-reported symptoms or abnormal vital signs)
Sood[22]	USA (California, Los Angeles)	10–14 April	Proprietary database representative of the county. A random sample of these residents was invited, with quotas for enrolment for subgroups based on age, sex, race and ethnicity distribution
Chamie et al.[33]	USA (California, San Francisco)	25–28 April	United States census tract 022 901 population-dense area (58% Latin American) in San Francisco Mission district, expanded to neighbouring blocks on 28 April
Bendavid et al.[19]	USA (California, Santa Clara)	2–3 April	Facebook advertisement with additional targeting by zip code
Biggs et al.[53]	USA (Georgia, DeKalb and Fulton)	28 April–3 May	Two-stage cluster sampling design used to randomly select 30 census blocks in DeKalb County and 30 census blocks in Fulton County, with a target of seven participating households per census block
McLaughlin et al.[46]	USA (Idaho, Blaine County)	4–19 May	Volunteers who registered via a secure web link, using prestratification weighting to the population distribution by age and sex within each zip code
Bryan et al.[9]	USA (Idaho, Boise)	Late April	People from the Boise, Idaho metropolitan area, part of the Crush the Curve initiative
Menachemi et al.[54]	USA (Indiana)	25–29 April	Stratified random sampling among all persons aged ≥ 12 years using Indiana's 10 public health preparedness districts as sampling strata
Feehan et al.[63]	USA (Louisiana, Baton Rouge)	15–31 July	Representative sample in a method developed by Public Democracy
Feehan et al.[37]	USA (Louisiana, Orleans and Jefferson Parish)	9–15 May	Pool of potential participants reflecting the demographics of the parishes was based on 50 characteristics, then a randomized subset of 150 000 people was selected, and 25 000 were approached with digital apps, and 2640 were recruited

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Author	Country (location)	Dates	Sampling and recruitment
Rosenberg et al.[23]	USA (New York)	19–28 April	Convenience sample of people ≥ 18 years living in New York State, recruited consecutively on entering 99 grocery stores and through an in-store flyer
Meyers et al.[56]	USA (New York)	2–30 March (Columbia University Medical Center, New York City); 13–28 March (CareMount central laboratory)	Discarded clinical samples in Columbia Medical Center, New York City ($n = 814$ in 24 February–30 March, 742 of those in the period 2–30 March) and samples from CareMount central laboratory (960 samples on 13/14 March, 505 samples on 20/21 March, and 376 samples on 27/28 March) from its network of clinics in five counties north of New York City
Reifer et al.[27]	USA (New York, Brooklyn)	Early May	Patients seen in an urgent care facility in Brooklyn
Nesbitt et al.[45]	USA (Rhode Island)	27 April–11 May	Consecutive blood donors

COVID-19: coronavirus disease 19; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

[a] Sample collection time for some sub-cohorts may have exceeded 1 month, but more than half of the cases were already documented by polymerase chain reaction testing before any antibody testing and the last death occurred on 20 April.

Note: Some studies included additional data sets that did not fulfil the eligibility criteria (e.g. had sample size < 500 or were health-care workers) and they are not presented here.

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Table 2. **Sample size, types of antibodies assessed and population size in the studies included to assess COVID-19 infection fatality rate, 2020**

Country (location)	Sample size[a], no.	Antibody	Population,[b,c,d] no.	% of population < 70 years[c]
Argentina (Barrio Padre Mugica)[47]	873	IgG	49 983	99
Belgium[38]	3 391 (20–26 April)	IgG	11 589 623	86
Brazil (133 cities)[25]	24 995	IgG and IgM	74 656 499	94 (Brazil)
Brazil (Espirito Santo)[34]	4 608	IgG and IgM	4 018 650	94 (Brazil)
Brazil (Maranhao)[68]	3 156	IgG and IgM	7 114 598	92
Brazil (Rio de Janeiro), blood donors[41]	669 (24–27 April)	IgG and IgM	17 264 943	94 (Brazil)
Brazil (Rio Grande do Sul)[17]	4 500	IgG	11 377 239	91
Brazil (Sao Paulo)[42]	517	IgG and IgM	298 240 (6 districts)	94 (Brazil)
Canada (British Columbia)[50]	885	IgG, IgM and IgA	5 071 000	94
Chile (Vitacura)[43]	1 244	IgG and IgM	85 000	92 (Chile)
China, blood donors[55]				
Wuhan	930 (3–23 February)	IgG and IgM	11 210 000	93 (China)
Shenzhen	3 507 (24 February–15 March)	IgG and IgM	13 030 000	93 (China)
Shijiazhuang	6 455 (10 February–1 March)	IgG and IgM	11 030 000	93 (China)
China (Wuhan)[14]	1 401	IgG and IgM	11 080 000	93 (China)
China (Wuhan)[32]	1 196 (4–8 April)	IgG and IgM	11 080 000	93 (China)
China (Guangzhou), blood donors[60]	2 199	IgG, IgM and IgA	115 210 000 (Guangdong)	93 (China)
China (several regions)[40]				
Hubei (not Wuhan)	979	IgG and IgM	48 058 000	93 (China)
Chongqing	993	IgG and IgM	31 243 200	93 (China)
Sichuan	9 442	IgG and IgM	83 750 000	93 (China)
Guangdong	1 005	IgG and IgM	115 210 000	93 (China)
Croatia[26]	1 494	IgG and IgM	4 076 000	86
Denmark blood donors[12]	20 640	IgG and IgM	5 771 876	86
Denmark (Faroe Islands)[52]	1 075	IgG and IgM	52 428	88
France (Crepy-en-Valois)[39]	1 340	IgG	5 978 000 (Hauts-de-France)	89
France (Oise)[13]	661	IgG	5 978 000 (Hauts-de-France)	89
Germany (Gangelt)[16]	919	IgG and IgA	12 597	86
Germany (Frankfurt)[21]	1 000	IgG	2 681 000[e]	84 (Germany)
Greece[62]	6 586 (4 511 in April)	IgG	10 412 967	84
Hungary[57]	10 504	IgG (also had RT-PCR)	9 657 451	88
Iceland[58]	30 576	Pan-Ig	366 854	90
India (Mumbai)[61]	6 904 (4 202 in slums, 2 702 not in slums)	IgG	1 414 917 (705 523 in slums, 709 394 in non-slums) in the 3 ward areas	98
India (Srinagar)[67]	2 906	IgG	1 500 000	97
Islamic Republic of Iran (Guilan)[8]	551	IgG and IgM	2 354 848	95
Italy (Apulia), blood donors[31]	909	IgG and IgM	4 029 000	84
Japan (Kobe)[11]	1 000	IgG	1 518 870	79 (Japan)
Japan (Tokyo)[29]	1 071	IgG	13 902 077	79 (Japan)
Japan (Utsunomiya City)[48]	742	IgG	518 610	79 (Japan)
Kenya, blood donors[44]	3 098	IgG	47 564 296	99
Luxembourg[20]	1 807	IgG and IgA[f]	615 729	90
Netherlands blood donors[15]	7 361	IgG, IgM and IgA	17 097 123	86
Netherlands (Rotterdam)[64]	729 (early April)	IgG	17 097 123 (Netherlands)	86
Pakistan (Karachi)[49]	1 004	IgG and IgM	16 700 000	98 (Pakistan)
Pakistan (urban)[66]	24 210	IgG and IgM	79 000 000 (urban)	98
Qatar[51]	937	IgG	2 800 000	99
Republic of Korea[59]	1 500	IgG	2 667 341	90 (Republic of Korea)
Spain[36]	61 075	IgG	46 940 000	85
Spain (Barcelona)[30]	874	IgG, IgM and IgA	7 566 000 (Catalonia)	86
Switzerland (Geneva)[10]	577 (20–27 April)	IgG	500 000	88

(*continues. . .*)

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Country (location)	Sample size[a], no.	Antibody	Population,[b,c,d] no.	% of population < 70 years[c]
Switzerland (Zurich)[28]	1 644 patients (1–15 April)	IgG	1 520 968 (Zurich canton)	88
Switzerland (Zurich and Lucerne)[28]	1 640 blood donors (May)	IgG	1 930 525 (Zurich and Lucerne)	88
United Kingdom (England)[65]	109 076	IgG	56 287 000	86
United Kingdom (Scotland), blood donors[18]	500	IgG	5 400 000	88
USA (10 states)[35]				
Washington, Puget Sound	3 264	Pan-Ig	4 273 548	90 (Washington)
Utah	1 132	Pan-Ig	3 282 120	92
New York, New York City	2 482	Pan-Ig	9 260 870	89
Missouri	1 882	Pan-Ig	6 110 800	88
Florida, south	1 742	Pan-Ig	6 345 345	86 (Florida)
Connecticut	1 431	Pan-Ig	3 562 989	88
Louisiana	1 184	Pan-Ig	4 644 049	92
California, San Francisco Bay	1 224	Pan-Ig	2 173 082	90
Pennsylvania, Philadelphia	824	Pan-Ig	4 910 139	90
Minnesota, Minneapolis	860	Pan-Ig	3 857 479	90
USA (California, Bay Area)[24]	1 000	IgG	7 753 000	90
USA (California, Los Angeles)[22]	863	IgG and IgM	7 892 000	92
USA (California, San Francisco)[33]	3 953	IgG and RT-PCR	5 174 (in census tract 022 901)	95
USA (California, Santa Clara)[19]	3 300	IgG and IgM	1 928 000	90
USA (Idaho, Boise)[9]	4 856	IgG	481 587 (Ada County)	92
USA (Georgia, DeKalb and Fulton Counties)[53]	696	Total Ig	1 806 672	88 (Georgia)
USA (Idaho, Blaine County)[46]	917	IgG	23 089	92
USA (Indiana)[54]	3 629	IgG and RT-PCR	6 730 000	89
USA (Louisiana, Baton Rouge)[63]	138	IgG	699 200 (East Baton Rouge, West Baton Rouge, Ascension, Livingston)	92 (Louisiana)
USA (Louisiana, Orleans and Jefferson Parish)[37]	2 640	IgG	825 057	92 (Louisiana)
USA (New York)[23]	15 101	IgG	19 450 000	90
USA, New York[56]				
Columbia University Medical Center, New York City	742 (2–30 March)	IgG and IgM	9 260 870	89
CareMount central laboratory, five New York state counties	1 841	IgG and IgM	10 189 130 (New York state excluding New York City)	89
USA (New York, Brooklyn)[27]	11 092	IgG	2 559 903	91
USA (Rhode Island), blood donors[45]	1 996	IgG and IgM	1 059 000	88

COVID-19: coronavirus disease 19; Ig: immunoglobin; RT-PCR: real-time polymerase chain reaction.

[a] Dates in brackets are the specific dates used when seroprevalence was evaluated at multiple consecutive time points or settings.

[b] Some studies focused on age-restricted populations of the specific location under study, for example: people 17–70 years in the Denmark blood donor study ($n = 3\,800\,000$); people 18–79 years in the Luxembourg study ($n = 483\,000$); people < 70 years in the Netherlands blood donor study ($n = 13\,745\,768$); people ≥ 18 years in the New York state study ($n = 15\,280\,000$); people > 19 years in the Utah population of the 10-state United States of America study ($n = 2\,173\,082$); people ≥ 18 years in Blaine County, Idaho ($n = 17\,611$); people 15–64 years in the Kenya blood donor study ($n = 27\,150\,165$); people > 14 years living in private premises in Hungary ($n = 8{,}283{,}810$); people > 18 years ($n = 551\,185$) in Baton Rouge, Louisiana; people 18–65 years working in urban locations in Pakistan ($n = 22\,100\,000$); and people > 18 years in Srinagar District, India ($n = 1\,020\,000$). In this table and subsequent analyses, the entire population in the location is considered for consistency across studies.

[c] Information in parentheses specifies the population.

[d] When the population of the relevant location was not given in a specific study, information on recent estimates of the pertinent population was obtained by standard online sources such as: populationpyramid.net, worldpopulationreview.com, worldometers.info/coronavirus, and Wikipedia.

[e] Participants were recruited from a large number of districts, but most districts had very few participants; here I included the population of the nine districts with > 1:10 000 sampling ratio (846/1000 participants came from these nine districts).

[f] Considered positive if both IgG and IgA were positive; in the other studies, detection of any antibody was considered positive.

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Centers for Disease Control and Prevention

COVID Data Tracker

Maps, charts, and data provided by CDC, updates daily by 8 pm ET

COVID-19 Home ›

CDC recommends use of COVID-19 Community Levels to determine the impact of COVID-19 on communities and take action. Community Transmission levels are provided for healthcare facility use only.

United States at a Glance Collapse

United States
At a Glance

Cases Total **81,391,274**
Case Trends

Deaths Total **993,341**
Death Trends

Current **Hosp.** **12,883**
Admission Trends

82.5% of People 5+ with At Least
One Vaccination

- Data Tracker Home
- Cases, Deaths, & Testing
- Case & Death Demographic Trends
- Vaccination Distribution & Coverage
- Vaccine Effectiveness & Breakthrough Surveillance
- Health Equity
- Pediatric
- Pregnancy
- People at Increased Risk
- Wastewater Surveillance
- Health Care Settings
- Social Impact & Prevention
- Variants & Genomic Surveillance

Trends in Number of COVID-19 Cases and Deaths in the US Reported to CDC, by State/Territory

Reported to the CDC by State or Territory; Maps, charts, and data provided by CDC, updates Mon-Sat by 8 pm ET†

View Footnotes and Download Data

Select a state or territory: The United States

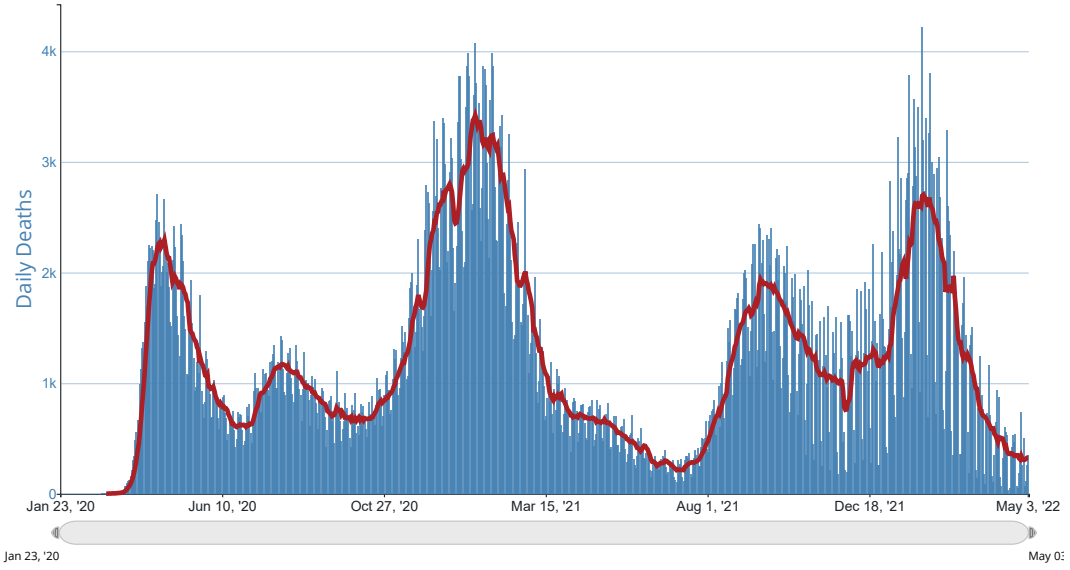
View(left axis): Daily Deaths

Show: ☑ 7-Day moving average

View(right axis): select one

The blue bars show daily deaths. The red line is the 7-day moving average of deaths.

Daily Trends in Number of COVID-19 Deaths in The United States Reported to CDC



Antibody Seroprevalence

Other COVID-19 Data

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Data Downloads and Footnotes

Expand each accordion to view data table and download data

Data Table for Daily Death Trends - The United States +

Footnotes +

Wondering what all the data mean?

CDC's new COVID Data Tracker Weekly Review helps you stay up-to-date on the pandemic with weekly visualizations, analysis, and interpretations of key data and trends.

Where can I see the number of deaths from death certificate data?

Death certificate data are reported directly to CDC's National Center for Health Statistics by state vital record offices as part of the National Vital Statistics System (NVSS). You can use NVSS data to look at trends in total deaths, COVID-19 deaths, leading causes and excess deaths by geography, age, sex, race/ethnicity, and comorbidities.

How many COVID-19 cases are there in your county?

View your county's data in the County View tab

View and Download COVID-19 Case Surveillance Public Use Data with Geography

Cite COVID Data Tracker

Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2022, May 05. https://covid.cdc.gov/covid-data-tracker

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All COVID-19 topics including prevention, travel, work, and school

Communicable Disease Service

New Jersey COVID-19 Dashboard

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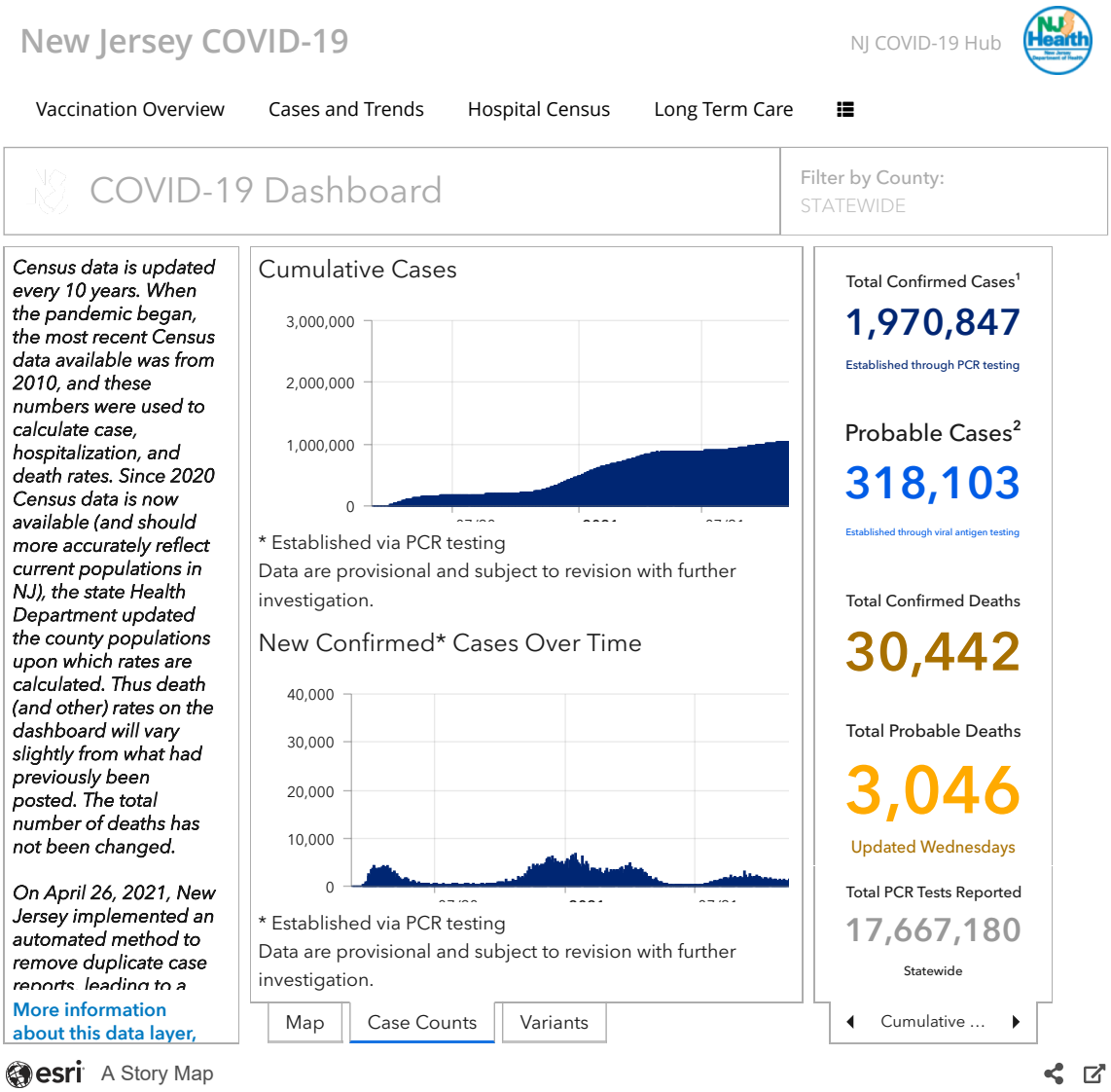

Department of Health
P. O. Box 360
Trenton, NJ 08625-0360

Last Reviewed: 10/19/2020

EXECUTIVE ORDER NO. 103

WHEREAS, Coronavirus disease 2019 ("COVID-19") is a contagious, and at times fatal, respiratory disease caused by the SARS-CoV-2 virus; and

WHEREAS, COVID-19 is responsible for the 2019 novel coronavirus outbreak, which was first identified in Wuhan, the People's Republic of China in December 2019 and quickly spread to the Hubei Province and multiple other countries; and

WHEREAS, symptoms of the COVID-19 illness include fever, cough, and shortness of breath, which may appear in as few as two or as long as 14 days after exposure, and can spread from person to person via respiratory droplets produced when an infected person coughs or sneezes; and

WHEREAS, on January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization declared the outbreak a "public health emergency of international concern," which means "an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response," and thereafter raised its global risk assessment of COVID-19 from "high" to "very high"; and

WHEREAS, on January 31, 2020, the United States Department of Health and Human Services Secretary declared a public health emergency for the United States to aid the nation's healthcare community in responding to COVID-19; and

WHEREAS, as of March 9, 2020, according to the Centers for Disease Control and Prevention ("CDC"), there were more than 114,000 confirmed cases of COVID-19 worldwide, with over 4,000 of those cases having resulted in death; and

WHEREAS, as of March 9, 2020, there were more than 500 confirmed cases of COVID-19 in the United States, with 22 of those cases having resulted in death; and

WHEREAS, as of March 9, 2020, there were 11 presumed positive cases of COVID-19 in New Jersey, with 24 additional "Persons Under Investigation" spread across the counties of Bergen, Camden, Cumberland, Essex, Hunterdon, Middlesex, Monmouth, Passaic, Union, and Sussex; and

WHEREAS, as of March 9, 2020, there were 142 positive cases of COVID-19 in the State of New York and seven presumptive positive cases in the Commonwealth of Pennsylvania; and

WHEREAS, the CDC expects that additional cases of COVID-19 will be identified in the coming days, including more cases in the United States, and that person-to-person spread is likely to continue to occur; and

WHEREAS, if COVID-19 spreads in New Jersey at a rate comparable to the rate of spread in other affected areas, it will greatly strain the resources and capabilities of county and municipal governments, including public health agencies, that provide essential services for containing and mitigating the spread of contagious diseases, such as COVID-19, and the situation may become too large in scope to be handled in its entirety by the normal county and municipal operating services in some parts of this State, and this situation may spread to other parts of the State; and

WHEREAS, the spread of COVID-19 may make it difficult or impossible for citizens to obtain consumer goods and other necessities of life due to supply chain disruption and price increases, as well as hamper the delivery of essential services such as police, fire, and first aid; and

WHEREAS, the State's public bidding act, N.J.S.A. 52:34-6 et seq., provides a public exigency exemption, N.J.S.A. 52:34-10(b), that in the event of a threat to the life, health, or safety to the public, advertised bidding is not required to obtain those

goods and services necessary to address the public exigency where the Division of Purchase of Property provides preapproval in accordance with Treasury Circular 18-14-DPP; and

WHEREAS, in the event of a declared emergency pursuant to Treasury Circular 19-10-DPP, the threshold for delegated purchasing by individual State Departments is raised to $100,000 such that purchases at or below that amount do not require prior approval or action by DPP; and

WHEREAS, the spread of COVID-19 may disrupt the timely delivery of State contracted goods or services, the immediate delivery and fulfillment of which is necessary for the life, safety, or health of the public; and

WHEREAS, the State of New Jersey has been working closely with the CDC, local health departments, and healthcare facilities to monitor, plan for and mitigate the spread of COVID-19 within the State; and

WHEREAS, through Executive Order No. 102, which I signed on February 3, 2020, I created the State's Coronavirus Task Force, chaired by the Commissioner of the New Jersey Department of Health ("DOH"), in order to coordinate the State's efforts to appropriately prepare for and respond to the public health hazard posed by COVID-19; and

WHEREAS, it is critical to prepare for and respond to suspected or confirmed COVID-19 cases in New Jersey, to implement appropriate measures to mitigate the spread of COVID-19, and to prepare in the event of an increasing number of individuals requiring medical care or hospitalization; and

WHEREAS, the State of New Jersey also acts as an employer with tens of thousands of employees, and the spread of COVID-19 requires preparedness for staffing shortages and flexibility in work rules to ensure that its employees can fully comply with all

medically appropriate measures while also ensuring the continuous delivery of State services performed by Executive branch agencies; and

WHEREAS, the continuous delivery of services at the county and municipal level performed by those governments and their employees is also essential; and

WHEREAS, the spread of COVID-19 within New Jersey constitutes an imminent public health hazard that threatens and presently endangers the health, safety, and welfare of the residents of one or more municipalities or counties of the State; and

WHEREAS, it is necessary and appropriate to take action against this public health hazard to protect and maintain the health, safety, and welfare of New Jersey residents and visitors; and

WHEREAS, the facts as set forth above and consultation with the Commissioner of DOH confirms that there exists a public health emergency in the State; and

WHEREAS, New Jersey's Consumer Fraud Act, N.J.S.A. 56:8-107 et seq., prohibits excessive price increases during a declared state of emergency, or for 30 days after the termination of the state of emergency; and

WHEREAS, the Constitution and statutes of the State of New Jersey, particularly the provisions of N.J.S.A. 26:13-1 et seq., N.J.S.A. App. A: 9-33 et seq., N.J.S.A. 38A:3-6.1, and N.J.S.A. 38A:2-4 and all amendments and supplements thereto, confer upon the Governor of the State of New Jersey certain emergency powers;

NOW, THEREFORE, I, PHILIP D. MURPHY, Governor of the State of New Jersey, in order to protect the health, safety and welfare of the people of the State of New Jersey, DO DECLARE and PROCLAIM that a Public Health Emergency and State of Emergency exist in the State of New Jersey, and I hereby ORDER and DIRECT the following:

1. I authorize and empower the State Director of Emergency Management, who is the Superintendent of State Police, in conjunction with the Commissioner of DOH, to take any such emergency measures as the State Director may determine necessary, including the implementation of the State Emergency Operations Plan and directing the activation of county and municipal emergency operations plans, in order to fully and adequately protect the health, safety and welfare of the citizens of the State of New Jersey from any actual or potential threat or danger that may exist from the possible exposure to COVID-19. The State Director of Emergency Management, in conjunction with the Commissioner of DOH, is authorized to coordinate the relief effort from this emergency with all governmental agencies, volunteer organizations, and the private sector.

2. The State Director of Emergency Management, in conjunction with the Commissioner of DOH, shall also supervise and coordinate all activities of all State, regional and local political bodies and agencies in order to ensure the most effective and expeditious implementation of this order, and, to this end, may call upon all such agencies and political subdivisions for any assistance necessary.

3. Given the concurrent invocation of both a State of Emergency pursuant to N.J.S.A. App.A.:9-33 et seq. and a Public Health Emergency as contemplated by N.J.S.A. 26:13-1 et seq., I reserve the right as specifically contemplated by N.J.S.A. 26:13-3 to exercise the authority and powers specific to the Emergency Health Powers Act as I deem necessary and appropriate to ensure the public health for New Jersey's residents.

4. It shall be the duty of every person or entity in this State or doing business in this State and of the members of the governing body and every official, employee, or agent of every

political subdivision in this State and of each member of all other governmental bodies, agencies, and authorities in this State of any nature whatsoever, to cooperate fully with the State Director of Emergency Management and the Commissioner of DOH in all matters concerning this state of emergency.

5. The Coronavirus Task Force established under Executive Order No. 102 is continued with the Commissioner of DOH as the chair, and shall provide assistance on the State's efforts preparing for and responding to the public health hazard posed by COVID-19.

6. I authorize and empower the executive head of any agency or instrumentality of the State government with authority to promulgate rules to waive, suspend, or modify any existing rule, where the enforcement of which would be detrimental to the public welfare during this emergency, notwithstanding the provisions of the Administrative Procedure Act or any law to the contrary for the duration of this Executive Order, subject to my prior approval and in consultation with the State Director of Emergency Management and the Commissioner of DOH. Any such waiver, modification, or suspension shall be promulgated in accordance with N.J.S.A. App. A:9-45.

7. All State agencies, and specifically the Departments of Banking and Insurance, Health, Human Services, Education, and the Civil Service Commission are authorized to take appropriate steps to address the public health hazard of COVID-19, including increasing access and eliminating barriers to medical care, protecting the health and well-being of students, and protecting the health and well-being of State, county, and municipal employees while ensuring the continuous delivery of State, county, and municipal services.

8. I authorize and empower the State Director of Emergency Management, in conjunction with the Commissioner of DOH, to order the evacuation of all persons, except for those emergency and governmental personnel whose presence the State Director deems necessary, from any area where their continued presence would present a danger to their health, safety, or welfare because of the conditions created by this emergency.

9. I authorize and empower the State Director of Emergency Management, in conjunction with the Commissioner of DOH, to utilize all property, equipment, and facilities owned, rented, operated, and maintained by the State of New Jersey to house and shelter persons who may need to be evacuated from a residence, dwelling, building, structure, or vehicle during the course of this emergency.

10. I authorize and empower the Adjutant General, in accordance with N.J.S.A. 38A:2-4 and N.J.S.A. 38A:3-6.1, to order to active duty such members of the New Jersey National Guard who, in the Adjutant General's judgment, are necessary to provide aid to those localities where there is a threat or danger to the public health, safety, and welfare and to authorize the employment of any supporting vehicles, equipment, communications, or supplies as may be necessary to support the members so ordered.

11. In accordance with the N.J.S.A. App. A:9-34 and N.J.S.A. App. A:9-51, I reserve the right to utilize and employ all available resources of the State government and of each and every political subdivision of the State, whether of persons, properties, or instrumentalities, and to commandeer and utilize any personal services and any privately-owned property necessary to protect against this emergency.

12. In accordance with N.J.S.A. App. A:9 40, no municipality, county, or any other agency or political subdivision of this State shall enact or enforce any order, rule, regulation, ordinance, or resolution which will or might in any way conflict with any of the provisions of this Order, or which will in any way interfere with or impede the achievement of the purposes of this Order.

13. In accordance with N.J.S.A. App. A:9-34, N.J.S.A. App. A:9-40.6, and N.J.S.A. 40A:14-156.4, no municipality or public or semipublic agency shall send public works, fire, police, emergency medical, or other personnel or equipment into any non-contiguous impacted municipality within this State, nor to any impacted municipality outside this State, unless and until such aid has been directed by the county emergency management coordinator or his or her deputies in consultation with the State Director of Emergency Management in conjunction with the Commissioner of DOH.

14. This Order shall take effect immediately and shall remain in effect until such time as it is determined by me that an emergency no longer exists.

GIVEN, under my hand and seal this 9th day of March, Two Thousand and Twenty, and of the Independence of the United States, the Two Hundred and Forty-Fourth.

[seal]

/s/ Philip D. Murphy

Governor

Attest:

/s/ Matthew J. Platkin

Chief Counsel to the Governor

EXECUTIVE ORDER NO. 292

WHEREAS, on March 9, 2020, I issued Executive Order No. 103, declaring the existence of a Public Health Emergency, pursuant to the Emergency Health Powers Act ("EHPA"), N.J.S.A. 26:13-1 et seq., and a State of Emergency, pursuant to the New Jersey Civilian Defense and Disaster Control Act ("Disaster Control Act"), N.J.S.A. App A:9-33 et seq., in the State of New Jersey for Coronavirus disease 2019 ("COVID-19"), the facts and circumstances of which are adopted by reference herein; and

WHEREAS, through Executive Order Nos. 119, 138, 151, 162, 171, 180, 186, 191, 200, 210, 215, 222, 231, 235, and 240, which were issued each month between April 7, 2020 and May 14, 2021, the facts and circumstances of which are adopted by reference herein, I declared that the COVID-19 Public Health Emergency in effect at the time continued to exist; and

WHEREAS, Executive Order No. 111, issued March 28, 2020, requires that health care facilities report their capacity and supplies, including bed capacity, ventilators, and Personal Protective Equipment ("PPE") on a daily basis; and

WHEREAS, Executive Order No. 112, issued April 1, 2020, granted the Department of Law and Public Safety, Division of Consumer Affairs, the authority to temporarily reactivate certain inactive health care licenses and allow the licensure of physicians licensed, and in good standing, in another country; suspended and waived certain licensure requirements for advanced practice nurses and physician assistants; relaxed registration requirements for the Prescription Monitoring Program; waived signature requirements for funeral agreements and authorizations; and provided certain healthcare professionals with civil or criminal immunity; and

WHEREAS, Executive Order No. 207, issued December 4, 2020, requires all individuals, regardless of age, to be automatically enrolled in the New Jersey Immunization Information System ("NJIIS"), the statewide electronic immunization registry, upon receipt of a COVID-19 vaccination; and

WHEREAS, New Jersey made significant progress in responding to COVID-19 and mitigating its devastating effects, in particular in light of the advent of three effective vaccines that, among other things, had significantly reduced the likelihood of both contracting and transmitting the variants of COVID-19 that were present in the United States at the time; and

WHEREAS, on June 4, 2021, in light of these developments, I signed Assembly Bill No. 5820 into law as P.L.2021, c.103, and issued Executive Order No. 244, which terminated the Public Health Emergency declared in Executive Order No. 103 (2020); and

WHEREAS, P.L.2021, c.103 sought to enable the State to bring an end to its prior Public Health Emergency while still allowing for an orderly continuation of the Administration's ability to order certain public health measures relating to COVID-19, including but not limited to vaccine distribution, administration, and management, COVID-19 testing, health resource and personnel allocation, data collection, and implementation of recommendations of the Centers for Disease Control and Prevention ("CDC") to prevent or limit the transmission of COVID-19, including in specific settings; and

WHEREAS, P.L.2021, c.103 explicitly maintained the State of Emergency declared in Executive Order No. 103 (2020), and stated it would in no way diminish, limit, or impair the powers of the Governor to respond to any of the threats presented by COVID-19 pursuant to the Disaster Control Act; and

WHEREAS, in addition to leaving the prior State of Emergency in effect, nothing in P.L.2021, c.103 prevented the Governor from declaring any new public health emergency under the EHPA, N.J.S.A. 26:13-1 et seq., should the evolving circumstances on the ground require such a declaration; and

WHEREAS, Executive Order No. 251, issued August 6, 2021, requires all public, private, and parochial preschool programs and elementary and secondary schools, including charter and renaissance schools (collectively "school districts"), to maintain a policy regarding mandatory use of face masks by staff, students, and visitors in the indoor portion of the school district premises, except in certain specified circumstances; and

WHEREAS, Executive Order No. 252, issued August 6, 2021, required all covered health care and high-risk congregate settings ("covered settings") to maintain a policy that required all covered workers to either provide adequate proof to the covered settings that they have been fully vaccinated or submit to COVID-19 testing at minimum one to two times weekly beginning September 7, 2021; and

WHEREAS, Executive Order No. 253, issued August 23, 2021, requires school districts to maintain a policy that requires all covered workers to either provide adequate proof to the school district that they have been fully vaccinated or submit to COVID-19 testing at minimum one to two times weekly beginning October 18, 2021; and

WHEREAS, Executive Order No. 264, issued September 20, 2021, requires all child care centers and other child care facilities (collectively "child care settings") to maintain a policy regarding mandatory use of face masks by staff, child enrollees, and visitors in the indoor portion of the child care setting premises, except in certain specified circumstances; and

WHEREAS, Executive Order No. 264 (2021) further requires all child care settings to maintain a policy that requires all covered workers to either provide adequate proof to the child care settings that they have been fully vaccinated or submit to COVID-19 testing at minimum one to two times weekly beginning November 1, 2021; and

WHEREAS, Executive Order No. 271, issued October 20, 2021, requires that each executive department and agency, including an independent authority, ensure that certain new contracts, new solicitation for a contract, extension or renewal of existing contracts, and exercise of an option on existing contracts, include a clause that the contractor or any subcontractors, at any tier, that is party to the contract, must maintain a policy that requires all covered workers to either provide adequate proof to the covered contractor that they have been fully vaccinated or submit to COVID-19 testing at minimum one to two times weekly; and

WHEREAS, as the CDC has recognized, viruses can change through mutation and mutations can result in a new variant of the virus, and these variants can have meaningfully distinct impacts from the original virus; and

WHEREAS, as the CDC has recognized, some variants spread more easily and quickly than other variants of the same virus, which may lead to more cases of COVID-19, increased strain on healthcare resources, more hospitalizations, and more deaths; and

WHEREAS, new variants are classified based on how easily the variant spreads, how severe its symptoms are, how it responds to treatments, and how well vaccines protect against the variant; and

WHEREAS, since Executive Order No. 244 (2021) took effect, the CDC has reported that new variants of concern of COVID-19 have been identified in the United States, particularly the B.1.617.2 (Delta) variant and most recently the B1.1.529 (“Omicron”) variant; and

WHEREAS, although New Jersey was able to end the prior Public Health Emergency on account of the effectiveness of vaccines in reducing transmissibility of COVID-19, the Omicron variant spread more easily than other variants and required additional action to protect the public; and

WHEREAS, on January 11, 2022, I issued Executive Order No. 280, declaring the existence of a new Public Health Emergency, pursuant to the EHPA, N.J.S.A. 26:13-1 et seq., and continuing the State of Emergency declared in Executive Order No. 103 (2020) pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq., in the State of New Jersey due to the surge of cases and hospitalizations tied to the new variants of COVID-19; and

WHEREAS, on January 11, 2022, I issued Executive Order No. 281, extending various orders to ensure the State continues to have the necessary resources in place to respond to the new variants of COVID-19; and

WHEREAS, on January 19, 2022, I issued Executive Order No. 283, requiring all covered settings to maintain a policy that requires all covered workers to provide adequate proof to the covered settings that they have are up to date with their COVID-19 vaccinations, including any booster shots for which they are eligible; and

WHEREAS, N.J.S.A. 26:13-3(b) establishes that a Public Health Emergency declared by the Governor shall automatically terminate after 30 days, unless renewed for an additional 30 days through a declaration of the Governor; and

WHEREAS, on February 10, 2022, I issued Executive Order No. 288, which declared that the Public Health Emergency declared in Executive Order No. 280 (2022) continues to exist; and

WHEREAS, through Executive Order No. 288 (2022), I declared all Executive Orders issued, as well as actions taken by any Executive Branch department and agency, in whole or in part in response to the COVID-19 Public Health Emergency remained in full force and effect; and

WHEREAS, on March 2, 2022, I issued Executive Order No. 290, clarifying and extending the timeframes within which covered settings must require their covered workers to comply with the vaccination and booster requirements set forth in Executive Order No. 283 (2020); and

WHEREAS, as the State has taken significant emergency measures in the last two months in response to the Omicron variant, there has been a substantial decrease in the rate of reported new cases of COVID-19 in New Jersey, in the total number of individuals being admitted to hospitals for COVID-19, and in the rate of transmission for COVID-19 infections in New Jersey; and

WHEREAS, the fact that the spread of COVID-19 has slowed over the last two months does not by itself suggest that the Public Health Emergency had dissipated, because absent certain mitigation measures, particularly increased rates of vaccinations and COVID-19 testing, public health experts anticipated that the spread of COVID-19 would continue to significantly increase; and

WHEREAS, over the last two months, the number of hospitalized patients has gone from over 6,075 to under 730, the number of patients in intensive care has gone from over 900 to under 140, and the number of ventilators in use has gone from over 500 to under 85; and

WHEREAS, over the last two months, the number of individuals testing positive for COVID-19 has gone from approximately 33,400 per day to 887 per day, and the weekday spot positivity of COVID-19 tests has gone from over 39 percent to under 2 percent; and

WHEREAS, the rate of transmission in the State has moved significantly below 1; and

WHEREAS, the COVID-19 Activity Level Report ("CALI Report") issued by the New Jersey Department of Health ("DOH"), Communicable Disease Service calculates COVID-19 activity levels throughout the State using the case rate, percent of COVID-like illness, and percent positivity; and

WHEREAS, for the first time since April 2020, the CALI Report reached the "Very High" score throughout the entire State the week of January 10, 2022; and

WHEREAS, the CALI Report for the week ending March 4, 2022, presented activity levels of "Moderate" and "Low" throughout the State; and

WHEREAS, because vaccines are effective at preventing severe illness, hospitalizations, and death, including from the Omicron variant, the CDC has noted that the recent emergence of this variant emphasizes the importance of vaccination and boosters, particularly as we move toward the next phase of the State's COVID-19 response; and

WHEREAS, according to the CDC, studies show after getting the primary series of a COVID-19 vaccine, protection against the virus and the ability to prevent infection may decrease over time, in particularly due to changes in variants; and

WHEREAS, although the COVID-19 vaccines remain effective in preventing severe disease, recent data suggests their effectiveness at preventing infection or severe illness wanes over time; and

WHEREAS, the CDC has reported that vaccinated people who receive a COVID-19 booster are likely to have a stronger protection against contracting and transmitting COVID-19, particularly the

Omicron variant, and stronger protection against serious illness, including hospitalizations and death; and

WHEREAS, New Jersey has administered over 13.7 million doses of the COVID-19 vaccine in the State to date, with over 6.8 million New Jerseyans having received the primary series of a vaccine; and

WHEREAS, as of March 3, 2022, only 54 percent of eligible individuals statewide have received their booster shot; and

WHEREAS, in addition to vaccination, testing for COVID-19 remains one of the strongest tools to prevent the further spread of COVID-19 and ensure the State can move into the next phase of its COVID-19 response; and

WHEREAS, because the number of hospitalized patients, patients in intensive care, and ventilators in use, and the spot positivity of COVID-19 tests have decreased considerably over the past two months, the State can begin to responsibly lift certain mitigation protocols in place, including requiring that face masks be worn in schools and child care settings, as the State moves into the next phase of the COVID-19 response; and

WHEREAS, given the progress the State has made and the decisive decrease in key statistics, such as the number of hospitalized patients in the State, the number of daily positive COVID-19 cases, spot positivity, and the rate of transmission, and in consultation with the Commissioner of DOH, I find that the Public Health Emergency declared in Executive Order No. 280 (2022) can be safely and responsibly lifted; and

WHEREAS, despite the extensive progress made in combatting COVID-19, and the ability to lift the Public Health Emergency and certain mitigation protocols, there remains an ongoing threat necessitating that certain actions taken by the State in response to COVID-19 and the Omicron variant, including to ensure COVID-19

testing and vaccine management, administration, and tracking, can all remain in place as the State moves toward the next phase of our COVID-19 response; and

WHEREAS, due to the ongoing threat, health care workers must continue to have the staffing and resources that are essential to maintaining the operations of the State's essential health care services to protect public health, which include but are not limited to critical and emergency health care, vaccine administration, COVID-19 testing, contact tracing, acquiring and maintaining stockpiles of PPE, ventilators, and other critical supplies to remain prepared for the ongoing threat; and

WHEREAS, it remains crucial that the State understand the health care system's existing capacity and its gaps through continued reporting, which will allow additional resources to be deployed where they are most needed; and

WHEREAS, continued automatic enrollment in the NJIIS for individuals receiving a COVID-19 vaccine will facilitate and track progress relative to New Jersey's vaccination targets; and

WHEREAS, ongoing oversight of the State's vaccination program is particularly important as the rollout continues during the next phase of the State's COVID-19 response, especially in ensuring that all residents in New Jersey have access to the booster doses, and as the State prepares for additional groups of New Jerseyans to become eligible for vaccination; and

WHEREAS, on July 6, 2021, the U.S. Department of Justice's Office of Legal Counsel issued an opinion concluding that Section 564 of the Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3 does not prohibit public or private entities from imposing vaccination requirements while vaccinations are only available pursuant to Emergency Use Authorization (EUA); and

WHEREAS, the American Academy of Pediatrics (AAP) continues to emphasize that in-person learning is critical for educational and social development of children, as evidence demonstrates that remote learning has been detrimental to the educational attainment of students of all ages and has exacerbated the mental health crisis among children and adolescents; and

WHEREAS, the CDC has also cited evidence that suggests virtual learning can lead to learning loss for children and worsening mental health problems for the younger population; and

WHEREAS, child care centers provide critical support to tens of thousands of families across the State who rely on safe, in-person environments for their children during the work day; and

WHEREAS, continuing to require workers in schools and child care settings to receive a COVID-19 vaccine or undergo regular testing can help prevent outbreaks and reduce transmission to children, including those who have not received or are not yet eligible to receive a vaccination; and

WHEREAS, preventing transmission of COVID-19 is critical to ensuring that we can safely lift the mask requirements and to keeping schools and child care settings open for in-person instruction; and

WHEREAS, school districts have access to multiple sources of funding to address costs associated with worker vaccination efforts and testing, including three rounds of federal Elementary and Secondary School Emergency Relief funds and Emergency Assistance for Nonpublic Schools within the Governor's Emergency Education Relief funds; and

WHEREAS, the CDC has repeatedly emphasized the importance of heightened mitigation protocols in certain covered settings because of the significant risk of spread and vulnerability of the populations served; and

WHEREAS, continuing to require workers in those covered settings to receive a COVID-19 vaccine, including a booster shot when eligible, can help prevent outbreaks and reduce transmission to vulnerable individuals who may be at higher risk of severe disease; and

WHEREAS, parties that contract with the State government provide essential services to the public and interact with the public on a regular basis, and because of the nature of their work, a significant portion of their workers are not able to work remotely; and

WHEREAS, continuing to require contractors to maintain a policy that requires its covered workers to either provide proof of vaccination status or submit to regular testing continues to be essential for continued operation and service to the public; and

WHEREAS, this continues to ensure that contractors are held to the same requirements as the State workforce, which the Executive Branch in its capacity as an employer has required to receive a COVID-19 vaccine or undergo regular testing; and

WHEREAS, while the State has significantly curtailed the immediate public health threat of the virus, the economic and social impacts of the virus, as part of the next phase of the State's COVID-19 response, will also require ongoing management and oversight; and

WHEREAS, as we evaluate the appropriate response and resources needed to continue to manage and oversee the next phase of the COVID-19 response, I have consulted with the Executive Branch departments and agencies as to what administrative orders, directives, and waivers are necessary to continue; and

WHEREAS, it is critical that the Executive Orders and Administrative Orders, Directives, and Waivers continue at this time to ensure that an orderly transition to the next phase of the

State's COVID-19 recovery is done in a measured and thoughtful manner; and

WHEREAS, the State of Emergency declared in Executive Order No. 103 (2020) and continued in Executive Order No. 280 (2022) pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq., must remain in effect to allow for the continued management of New Jersey's recovery from and response to the COVID-19 pandemic; and

WHEREAS, the Constitution and statutes of the State of New Jersey, particularly the provisions of N.J.S.A. 26:13-1 et seq., N.J.S.A. App. A: 9-33 et seq., N.J.S.A. 38A:3-6.1, and N.J.S.A. 38A:24 and all amendments and supplements thereto, confer upon the Governor of the State of New Jersey certain emergency powers, which I have invoked;

NOW, THEREFORE, I, PHILIP D. MURPHY, Governor of the State of New Jersey, by virtue of the authority vested in me by the Constitution and by the Statutes of this State, do hereby DECLARE and PROCLAIM and ORDER and DIRECT:

1. The Public Health Emergency declared in Executive Order No. 280 (2022) pursuant to the EHPA, N.J.S.A. 26:13-1 et seq., is hereby terminated.

2. The State of Emergency declared in Executive Order No. 103 (2020) and continued in Executive Order No. 280 (2022) pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq., continues to exist in the State of New Jersey.

3. Executive Order Nos. 111, 112, and 207 (2020), Nos. 252, 253, and 271 (2021), and Nos. 283 and 290 (2022) remain in full force and effect pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq, except that any civil or criminal immunity related to the COVID-19 response bestowed by Executive Order No. 112 shall not be in effect.

4. Executive Order No. 251 (2021) is hereby rescinded.

5. Executive Order No. 264 (2021) remains in full force and effect pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq., except that paragraphs 11 and 13 are hereby rescinded.

6. All actions taken by any Executive Branch departments and agencies in whole or in part to respond to the Public Health Emergency presented by the COVID-19 outbreak, and extended pursuant to Executive Order No. 281 (2022) and attached in the Appendix thereto, including but not limited to any Administrative Orders, Directives, and Waivers, remain in full force and effect pursuant to the Disaster Control Act, N.J.S.A. App. A:9-33 et seq, until revoked or modified by the department or agency head, or until the State of Emergency is no longer in effect, whichever is sooner, except that any Administrative Order, Directive, or Waiver extended pursuant to Executive Order No. 281 (2022) that was revoked after the effective date of Executive Order No. 281 shall not remain in full force and effect.

7. Notwithstanding paragraph 6 of this Order, Executive Directive 21-003, Youth Camp Requirements, issued April 28, 2021, provided in the Appendix to Executive Order No. 281 (2022) shall no longer be in full force and effect.

8. For purposes of this Order, "Executive Branch departments and agencies" shall mean any of the principal departments in the Executive Branch of State government and any agency, authority, board, bureau, commission, division, institution, office, or other instrumentality within or created by any such department, and any independent State authority, commission, instrumentality, or agency over which the Governor exercises executive authority, as determined by the Attorney General.

9. It shall be the duty of every person or entity in this State or doing business in this State and of the members of the governing body and every official, employee, or agent of every political subdivision in this State and of each member of all other governmental bodies, agencies, and authorities in this State of any nature whatsoever, to cooperate fully in all matters concerning this Order, and to cooperate fully with any Administrative Orders issued pursuant to this Order.

10. No municipality, county, or any other agency or political subdivision of this State shall enact or enforce any order, rule, regulation, ordinance, or resolution which will or might in any way conflict with any of the provisions of this Order, or which will or might in any way interfere with or impede its achievement.

11. Penalties for violations of this Order may be imposed under, among other statutes, N.J.S.A. App. A:9-49 and -50.

12. This Order shall take effect at 12:01 a.m. on March 7, 2022, and shall remain in effect until revoked or modified by the Governor.

GIVEN, under my hand and seal this 4th day of March, Two Thousand and Twenty-two, and of the Independence of the United States, the Two Hundred and Forty-Sixth.

[seal]

/s/ Philip D. Murphy

Governor

Attest:

/s/ Parimal Garg

Chief Counsel to the Governor

Centers for Disease Control and Prevention

COVID-19

What You Need to Know About Variants

Updated Apr. 26, 2022

Omicron Spread

CDC is monitoring the current surge of COVID-19 cases. Learn more about the Omicron variant and its expected impact on hospitalizations.

Omicron Variant | Hospitalization Forecast

What You Need to Know

- New variants of the virus are expected to occur.
- Slowing the spread of the virus, by protecting yourself and others, can help slow the emergence of new variants.
- The Omicron variant causes more infections and spreads faster than the original SARS-CoV-2 strain of the virus that causes COVID-19.
- CDC is working with state and local public health officials to monitor the spread of all variants, including Omicron.
- Getting a vaccine reduces your risk of severe illness, hospitalization, and death from COVID-19. Staying up to date on your COVID-19 vaccines, which includes getting a booster when eligible, further improves your protection.

Variants Are Expected

Viruses constantly change through mutation and sometimes these mutations result in a new variant of the virus. Some variants emerge and disappear while others persist. New variants will continue to emerge. CDC and other public health organizations monitor all variants of the virus that causes COVID-19 in the United States and globally.

Scientists monitor all variants but may classify certain ones as variants being monitored, variants of interest, variants of concern and variants of high consequence. Some variants spread more easily and quickly than other variants, which may lead to more cases of COVID-19. Even if a variant causes less severe disease in general, an increase in the overall number of cases could cause an increase in hospitalizations, put more strain on healthcare resources and potentially lead to more deaths.

Variants of Concern

Omicron - B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5

First identified: South Africa

Spread: Spreads more easily than other variants. CDC is working with state and local public health officials to monitor the spread of Omicron.

Symptoms: Please refer to Symptoms of COVID-19 | CDC

Severe illness and death: Data suggest that Omicron is less severe in general. However, a surge in cases may lead to significant increases in hospitalization and death. More data are needed to fully understand the severity of illness and death associated with this variant.

Vaccine: Breakthrough infections in people who are vaccinated are expected, but being up to date on recommended vaccines is effective at preventing severe illness, hospitalizations, and death. The emergence of the Omicron variant further emphasizes the importance of vaccination and boosters.

Treatments: Some, but not all, monoclonal antibody treatments remain effective against Omicron. Public health agencies work with healthcare providers to ensure that effective treatments are used appropriately to treat patients.

Learn more about the Omicron variant

We Have the Tools to Fight COVID-19

Vaccines

- Vaccines reduce the risk of severe illness, hospitalization, and death from COVID-19.
- People who are up to date on vaccines, including booster doses when eligible are likely to have stronger protection against COVID-19 variants, including Omicron. CDC recommends everyone eligible get vaccinated and a booster shot.

Masks

When to wear a mask

- Wear a well-fitting mask with the best fit, protection, and comfort for you.
- If you are in an area with a high COVID-19 Community Level and are ages 2 or older, wear a well-fitting mask indoors in public.
- If you are sick and need to be around others, or are caring for someone who has COVID-19, wear a mask.
- If you are at increased risk for severe illness, or live with or spend time with someone at higher risk, speak to your healthcare provider about wearing a mask at medium COVID-19 Community Levels.

Testing

- Tests for COVID-19 tell you if you have an infection at the time of the test. This type of test is called a “viral” test because it looks for viral infection. Antigen or Nucleic Acid Amplification Tests (NAATs) are viral tests.
  - Additional tests would be needed to determine which variant caused your infection, but these typically are not authorized for public use.
- As new variants emerge, scientists will continue to evaluate how well tests detect current infection.
- Self-tests may be used if you have COVID-19 symptoms or have been exposed or potentially exposed to an individual with COVID-19.
  - Even if you don’t have symptoms and have not been exposed to an individual with COVID-19, using a self-test before gathering indoors with others can give you information about the risk of spreading the virus that causes COVID-19.

Related Pages

- Omicron Variant
- Variant Proportions
- SARS-CoV-2 Sequences
- Symptoms of COVID-19

Last Updated Apr. 26, 2022

Centers for Disease Control and Prevention

Stay Up to Date with Your COVID-19 Vaccines

Updated May 6, 2022

What You Need to Know

- CDC recommends that everyone ages 5 years and older get their primary series of COVID-19 vaccine, and everyone ages 12 years and older also receive a booster. Some people can receive two boosters.
- People who are moderately or severely immunocompromised have specific COVID-19 vaccine recommendations, including recommendations for a booster. Learn more about COVID-19 vaccine recommendations for people who are moderately or severely immunocompromised.
- The following COVID-19 vaccine and booster recommendations may be updated as CDC continues to follow data related to vaccine effectiveness and safety, waning immunity, and protection against variants.

About COVID-19 Vaccines

COVID-19 vaccines available in the United States are effective at protecting people from getting seriously ill, being hospitalized, and even dying—especially people who are boosted. As with other diseases, you are protected best from COVID-19 when you stay up to date with recommended vaccines.

Approved or Authorized Vaccines

Three COVID-19 vaccines are authorized or approved for use in the United States to prevent COVID-19. Pfizer-BioNTech or Moderna are COVID-19 mRNA vaccines and are preferred. You may get Johnson & Johnson's Janssen COVID-19 vaccine in some situations.

Pfizer-BioNTech | Moderna | Johnson & Johnson's Janssen

When Are You Up to Date?

You are **up to date** with your COVID-19 vaccines when you have received all doses in the primary series and one booster when eligible, as shown below.

- Getting a second booster is not necessary to be considered up to date at this time.
- The recommendations will be different depending on your age, your health status, what vaccine you first received, and when you first got vaccinated.

Adults ages 18 or older

Pfizer-BioNTech

Primary Series:
2 doses of Pfizer-BioNTech given 3–8 weeks apart [1]

Fully Vaccinated: 2 weeks after final dose in primary series

Boosters:

- 1 booster of either Pfizer-BioNTech or Moderna COVID-19 vaccine is recommended at least 5 months after the final dose in the primary series
- Adults ages 50 years and older can choose to receive a 2nd booster dose of either Pfizer-BioNTech or Moderna COVID-19 vaccine at least 4 months after the 1st booster

Up to Date: Immediately after getting 1st booster [2]

Moderna

Primary Series:
2 doses of Moderna given 4–8 weeks apart [1]

Fully Vaccinated: 2 weeks after final dose in primary series

Boosters:

- 1 booster of either Pfizer-BioNTech or Moderna COVID-19 vaccine is recommended at least 5 months after the final dose in the primary series
- Adults ages 50 years and older can choose to receive a 2nd booster dose of either Pfizer-BioNTech or Moderna COVID-19 vaccine at least 4 months after the 1st booster

Up to Date: Immediately after getting 1st booster [2]

Johnson & Johnson's Janssen

Primary Series:
1 dose of Johnson & Johnson's Janssen

Fully Vaccinated: 2 weeks after vaccination

Boosters:

- 1 booster of either Pfizer-BioNTech or Moderna COVID-19 vaccine is recommended at least 2 months after a J&J/Janssen COVID-19 vaccine
- Anyone who received a J&J/Janssen COVID-19 vaccine for both their primary dose and booster may receive a 2nd booster of either Pfizer-BioNTech or Moderna COVID-19 vaccine at least 4 months after their 1st booster
- Adults ages 50 years and older can choose to receive a 2nd booster of either Pfizer-BioNTech or Moderna COVID-19 vaccine at least 4 months after the 1st booster

Up to Date: Immediately after getting 1st booster [2]

Children and teens ages 12–17 years

Pfizer-BioNTech

Primary Series:
2 doses of Pfizer-BioNTech given 3–8 weeks apart [1]

Fully Vaccinated: 2 weeks after final dose in primary series

Boosters:
1 booster of Pfizer-BioNTech COVID-19 vaccine is recommended at least 5 months after the final dose in the primary series

Up to Date: Immediately after getting 1st booster [2]

Children ages 5–11 years

Pfizer-BioNTech

Primary Series:
2 doses of Pfizer-BioNTech given 3 weeks apart [1]

COVID-19

[1] Talk to your healthcare or vaccine provider about the timing for the second dose in your primary series.

- **People ages 12 through 64 years, and especially males ages 12 through 39 years**, may consider getting the second dose of an mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna) 8 weeks after the first dose. A longer time between the first and second doses may increase how much protection the vaccines offer, and further minimize the already rare risk of heart problems, including myocarditis and pericarditis.
- **People ages 5 through 11 years, people ages 65 years and older, people more likely to get very sick from COVID-19, or anyone wanting protection due to high levels of community transmission** should get the second dose of **Pfizer-BioNTech** COVID-19 vaccine **3 weeks (or 21 days)** after the first dose, or the second dose of **Moderna** COVID-19 vaccine **4 weeks (or 28 days)** after the first dose.

[2] If you have completed your primary series—but are not yet eligible for a booster—you are also considered up to date. Stay up to date by getting one booster when you are eligible. Getting a second booster is not necessary to be considered up to date at this time.

Mixing COVID-19 Vaccine Products

CDC does not recommend mixing products for your primary vaccine series.

If you received a Pfizer-BioNTech or Moderna COVID-19 vaccine, you should get the same product for your second shot in the primary series. People eligible for a booster who are ages 18 years and older may get a different product for their booster. People eligible for a booster who are ages 12 through 17 years must get the same product (Pfizer-BioNTech) for their booster.

Timing of COVID-19 Vaccination After Infection

People who have COVID-19 should wait to receive any vaccine, including a COVID-19 vaccine, until after they recover and complete their isolation period.

Additionally, people who recently had COVID-19 *may* consider delaying their next booster by 3 months from when their symptoms started or, if they had no symptoms, when they first received a positive test. Reinfection is less likely in the weeks to months after infection. However, certain factors, such as personal risk of severe disease, local COVID-19 community level, and the dominant COVID-19 variant, could be reasons to get a vaccine sooner rather than later.

Talk to your healthcare professional if you have questions about when to get your next COVID-19 vaccine.

Vaccination Outside the United States

If you received COVID-19 vaccines outside the United States, whether you are up to date depends on which COVID-19 vaccine (and how many doses) you received. Learn more about when people vaccinated outside the United States are considered fully vaccinated.

Allergic Reaction to a COVID-19 Vaccine Product

If you had a severe allergic reaction after a previous dose of a COVID-19 vaccine or if you have a known (diagnosed) allergy to a COVID-19 vaccine ingredient, you should not get that vaccine. If you have been instructed not to get one type of COVID-19 vaccine, you may still be able to get another type.

Scheduling Your COVID-19 Vaccines

Find a COVID-19 vaccine or booster: Search vaccines.gov, text your ZIP code to 438829, or call 1-800-232-0233 to find locations near you.

There are several ways you can find a vaccine provider. You can get your COVID-19 vaccines at the same location, or different locations.

- If you need help scheduling your second shot or your booster, contact the location that set up your previous appointment.
- Some community vaccination clinics have closed. You can get your second shot or your booster at a different location.

Learn more about getting your COVID-19 vaccine.

For Healthcare and Public Health

COVID-19 Clinical and Professional Resources

Related Pages

- Getting a COVID-19 Vaccine
- How COVID-19 Vaccines Work
- Possibility of COVID-19 after Vaccination: Breakthrough Infections
- Meeting Materials for the Advisory Committee on Immunization Practices

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Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection

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ABSTRACT

BACKGROUND

The duration and effectiveness of immunity from infection with and vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are relevant to pandemic policy interventions, including the timing of vaccine boosters.

METHODS

We investigated the duration and effectiveness of immunity in a prospective cohort of asymptomatic health care workers in the United Kingdom who underwent routine polymerase-chain-reaction (PCR) testing. Vaccine effectiveness (≤10 months after the first dose of vaccine) and infection-acquired immunity were assessed by comparing the time to PCR-confirmed infection in vaccinated persons with that in unvaccinated persons, stratified according to previous infection status. We used a Cox regression model with adjustment for previous SARS-CoV-2 infection status, vaccine type and dosing interval, demographic characteristics, and workplace exposure to SARS-CoV-2.

RESULTS

Of 35,768 participants, 27% (9488) had a previous SARS-CoV-2 infection. Vaccine coverage was high: 95% of the participants had received two doses (78% had received BNT162b2 vaccine [Pfizer–BioNTech] with a long interval between doses, 9% BNT162b2 vaccine with a short interval between doses, and 8% ChAdOx1 nCoV-19 vaccine [AstraZeneca]). Between December 7, 2020, and September 21, 2021, a total of 2747 primary infections and 210 reinfections were observed. Among previously uninfected participants who received long-interval BNT162b2 vaccine, adjusted vaccine effectiveness decreased from 85% (95% confidence interval [CI], 72 to 92) 14 to 73 days after the second dose to 51% (95% CI, 22 to 69) at a median of 201 days (interquartile range, 197 to 205) after the second dose; this effectiveness did not differ significantly between the long-interval and short-interval BNT162b2 vaccine recipients. At 14 to 73 days after the second dose, adjusted vaccine effectiveness among ChAdOx1 nCoV-19 vaccine recipients was 58% (95% CI, 23 to 77) — considerably lower than that among BNT162b2 vaccine recipients. Infection-acquired immunity waned after 1 year in unvaccinated participants but remained consistently higher than 90% in those who were subsequently vaccinated, even in persons infected more than 18 months previously.

CONCLUSIONS

Two doses of BNT162b2 vaccine were associated with high short-term protection against SARS-CoV-2 infection; this protection waned considerably after 6 months. Infection-acquired immunity boosted with vaccination remained high more than 1 year after infection. (Funded by the U.K. Health Security Agency and others; ISRCTN Registry number, ISRCTN11041050.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Hopkins can be contacted at susan.hopkins1@ukhsa.gov.uk.

*A complete list of the SIREN Study Group investigators is provided in the Supplementary Appendix, available at NEJM.org.

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A Quick Take is available at NEJM.org

Real-world studies have shown the short-term effectiveness of vaccines with respect to symptomatic and asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the severity of coronavirus disease 2019 (Covid-19), and secondary transmission.[1-4] The duration of this protection over longer periods remains uncertain and warrants ongoing study.

The population uptake of two doses of Covid-19 vaccines in the United Kingdom (in persons >12 years of age) as of February 2022 was 84.5%,[5] and it has now been more than 6 months since the second dose was administered to prioritized groups (health care and social workers and clinically vulnerable persons). Given the sustained high levels of community infection[5] and concerns about the potential waning of immunity,[6-10] the government of the United Kingdom initiated a rollout of booster vaccination in prioritized groups in September 2021.[11] Improved understanding and characterization of vaccine effectiveness at longer dose intervals and of potential variation in effectiveness according to demographic factors, vaccination schedules, and history of SARS-CoV-2 infection are urgently needed to inform vaccination strategies.

In the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study, which involved a large cohort of asymptomatic health care workers who underwent polymerase-chain-reaction (PCR) testing every 2 weeks, more than 30% of the participants were seropositive for SARS-CoV-2 at enrollment.[4,12,13] In this analysis, we aimed to determine the level and durability of protection against SARS-CoV-2 infection in the study cohort from March 2020 through September 2021 by estimating vaccine effectiveness after two doses of Covid-19 vaccine, according to the type of vaccine and dosing interval, in participants without previous infection. We also evaluated immunity against reinfection conferred by previous infection plus Covid-19 vaccine.

Methods

Study Design and Oversight

The SIREN study is an ongoing, multicenter, prospective cohort study involving health care workers (≥18 years of age) in the United Kingdom. This study received approval from the Berkshire Research Ethics Committee, and the results were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[15] All the authors vouch for the accuracy and completeness of the data and for the fidelity of the study to the protocol.

Study Participants and Data

Participants underwent PCR testing for SARS-CoV-2, supplemented by widespread lateral-flow testing, every 2 weeks, as well as monthly antibody testing. Every 2 weeks, they also completed questionnaires that included questions about symptoms. This data collection has been described elsewhere.[4]

Vaccination data (the type of vaccine and dates of administration) were obtained through personal identifiers from each health administration, linked to a national vaccination register, and directly from the participants in questionnaires completed every 2 weeks. The dosing interval was categorized as "short" if the second dose was administered up to 6 weeks after the first dose and "long" if the second dose was administered 6 weeks or more after the first dose.[14]

Serum samples obtained from all the participants at baseline visits were collected centrally. These samples were tested at the U.K. Health Security Agency (formerly Public Health England) central testing laboratory at Porton Down with the use of the semiquantitative Elecsys Anti-SARS-CoV-2 nucleocapsid (N) protein assay and the fully quantitative Elecsys Anti-SARS-CoV-2 spike (S) protein assay (both manufactured by Roche Diagnostics).

Explanatory Variables and Exclusion Criteria

At the beginning of the analysis, the participants were assigned to one of two cohorts: participants with no history of SARS-CoV-2 infection (the previously uninfected cohort) and those who had ever received a PCR test result or an antibody test result consistent with previous SARS-CoV-2 infection (the previously infected cohort). Participants were excluded from this analysis if the cohort assignment could not be accurately completed or if the outcome could not be determined (e.g., if they did not undergo PCR testing during the follow-up period), if they had previous infection that occurred on or after the vaccination date, or if the date of onset of the primary infection, based on either a positive PCR test or Covid-19 symptoms, was not avail-

able. Participants were also excluded if they had received a Covid-19 vaccine other than the BNT162b2 vaccine (Pfizer–BioNTech) or the ChAdOx1 nCoV-19 vaccine (AstraZeneca) because of the small numbers of persons who had received other vaccines.

PRIMARY OUTCOME

The primary outcome was a PCR-confirmed SARS-CoV-2 infection, irrespective of the participant's symptom status. This outcome was defined as a primary infection in the previously uninfected cohort or a reinfection in the previously infected cohort (two PCR-positive samples ≥90 days apart or a new PCR-positive sample ≥28 days after an antibody-positive result consistent with previous infection).

PERSON-TIME AT RISK

Follow-up began on December 7, 2020 (the day before Covid-19 vaccination was introduced in the United Kingdom), and continued until September 21, 2021, a period that covered 10 calendar months. All the participants who were enrolled on or before December 7, 2020, were followed from that date onward. Participants who were enrolled after December 7, 2020, (i.e., those with delayed entry) were followed from the date of their enrollment. Unvaccinated participants who had a primary infection during follow-up were moved into the previously infected cohort 90 days after their PCR-positive date, at which point they were considered to be at risk for reinfection. For individual participants, the end of follow-up was the date of primary infection (in the previously uninfected cohort), the date of reinfection (in the previously infected cohort), or the date of the last PCR-negative test.

STATISTICAL ANALYSIS

In our Cox proportional-hazards model with delayed entry of some participants, the outcome was time to PCR-positive SARS-CoV-2 infection, stratified according to age group, geographic region, workplace setting, and frequency of exposure to persons with Covid-19. We chose stratification based on these categorical predictors because they were statistically significant when controlled for but did not satisfy the proportional-hazards assumption (Schoenfeld test, according to predictor and global fit). We also controlled for sex and race or ethnic group because we observed that these predictors were statistically significant, led to an increase in the likelihood value and Wald statistic, and satisfied the proportional-hazards assumptions.

The model accounted for calendar time, given the varying infection rate, through the baseline hazard, which could take any functional form. In this model, the hazard is assumed to be

$$H_i(t)=h_{oi}(t)exp\ (\beta_1 x_1 + \ldots + \beta_k x_k),$$

with a time-varying baseline hazard $h_{oi}(t)$ for each stratum. We estimated the parameter β, report the hazard ratio HR=exp(β), and report vaccine effectiveness and protection from primary infection calculated as 1 minus the hazard ratio, along with Wald statistic confidence intervals. The estimates of the hazard ratios are independent of the baseline hazard, on which no assumption was made.

The analysis began on December 7, 2020, shortly before the second wave of SARS-CoV-2 infection peaked in the United Kingdom, and continued through the spring of 2021 and into the third wave (Fig. S3 in the Supplementary Appendix, available with the full text of this article at NEJM.org); thus, it was crucial to account for a varying hazard rate.

The main predictors — vaccination status and previous infection status — were categorical and varied according to time. We grouped these predictors according to the time since vaccination and divided the follow-up time into unvaccinated and postvaccination time intervals. We also grouped previous infection status into three categories: before primary infection, up to 12 months after the primary infection, and more than 12 months after the primary infection. We used robust variance estimates to guard against the potential for unmeasured confounders at the hospital organization (site) level.

We fitted the model first in the previously uninfected cohort, estimating vaccine effectiveness over time. Here, postvaccination intervals were categorized according to vaccine type and dosing interval, the latter to explore differences in protection in participants who received the second dose closer in time to their first dose. We then focused on all the recipients of the BNT162b2 vaccine, including those who were infected before vaccination, and fitted a model with interaction of the time since the primary infection and the time since vaccination. Recipients of the ChAdOx1 nCoV-19 vaccine and the

categorization according to dosing interval for the BNT162b2 vaccine were excluded because of small numbers in the previously infected cohort. This allowed us to investigate vaccine effectiveness in previously infected persons. We report these estimates as well as estimates from an unadjusted model, without stratifying or controlling for any predictor other than the time since vaccination and infection. Goodness of fit was assessed with the use of the likelihood ratio test (against the null model) and Akaike information criterion values. The widths of the confidence intervals have not been adjusted for multiplicity and cannot be used to infer effects.

We performed sensitivity analyses to assess the extent of depletion-of-susceptibles bias and the effect of excluding participants in the previously infected cohort who did not have a reliable date of primary infection. All the sensitivity analyses provided results that were similar to those presented here, but the estimates were more uncertain (see Tables S6 through S11). All the analyses were conducted with the use of Stata software, version 15.1 (StataCorp). The results were independently replicated with the use of R software, version 4.1.1, survival package v.3.2-13 (R Foundation for Statistical Computing). Our annotated code is available at https://github.com/SIREN-study/SARS-CoV-2-Immunity.

RESULTS

STUDY POPULATION

A total of 44,546 participants were enrolled between June 18, 2020, and April 23, 2021, from 135 sites across the United Kingdom; 35,768 met the inclusion criteria for this analysis (Fig. S1). The characteristics of the participants are shown in Table 1; most participants were women (84%), and the median age was 46 years (interquartile range, 36 to 54). Table S2 shows a comparison of these characteristics with those of the national population.

At the beginning of the analysis, we assigned 26,280 participants to the previously uninfected cohort and 9488 to the previously infected cohort. The participants in the previously infected cohort were more likely than those in the previously uninfected cohort to be male, younger, from Black, Asian, or ethnic minority backgrounds, to work in clinical roles (e.g., to be doctors, nurses, or allied health professionals), and to report more frequent exposure to patients with Covid-19 (Table 1).

By the end of the analysis, 94.9% of the participants had received two doses of vaccine: 78.5% had received the BNT162b2 vaccine with a long interval between doses, 8.6% had received the BNT162b2 vaccine with a short interval between doses, and 7.8% had received the ChAdOx1 nCoV-19 vaccine (Table 1 and Fig. S2). We did not identify any major demographic differences among the participants according to vaccination schedule (Table S3).

Follow-up time varied according to participant, with a total of 7,482,388 participant person-days, of which 998,270 involved unvaccinated participants and 6,430,118 involved vaccinated participants (from the date of the first dose). A total of 62,291 PCR tests were performed during the "unvaccinated follow-up period," which included follow-up time before vaccination in participants who were vaccinated during the analysis period and the total follow-up time in those who remained unvaccinated at the end of the analysis . A total of 427,951 PCR tests were performed during the period of the analysis in which participants were vaccinated (i.e., the "vaccinated follow-up period"). The average test interval was 16 days in the unvaccinated period and 15 days in the vaccinated period. In the previously uninfected cohort, 358,346 tests (average test interval, 14.8 days) were performed, and 131,896 tests were performed in the previously infected cohort (average test interval, 14.3 days).

PRIMARY OUTCOME

The primary outcome was PCR-confirmed SARS-CoV-2 infection. Primary infections were noted in 2747 participants during follow-up, and reinfections were seen in 210, with cases peaking at the end of December 2020, declining by March and April 2021, and increasing in May 2021, a pattern that mirrored national trends (Fig. S3). At 14 days before or after the date of the positive PCR test, among the participants with primary infections, 1673 (61%) reported Covid-19–related symptoms, 368 (13%) reported other symptoms, 118 (4%) reported no symptoms, and 588 (21%) did not provide data on symptoms. In contrast, among the participants with reinfections, 71 (34%) reported Covid-19–related symptoms, 42 (20%) reported other symptoms, 45 (21%) reported no symptoms, and 52 (25%) did not provide data on

symptoms. A total of 357 participants (13%) with primary infection reported a hospital visit for Covid-19–related symptoms, as compared with 18 (9%) of those with reinfection.

VACCINE EFFECTIVENESS AGAINST PRIMARY INFECTION

Among the participants without previous SARS-CoV-2 infection, two doses of BNT162b2 vaccine administered with a long interval between doses was associated with a decrease in the risk of infection of 85% (95% confidence interval [CI], 72 to 92) (i.e., the adjusted vaccine effectiveness in the first 2 months after the development of the full immune response, 14 to 73 days after the second dose) (Tables 2 and S4 and Fig. 1). Over time, the adjusted vaccine effectiveness declined but remained high, at 68% (95% CI, 54 to 77), 134 to 193 days after the second dose. At a median of 201 days (interquartile range, 197 to 205) after the second dose, we observed evidence of waning of protection, with an adjusted vaccine effectiveness of 51% (95% CI, 22 to 69).

A similar trend was observed in the participants who received a second dose of BNT162b2 vaccine with a short interval between doses, with high protection at 14 to 73 days (adjusted vaccine effectiveness, 89%; 95% CI, 78 to 94) that decreased to 53% (95% CI, 28 to 69) at a median of 238 days (interquartile range, 220 to 249) after the second dose. We found no significant difference between the BNT162b2 vaccine participants who had a long interval and those who had a short interval between doses with respect to protection after the second dose, with a hazard ratio for infection of 1.34 (95% CI, 0.58 to 3.10) at 14 to 73 days with the use of the short interval as the reference group.

The adjusted effectiveness of two doses of the ChAdOx1 nCoV-19 vaccine was 58% (95% CI, 23 to 77) 14 to 73 days after the second dose. The effectiveness did not differ considerably with longer periods of time after the second dose, with overlapping confidence intervals of vaccine effectiveness reflecting the small number of participants with data used to calculate this estimate (Table 2 and Fig. 1). At 14 to 73 days after the second dose, the BNT162b2 vaccine with a short interval between doses was 74% more effective (95% CI, 36 to 89) and the BNT162b2 vaccine with a long interval between doses was 65% more effective (95% CI, 21 to 85) than the ChAdOx1 nCoV-19 vaccine. The Wald chi-square test of the model was 371.46 (31 degrees of freedom), with an Akaike information criterion of 15,367.

DURABILITY OF PROTECTION AFTER PRIMARY INFECTION

A total of 6169 participants in the previously infected cohort were followed in the unvaccinated follow-up period and up to 1 year after a primary infection. These participants were predominantly infected in the spring of 2020 and were followed in the period before emergence of the delta (B.1.617.2) variant. The risk of reinfection among these participants was 86% (95% CI, 81 to 89) lower than the risk of primary infection among the unvaccinated participants in the previously uninfected cohort (Table 3 and Fig. 2). There was evidence of considerable waning of protection more than 1 year after infection, with a reduction to 69% (95% CI, 38 to 84); protection during the first year after infection was 54% (95% CI, 3 to 78) higher than that after more than 1 year.

DURABILITY OF PROTECTION CONFERRED BY INFECTION AND VACCINATION

In the previously infected cohort, with unvaccinated participants in the previously uninfected cohort as the reference group (Table 3 and Fig. 2), a beneficial boosting of infection-acquired immunity was apparent, with combined protection of more than 90% after vaccination (after both the first and second doses). Waning of protection was not observed more than 1 year after infection or more than 6 months after vaccination. The Wald chi-square of the model was 789.68 (30 degrees of freedom), with an Akaike information criterion of 14,841.

DISCUSSION

A total of 18 months after the emergence of SARS-CoV-2 and 10 months after the rapid deployment of Covid-19 vaccines, we assessed the durability of protection against SARS-CoV-2 infection conferred by both infection-acquired and vaccine-acquired immunity. Most of our cohort of 26,280 previously uninfected health care workers received two doses of BNT162b2 vaccine, which was administered with a long interval between doses; this regimen was associated with

Table 1. Demographic Characteristics of the Participants at Baseline and Vaccination Status as of September 21, 2021.*

Characteristic	Previously Uninfected Cohort (N=26,280)	Previously Infected Cohort (N=9,488)	Total (N=35,768)
		number (percent)	
Age group			
<25 yr	935 (3.6)	362 (3.8)	1,297 (3.6)
25–34 yr	5,023 (19.1)	2,083 (22.0)	7,106 (19.9)
35–44 yr	6,580 (25.0)	2,268 (23.9)	8,848 (24.7)
45–54 yr	8,007 (30.5)	2,867 (30.2)	10,874 (30.4)
55–64 yr	5,283 (20.1)	1,802 (19.0)	7,085 (19.8)
≥65 yr	452 (1.7)	106 (1.1)	558 (1.6)
Sex			
Male	4,051 (15.4)	1,648 (17.4)	5,699 (15.9)
Female	22,190 (84.4)	7,827 (82.5)	30,017 (83.9)
Nonbinary, other, or prefer not to say	39 (0.1)	13 (0.1)	52 (0.1)
Race or ethnic group†			
White	23,610 (89.8)	8,024 (84.6)	31,634 (88.4)
Asian	1,581 (6.0)	905 (9.5)	2,486 (7.0)
Black	381 (1.4)	240 (2.5)	621 (1.7)
Mixed race	380 (1.4)	155 (1.6)	535 (1.5)
Other ethnic group	278 (1.1)	149 (1.6)	427 (1.2)
Prefer not to say	50 (0.2)	15 (0.2)	65 (0.2)
Medical conditions			
None	19,569 (74.5)	7,101 (74.8)	26,670 (74.6)
Immunosuppression	623 (2.4)	180 (1.9)	803 (2.2)
Chronic respiratory condition	3,306 (12.6)	1,133 (11.9)	4,439 (12.4)
Chronic nonrespiratory condition	2,782 (10.6)	1,074 (11.3)	3,856 (10.8)
Occupation			
Administrative or executive, office-based occupation	4,280 (16.3)	1,154 (12.2)	5,434 (15.2)
Nursing	8,658 (32.9)	3,526 (37.2)	12,184 (34.1)
Health care assistant	1,994 (7.6)	907 (9.6)	2,901 (8.1)
Doctor	3,053 (11.6)	1,195 (12.6)	4,248 (11.9)
Midwife	582 (2.2)	195 (2.1)	777 (2.2)
Physiotherapist, occupational therapist, or speech and language therapist	996 (3.8)	442 (4.7)	1,438 (4.0)
Nonclinical support staff: maintenance staff, security guard, or hospital porter	389 (1.5)	141 (1.5)	530 (1.5)
Pharmacist	582 (2.2)	155 (1.6)	737 (2.1)
Health care scientist	1,147 (4.4)	243 (2.6)	1,390 (3.9)
Medical, nursing, midwifery, or other student	867 (3.3)	333 (3.5)	1,200 (3.4)
Other	3,732 (14.2)	1,197 (12.6)	4,929 (13.8)
Occupational setting			
Office	5,481 (20.9)	1,521 (16.0)	7,002 (19.6)
Nonclinical setting	1,064 (4.0)	314 (3.3)	1,378 (3.9)
Outpatient setting	5,662 (21.5)	1,679 (17.7)	7,341 (20.5)
Maternity or labor ward	361 (1.4)	116 (1.2)	477 (1.3)
Ambulance, emergency department, inpatient ward	4,225 (16.1)	2,231 (23.5)	6,456 (18.0)
Intensive care	1,273 (4.8)	396 (4.2)	1,669 (4.7)
Operating room	657 (2.5)	209 (2.2)	866 (2.4)
Other	7,557 (28.8)	3,022 (31.9)	10,579 (29.6)

Table 1. (Continued.)

Characteristic	Previously Uninfected Cohort (N = 26,280)	Previously Infected Cohort (N = 9,488)	Total (N = 35,768)
		number (percent)	
Patient contact			
No	4,053 (15.4)	1052 (11.1)	5,105 (14.3)
Yes	22,227 (84.6)	8,436 (88.9)	30,663 (85.7)
Frequency of contact with patient with Covid-19			
Every day	5,585 (21.3)	3,212 (33.9)	8,797 (24.6)
Once per week	4,340 (16.5)	1,889 (19.9)	6,229 (17.4)
Once per month	2,368 (9.0)	889 (9.4)	3,257 (9.1)
Less than once per month	3,697 (14.1)	1,036 (10.9)	4,733 (13.2)
Never	10,290 (39.2)	2,462 (25.9)	12,752 (35.7)
Index of multiple deprivation‡			
5	6,563 (25.0)	2,308 (24.3)	8,871 (24.8)
4	5,982 (22.8)	2,091 (22.0)	8,073 (22.6)
3	5,537 (21.1)	1,978 (20.8)	7,515 (21.0)
2	4,408 (16.8)	1,612 (17.0)	6,020 (16.8)
1	2,680 (10.2)	1,178 (12.4)	3,858 (10.8)
Not known	1,110 (4.2)	321 (3.4)	1,431 (4.0)
Region			
East Midlands	1,963 (7.5)	862 (9.1)	2,825 (7.9)
East of England	2,415 (9.2)	948 (10.0)	3,363 (9.4)
London	2,432 (9.3)	1,256 (13.2)	3,688 (10.3)
Northeast	453 (1.7)	194 (2.0)	647 (1.8)
Northwest	2,174 (8.3)	1,255 (13.2)	3,429 (9.6)
Southeast	2,568 (9.8)	980 (10.3)	3,548 (9.9)
Southwest	4,503 (17.1)	1,037 (10.9)	5,540 (15.5)
West Midlands	1,900 (7.2)	817 (8.6)	2,717 (7.6)
Yorkshire and Humber	1,765 (6.7)	879 (9.3)	2,644 (7.4)
Scotland	4,646 (17.7)	803 (8.5)	5,449 (15.2)
Northern Ireland	888 (3.4)	239 (2.5)	1,127 (3.2)
Wales	573 (2.2)	218 (2.3)	791 (2.2)
Vaccination status as of September 21, 2021			
Vaccinated			
Second dose of BNT162b2 vaccine, long interval between doses	20,843 (79.3)	7,235 (76.3)	28,078 (78.5)
Second dose of BNT162b2 vaccine, short interval between doses	2,450 (9.3)	609 (6.4)	3,059 (8.6)
Second dose of ChAdOx1 nCoV-19 vaccine	1,895 (7.2)	908 (9.6)	2,803 (7.8)
First dose of any vaccine	630 (2.4)	307 (3.2)	937 (2.6)
Unvaccinated	462 (1.8)	429 (4.5)	891 (2.5)

* Baseline was defined as the date of cohort assignment between December 2020 and April 2021. In the cohort of previously infected participants, 83% were seropositive (72% on U.K. Health Security Agency testing) and 17% were seronegative but had had a previous positive antibody or polymerase-chain-reaction (PCR) test. In this cohort of 9488 participants, 6815 (72%) had a primary infection in the period between February 2020 and May 2020, a total of 272 (3%) had a primary infection in the period between June and August 2020, and 2401 (25%) had a primary infection in the period between September 2020 and March 2021; the date of infection was either the date of the first positive PCR test or the date of onset of coronavirus disease 2019 (Covid-19) symptoms..

† Race or ethnic group was reported by the participants.

‡ The index of multiple deprivation, which is a measure of neighborhood relative deprivation calculated by the Office of National Statistics, was obtained through linkage with participant postal codes; the index ranges from 1 (most deprived) to 5 (least deprived).

Table 2. Incidence of SARS-CoV-2 Infection and Effectiveness of Covid-19 Vaccines against Symptomatic and Asymptomatic Infection in Participants without Previous SARS-CoV-2 Infection, December 7, 2020, through September 21, 2021.*

Vaccination Status and Time since Vaccination	Participants	Days of Follow-up	Participants with Primary Infection	Crude Incidence Rate	Vaccine Effectiveness (95% CI)	Adjusted Vaccine Effectiveness (95% CI)
	no.	*no.*	*no.*	*no. of infections/ 10,000 person-days at risk*	%	%
Unvaccinated	18,094	649,643	1,038	15.98	—	—
Vaccinated with first dose						
BNT162b2 vaccine						
21–27 days	15,549	102,894	52	5.05	0.59 (0.44 to 0.71)	0.59 (0.42 to 0.71)
28–41 days	15,247	201,531	60	2.98	0.64 (0.47 to 0.76)	0.66 (0.52 to 0.76)
42–55 days	15,691	207,857	29	1.4	0.71 (0.56 to 0.81)	0.70 (0.54 to 0.81)
56–280 days	16,376	341,183	53	1.55	0.67 (0.53 to 0.77)	0.63 (0.46 to 0.75)
ChAdOx1 nCoV-19 vaccine						
21–27 days	1,471	10,204	2	1.96	0.63 (–0.61 to 0.92)	0.63 (–0.80 to 0.92)
28–41 days	1,495	20,496	1	0.49	0.87 (0.13 to 0.98)	0.85 (0.16 to 0.97)
42–55 days	1,494	20,445	3	1.47	0.42 (–0.66 to 0.80)	0.32 (–0.87 to 0.75)
56–249 days	1,470	38,308	10	2.61	0.24 (–0.56 to 0.63)	0.09 (–0.87 to 0.55)
Vaccinated with second dose						
BNT162b2 vaccine, long interval between doses						
14–73 days	18,562	1,063,102	16	0.15	0.85 (0.71 to 0.93)	0.85 (0.72 to 0.92)
74–133 days	17,332	950,734	264	2.78	0.70 (0.60 to 0.78)	0.66 (0.53 to 0.75)
134–193 days	13,539	528,245	479	9.07	0.73 (0.64 to 0.79)	0.68 (0.54 to 0.77)
194–239 days	2,261	20,774	81	38.99	0.46 (0.19 to 0.64)	0.51 (0.22 to 0.69)
BNT162b2 vaccine, short interval between doses						
14–73 days	2,259	118,505	10	0.84	0.85 (0.70 to 0.92)	0.89 (0.78 to 0.94)
74–133 days	2,238	130,389	6	0.46	0.62 (0.19 to 0.82)	0.58 (0.18 to 0.79)
134–193 days	2,122	118,192	47	3.98	0.58 (0.39 to 0.70)	0.50 (0.26 to 0.67)
194–265 days	1,706	69,352	87	12.54	0.62 (0.45 to 0.74)	0.53 (0.28 to 0.69)
ChAdOx1 nCoV-19 vaccine						
14–73 days	1,414	79,806	15	1.88	0.52 (0.15 to 0.73)	0.58 (0.23 to 0.77)
74–133 days	1,213	59,593	51	8.56	0.54 (0.32 to 0.68)	0.50 (0.29 to 0.65)
134–220 days	715	16,936	26	15.35	0.67 (0.40 to 0.82)	0.72 (0.39 to 0.87)

* Vaccine effectiveness was defined as 1 minus the hazard ratio. The crude incidence rate was not adjusted for the variable baseline hazard. The unadjusted vaccine effectiveness model was adjusted for the time since vaccination (combined with the dosing interval and type of vaccine) and baseline hazard only. The adjusted vaccine effectiveness model was adjusted for the baseline hazard time since vaccination (combined with the dosing interval and type of vaccine) and constant predictors (sex and race or ethnic group) and stratified across workplace setting, frequency of contact with patients with Covid-19, geographic area of the participant's workplace, and age. In order to provide an estimate of absolute protection, we defined the reference group as the unvaccinated participants in the previously uninfected cohort. Additional details are provided in Table S3. CI denotes confidence interval, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.

a considerably reduced risk of infection over the first 6 months that peaked in the first 2 months, with an adjusted vaccine effectiveness between 72% and 92%. However, we found evidence of considerable waning of immunity, with protection declining to between 22% and 69% after 6 months. We found no significant differences in the risk of infection when the BNT162b2 vaccine was administered with a short or long interval between doses, although we found considerably lower protection after two doses of the ChAdOx1 nCoV-19 vaccine than after two doses of the BNT162b2 vaccine. The period of waning of protection coincided with the period when the delta variant was the predominant circulating strain; this may account for the more pronounced waning of protection in our cohort, given the reported reduced vaccine effectiveness against the delta variant.[16]

Among unvaccinated participants, the risk of infection was between 81% and 89% lower up to a year after infection among those who were previously infected than among those who were previously uninfected, but we found evidence of waning of protection more than 1 year after infection. Vaccination after previous infection appeared to boost and extend immunity, and we found no indication of waning of this immunity even more than 1 year after primary infection. Protection against symptomatic infection in the cohort of participants who were vaccinated after previous infection was similar to that reported after a three-course vaccination (two doses and a booster dose).[17]

Our finding of reduced protection from infection in previously uninfected participants after 6 months following the receipt of two doses of vaccine strengthens the accruing evidence base. Our design overcomes several biases of recent studies, including underestimation of the proportion of participants with previous infection.[18] Previous studies have typically investigated symptomatic infection and used test-negative case–control or retrospective cohort designs and national testing surveillance data.[6,8,10] These real-world studies have shown consistently lower protection and more pronounced waning than a recent clinical trial of BNT162b2 vaccine that showed an efficacy of 83.7% (95% CI, 74.7 to 89.9) against symptomatic infection 4 to 6 months after the second dose[19]; this reduced protection was probably related to the reduced vaccine effectiveness reported against the delta variant.[16] The considerably lower protection observed after ChAdOx1 nCoV-19 vaccination than after BNT162b2 vaccination in the current study has also been reported in other recent studies.[6,19] Several studies have shown lower antibody titers after vaccination with ChAdOx1 nCoV-19 than after vaccination with BNT162b2[20,21]; a shorter interval to a reduction in titers below a putative protective antibody threshold from this lower baseline has been proposed as a causal mechanism for the lower vaccine effectiveness.[19] We found no significant difference between the BNT162b2 vaccine administered with a short interval between doses and that administered with a long interval between doses with respect to protection against infection after two doses, despite the findings of other studies showing considerably higher antibody, B-cell, and T-cell responses in participants who had long-interval regimens than in those who had short-interval regimens[14,22,23] and the findings of one observational study showing higher vaccine effectiveness against symptomatic infection associated with long-interval regimens.[14] It is plausible that the threshold for the prevention of all SARS-CoV-2 infections may be higher than that for the prevention of symptomatic infection.

Recent studies have shown that vaccination confers more durable protection against severe outcomes of hospitalization and death than against symptomatic and asymptomatic infection.[6,24] Although we have estimated vaccine effectiveness against all infections, including asymptomatic infections that have limited clinical significance, a reduction in vaccine effectiveness against infection will increase transmission to and the risk of infection among high-risk persons, some of whom may have progression to severe disease. Given the relatively young and healthy profile of our cohort and the rarity of severe disease observed in this study, we are unable to assess protection against severe outcomes.

Because of the limited length of follow-up, it remains unclear how long immune protection will last after previous infection; however, some studies have suggested that protection could last for up to 61 months, and others have shown protection ranging from 5 to 12 months.[20,25-28] We found that protection conferred by primary infection remained high at up to 1 year but then began to wane. Most follow-up investigations of

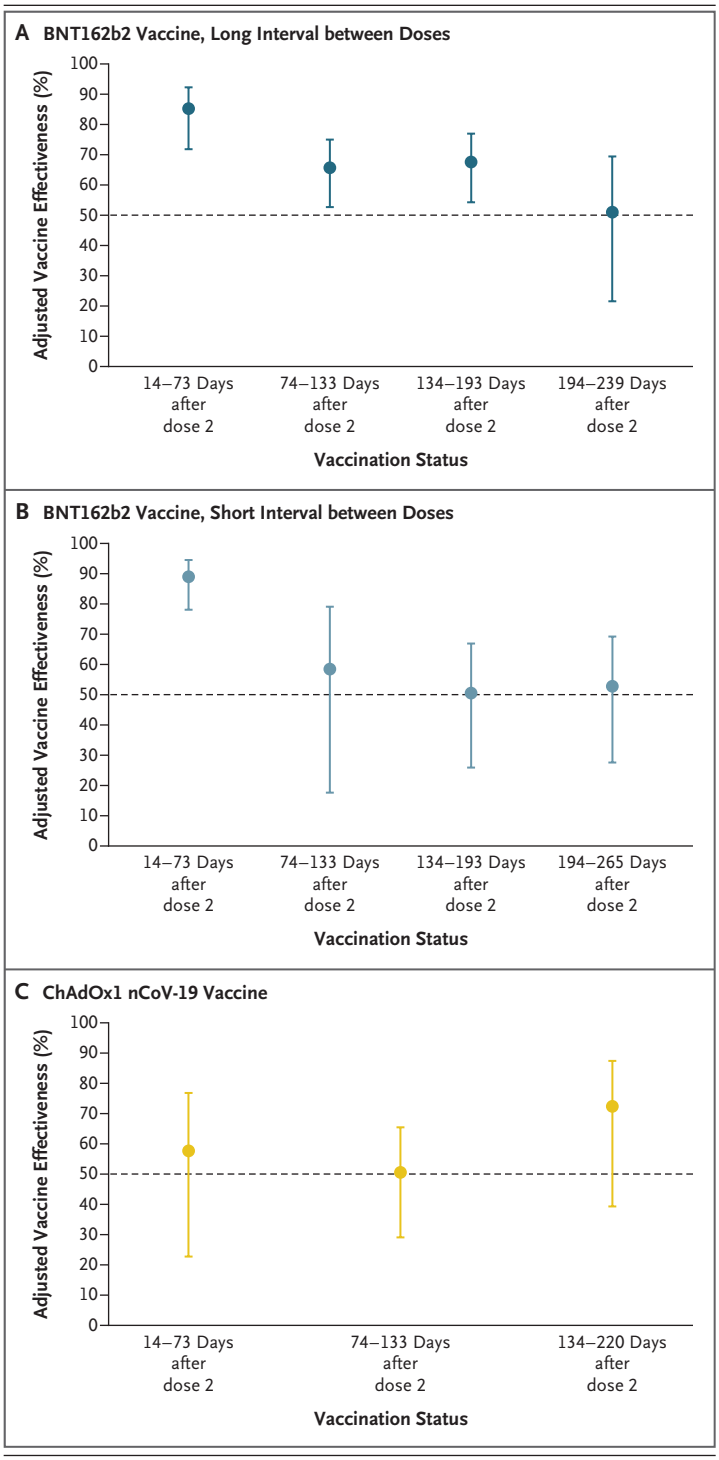

Figure 1. Adjusted Vaccine Effectiveness over Time in Previously Uninfected Participants, According to Vaccine Type and Dosing Interval.

Shown is the adjusted vaccine effectiveness of two doses of coronavirus disease 2019 (Covid-19) BNT162b2 vaccine with a long interval between doses (Panel A), BNT162b2 vaccine with a short interval between doses (Panel B), and ChAdOx1 nCoV-19 vaccine with short dose intervals and long dose intervals combined (Panel C) in participants without previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Data are for the period from December 7, 2020, through September 21, 2021. I bars indicate 95% confidence intervals.

unvaccinated, previously infected participants occurred before the delta variant wave, with most of this cohort infected in the spring of 2020 and vaccinated by the end of January 2021. Our ability to study infection-acquired immunity in unvaccinated persons at longer intervals was limited given the very small number of participants in our cohort who remained unvaccinated. It is possible that the sustained infection-acquired protection in our cohort was affected by repeated low-dose occupational exposure to Covid-19[29] and that it is therefore less generalizable to populations with lower exposure. It is also possible that sustained protection results from a broader diversity of T-cell immunity against different SARS-CoV-2 spike protein epitopes that emerges after infection, enhancing protection against variants and inducing long-lasting memory T-cell populations.[26,30,31] Although our finding of greater protection associated with infection-acquired immunity than with vaccine-acquired immunity has been reported by other authors,[32,33] others have reported that both types of immunity are equivalent[34,35] or that vaccine-acquired immunity is superior.[36] Although infection-acquired immunity is associated with a high level of protection, it wanes after 1 year in unvaccinated persons. In keeping with previous studies, we found an additional benefit of vaccination in previously infected participants,[33,37,38] and our finding of high levels of protection associated with immunity from infection plus vaccination has also been observed previously.[39] Until thresholds for protective antibody titers against SARS-CoV-2 infection are established, it will be challenging to accurately estimate how much vaccine-induced immunity is required to prevent reinfection at an individual level.

The key strengths of our study include the size of the cohort of participants who underwent frequent testing, independent of disease status,

Table 3. Incidence of SARS-CoV-2 Reinfection and Effectiveness of the BNT162b2 Vaccine against Symptomatic and Asymptomatic Reinfection among Participants with Previous SARS-CoV-2 Infection, December 7, 2020, through September 21, 2021.*

Infection and Vaccination Status and Time since Vaccination	Participants	Days of Follow-up	Participants with Reinfection	Crude Incidence Rate	Vaccine Effectiveness (95% CI)	Adjusted Vaccine Effectiveness (95% CI)
	no.	*no.*	*no.*	*no. of reinfections/ 10,000 person-days at risk*	%	%
Follow-up ≤1 yr after primary infection						
Unvaccinated	6,169	258,088	58	2.25	0.82 (0.76 to 0.87)	0.86 (0.81 to 0.89)
Vaccinated with first dose, 21–271 days	7,381	303,281	13	0.43	0.91 (0.84 to 0.95)	0.92 (0.86 to 0.95)
Vaccinated with second dose						
14–73 days	5,075	201,580	8	0.40	0.81 (0.60 to 0.91)	0.84 (0.67 to 0.92)
74–133 days	2,480	119,013	12	1.01	0.90 (0.82 to 0.95)	0.92 (0.83 to 0.96)
134–193 days	1,533	51,893	13	2.51	0.91 (0.85 to 0.95)	0.92 (0.85 to 0.95)
194–261 days	192	3,346	3	8.97	0.75 (–0.19 to 0.95)	0.86 (0.27 to 0.97)
Follow-up >1 yr after primary infection						
Unvaccinated	486	50,041	12	2.40	0.71 (0.42 to 0.85)	0.69 (0.38 to 0.84)
Vaccinated with first dose, 21–274 days	1,642	38,422	2	0.52	0.90 (0.60 to 0.97)	0.94 (0.62 to 0.99)
Vaccinated with second dose						
14–73 days	4,852	234,484	2	0.09	0.93 (0.72 to 0.98)	0.94 (0.75 to 0.99)
74–133 days	4,970	261,549	9	0.34	0.96 (0.92 to 0.98)	0.97 (0.93 to 0.98)
134–193 days	3,772	137,473	18	1.31	0.95 (0.91 to 0.97)	0.93 (0.89 to 0.96)
194–262 days	654	15,808	2	1.27	0.96 (0.84 to 0.99)	0.95 (0.82 to 0.99)

* The crude incidence rate was not adjusted for the variable baseline hazard. In order to provide an estimate of absolute protection, we defined the reference group as the unvaccinated participants in the previously uninfected cohort. Vaccine effectiveness in the unvaccinated group refers to protection against reinfection. Infection rates in the unvaccinated cohort with previous infection were compared with those in the unvaccinated cohort without previous infection. In the assessment of unadjusted absolute protection against reinfection, the model was adjusted for combinations of time since vaccination with BNT162b2 vaccine and since primary infection and the baseline hazard only. In the assessment of adjusted absolute protection against reinfection, the model was adjusted for the baseline hazard, combinations of time since vaccination with BNT162b2 vaccine and since primary infection, and constant predictors (sex and race or ethnic group) and was stratified across workplace setting, frequency of contact with patients with Covid-19, geographic area of the participant's workplace, and age. Additional details are provided in Table S4.

with an average PCR test interval of 16.6 days in the unvaccinated follow-up period and 14.5 days in the vaccinated follow-up period, supplemented by the widespread use of lateral-flow testing, which means we can be confident that most infections were detected. We were able to simultaneously investigate vaccination and previous infection status in this well-defined cohort and to adjust for important confounders, including workplace exposures. The most important limitation of our study is the relatively small number of participants who contributed follow-up data on key vaccination exposures; these participants included those who were unvaccinated, those who received the ChAdOx1 nCoV-19 vaccine, and those who received the BNT162b2 vaccine with a short interval between doses. This small number of participants particularly affected the precision of our estimates and our ability to assess potential waning after two doses of the ChAdOx1

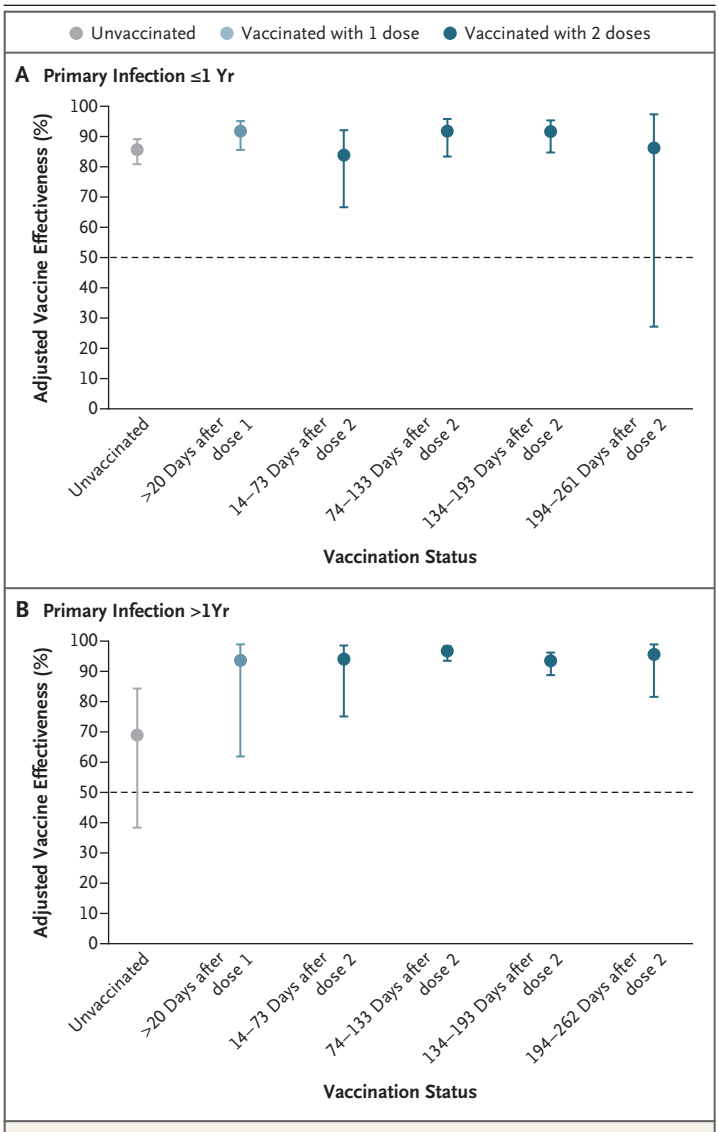

Figure 2. Protection against Reinfection with SARS-CoV-2 up to 18 Months after the Primary Infection.

Data are for the period from December 7, 2020, through September 21, 2021, for both the BNT162b2 and ChAdOx1 nCoV-19 vaccines and with all dosing intervals. I bars indicate 95% confidence intervals.

nCoV-19 vaccine. The strengths of our study design and the speed of vaccine deployment considerably limited the effect of depletion-of-susceptibles bias (which particularly affects studies on waning of immunity from vaccination).[18] Although the effect of this bias was not apparent in our sensitivity analysis (see the Supplementary Appendix), some residual confounding may remain.

BNT162b2 vaccine administered with a short or long interval between two doses was associated with a considerably reduced risk of SARS-CoV-2 infection (asymptomatic and symptomatic) in the short term, but this protection waned after 6 months, during a period when the delta variant predominated. Protection associated with two doses of ChAdOx1 nCoV-19 vaccine was considerably lower than that associated with the BNT162b2 vaccine overall. The highest and most durable protection was observed in participants who received one or two doses of vaccine after a primary infection. Strategic use of booster doses of vaccine to avert waning of protection (particularly in double-vaccinated, previously uninfected persons) may reduce infection and transmission in the ongoing response to Covid-19.

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APPENDIX

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Morbidity and Mortality Weekly Report

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

See table footnotes on the next page.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

See table footnotes on the next page.

Discussion

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

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

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

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

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

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

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

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

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

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

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

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

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

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

See table footnotes on the next page.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Summary

What is already known about this topic?

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

What is added by this report?

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

What are the implications for public health practice?

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

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Centers for Disease Control and Prevention

COVID-19

Possible Side Effects After Getting a COVID-19 Vaccine

Updated Jan. 12, 2022

COVID-19 vaccination helps protect people from getting COVID-19. Some people have side effects from the vaccine, which are normal signs that their body is building protection. These side effects may affect their ability to do daily activities, but they should go away in a few days. Some people have no side effects, and allergic reactions are rare.

Adverse effects that could cause a long-term health problem are extremely unusual following any vaccination, including COVID-19 vaccination. If adverse effects occur, they generally happen within six weeks of receiving a vaccine dose. For this reason, during clinical trials, the U.S. Food and Drug Administration (FDA) collected data on each of the authorized COVID-19 vaccines for a minimum of two months (eight weeks) after the final dose. CDC, FDA, and other federal agencies continue to monitor the safety of COVID-19 vaccines even now that the vaccines are in use.

Common Side Effects

On the arm where you got the shot:

- Pain
- Redness
- Swelling

Throughout the rest of your body:

- Tiredness
- Headache
- Muscle pain
- Chills
- Fever
- Nausea

Severe allergic reactions after COVID-19 vaccination are rare. Anyone who had a severe allergic reaction after getting an mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna) should not get another dose of either of the mRNA COVID-19 vaccines. Anyone who had a severe allergic reaction after receiving Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccine, should not receive another dose of that vaccine.

Learn about getting a different type of COVID-19 vaccine after an allergic reaction.

Helpful Tips to Relieve Side Effects

Talk to a doctor about taking over-the-counter medicine, such as ibuprofen, acetaminophen, aspirin (only for people ages 18 years or older), or antihistamines for any pain and discomfort experienced after getting vaccinated.

People can take these medications to relieve side effects after vaccination if they have no other medical reasons that prevent them from taking these medications normally. Ask your child's healthcare provider for advice on using a non-aspirin pain reliever and other steps you can take at home to comfort your child after vaccination.

It is not recommended to take these medicines before vaccination for the purpose of trying to prevent side effects.

To reduce pain and discomfort where the shot is given

- Apply a clean, cool, wet washcloth over the area.
- Use or exercise your arm.

To reduce discomfort from fever

- Drink plenty of fluids.
- Dress lightly.

After a Second Shot or a Booster Shot

Side effects after the second shot may be more intense than the ones experienced after the first shot. These side effects are normal signs that the body is building protection and should go away within a few days.

So far, reactions reported after getting a booster shot are similar to those after the two-dose or single-dose primary shots. Fever, headache, fatigue, and pain at the injection site were the most commonly reported side effects, and overall, most side effects were mild to moderate. However, as with the two-dose or single-dose primary shots, serious side effects are rare but can occur.

When to Call the Doctor

Side effects can affect you or your child's ability to do daily activities, but they should go away in a few days.

In most cases, discomfort from pain or fever is a normal sign that the body is building protection. Contact a doctor or healthcare provider:

- If the redness or tenderness where the shot was given gets worse after 24 hours
- If the side effects are worrying or do not seem to be going away after a few days

If you or your child get a COVID-19 vaccine and you think you or they might be having a severe allergic reaction after leaving the vaccination site, seek immediate medical care by calling 911. Learn more about COVID-19 vaccines and rare severe allergic reactions.

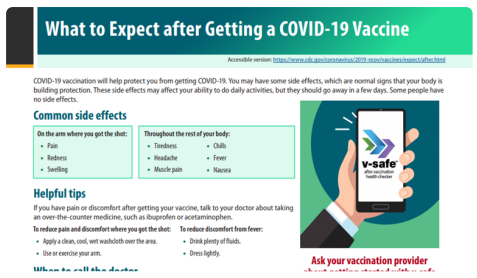
If You Have No Side Effects

Reactions after getting a COVID-19 vaccine can vary from person to person. Most people in clinical trials experienced only mild side effects, and some of them had no side effects at all. Those people still had a strong immune response to the vaccine. Vaccination protects you from severe COVID-19 infection whether or not you have side effects after vaccination.

Reporting Side Effects

V-safe provides quick and confidential health check-ins via text messages and web surveys so you can quickly and easily share with CDC how you or your dependent feel after getting a COVID-19 vaccine.

If you would like to report an adverse event, side effect, or reaction from the COVID-19 vaccine, please use the Vaccine Adverse Event Reporting System (VAERS) . Learn more about VAERS.



Fact sheet for healthcare workers to give after vaccination.

File Details: 199 KB, 1 page

View PDF in English

Other Languages

More Information

- Ensuring COVID-19 vaccine safety in the United States
- Benefits of getting a COVID-19 vaccine
- COVID-19 Vaccines for Children and Teens
- How to protect yourself and others
- Safety of COVID-19 Vaccines

Last Updated Jan. 12, 2022

Centers for Disease Control and Prevention

COVID-19

Allergic Reactions after COVID-19 Vaccination

Updated Feb. 3, 2022

If You Are Having a Severe Allergic Reaction to a COVID-19 Vaccine

Severe allergic reactions to vaccines are rare but can happen. If you get a COVID-19 vaccine and you think you might be having a severe allergic reaction after leaving the vaccination provider site, seek immediate medical care by calling 911.

A severe allergic reaction can cause

- difficulty breathing or wheezing,
- a drop in blood pressure,
- swelling of the tongue or throat, or
- a generalized rash or hives, which may include mucus membranes.

If You Had a Severe Allergic Reaction to a COVID-19 Vaccine

The Pfizer-BioNTech and Moderna COVID-19 vaccines are messenger RNA vaccines, also called mRNA vaccines. Johnson & Johnson's/Janssen (J&J/Janssen) COVID-19 vaccine is a viral vector vaccine. If you had a severe allergic reaction after receiving a particular type of COVID-19 vaccine (either mRNA or viral vector), you should not get another dose of that type of vaccine.

CDC recommends that people getting a booster get an mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna). However, if you had a severe allergic reaction after a dose of an mRNA COVID-19 vaccine or if you have had a severe allergic reaction to any ingredient in an mRNA COVID-19 vaccine, you may be able to get the J&J/Janssen COVID-19 vaccine.

Learn about getting a different type of COVID-19 vaccine after an allergic reaction.

If You Have Had an Immediate Allergic Reaction to Other Vaccines or Injectables

If you have had an immediate allergic reaction (a reaction that started within 4 hours) to any vaccine other than a COVID-19 vaccine or any injectable therapy, you may still be able to get a COVID-19 vaccine. However, your doctor may refer you to an allergy and immunology specialist for additional care or advice.

If You Had a Non-severe Allergic Reaction to a COVID-19 Vaccine

If you had an immediate allergic reaction (a reaction that started within 4 hours of getting vaccinated) to a COVID-19 vaccine, but the reaction was not considered severe by a medical professional, you likely can **receive another dose of the same vaccine**

under certain conditions. Your doctor may refer you to an allergy and immunology specialist for additional care or advice.

If You Had a Rash on the Arm where You Got a COVID-19 Shot

If you had a red, itchy, swollen, or painful rash where you got a COVID-19 shot, **you should still get another shot** at the recommended interval. This applies to second, additional, or booster shots. These rashes can start a few days to more than a week after your shot and are sometimes quite large. These rashes are also known as "COVID arm." Tell your vaccination provider that you experienced a rash or "COVID arm" after your shot. Your vaccination provider may recommend that you get your next COVID-19 vaccine in the opposite arm if possible.

If the rash is itchy, you can take an antihistamine. If it is painful, you can take a pain medication like acetaminophen or a non-steroidal anti-inflammatory drug (NSAID).

Safeguards Are in Place

- Everyone who gets a COVID-19 vaccine should be monitored on site for at least 15 minutes after vaccination.
- You should be monitored for 30 minutes if
  - You have had a severe allergic reaction called anaphylaxis due to any cause
  - You have had any type of immediate (within 4 hours) allergic reaction to a non-COVID-19 vaccine or injectable therapy
  - You had a severe allergic reaction to one type of COVID-19 vaccine (for example, an mRNA vaccine) and are now receiving another type of COVID-19 vaccine (for example, a viral vector). This vaccination should only be done in a health clinic, medical facility, or doctor's office.
  - You had an immediate (within 4 hours) allergic reaction that was not severe from a previous dose of that type of COVID-19 vaccine. This vaccination should only be done in a health clinic, medical facility, or doctor's office.
- Vaccination providers should have appropriate personnel, medications, and equipment—such as epinephrine, antihistamines, blood pressure monitor, and timing devices to check your pulse—at all COVID-19 vaccination provider sites.
- If you experience a severe allergic reaction after getting a COVID-19 vaccine, vaccination providers can provide care rapidly and call for emergency medical services. You should continue to be monitored in a medical facility for at least several hours.

CDC Is Monitoring Reports of Severe Allergic Reactions

If someone has a severe allergic reaction after getting vaccinated, their vaccination provider will send a report to the Vaccine Adverse Event Reporting System (VAERS). VAERS is a national system that collects reports from healthcare professionals, vaccine manufacturers, and the public about adverse events that happen after vaccination. Reports of adverse events that are unexpected, appear to happen more often than expected, or have unusual patterns are followed up with specific studies.

Learn more about how CDC and federal partners are monitoring reports of selected adverse events after COVID-19 vaccination.

Learn more about how federal partners are monitoring the safety of COVID-19 vaccines in the United States.

Related Pages

- Information about COVID-19 Vaccines for People with Allergies
- Possible Side Effects
- Ensuring the Safety of COVID-19 Vaccines

For Healthcare Professionals

- Interim Considerations: Preparing for the Potential Management of Anaphylaxis at COVID-19 Vaccination Sites

- Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States
- COVID-19 Clinical Resources

More Information

Research

Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020

Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021

More Information

Vaccine Adverse Event Reporting System (VAERS)

COVID-19 Vaccine Safety Publications

Last Updated Feb. 3, 2022

Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccines While Pregnant or Breastfeeding

Updated Mar. 3, 2022

What You Need to Know

- If you are pregnant or were recently pregnant, you are more likely to get very sick from COVID-19 compared to people who are not pregnant. Additionally, if you have COVID-19 during pregnancy, you are at increased risk of complications that can affect your pregnancy and developing baby.
- Getting a COVID-19 vaccine can help protect you from getting very sick from COVID-19.
- COVID-19 vaccination is recommended for people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future.
- People who are pregnant should stay up to date with their COVID-19 vaccines, including getting a COVID-19 booster shot when it's time to get one.
- Evidence continues to build showing that COVID-19 vaccination during pregnancy is safe and effective.
- There is currently no evidence that any vaccines, including COVID-19 vaccines, cause fertility problems in women or men.

Increased Risk for Severe Illness from COVID-19

Although the overall risks are low, if you are pregnant or were recently pregnant, you are more likely to get very sick from COVID-19 compared to people who are not pregnant. People who get very sick from COVID-19 may require hospitalization, admission to an intensive care unit (ICU), or use of a ventilator or special equipment to breathe. Severe COVID-19 illness can also lead to death. Additionally, if you have COVID-19 during pregnancy, you are at increased risk of complications that can affect your pregnancy and developing baby. For example, COVID-19 during pregnancy increases the risk of delivering a preterm or stillborn infant.

Safety and Effectiveness of COVID-19 Vaccination during Pregnancy

Evidence continues to build showing that COVID-19 vaccination before and during pregnancy is safe and effective. It suggests that the benefits of receiving a COVID-19 vaccine outweigh any known or potential risks of vaccination during pregnancy. Below is a brief summary of the growing evidence:

- **COVID-19 vaccines do not cause COVID-19 infection, including in people who are pregnant or their babies.** None of the COVID-19 vaccines contain live virus. They cannot make anyone sick with COVID-19, including people who are pregnant or their babies.
- **Data on the safety of receiving an mRNA COVID-19 vaccine, Moderna or Pfizer-BioNTech (Comirnaty), during pregnancy are reassuring.**
  - Early data from three safety monitoring systems did not find any safety concerns for people who received an mRNA COVID-19 vaccine late in pregnancy or for their babies.[1]

- Scientists have not found an increased risk for miscarriage among people who received an mRNA COVID-19 vaccine just before and during early pregnancy (before 20 weeks of pregnancy).[2-4]
- In a study of more than 40,000 pregnant women, COVID-19 vaccination during pregnancy was not associated with preterm birth or delivering an infant small for their gestational age.[5]
- The monitoring of COVID-19 vaccination during pregnancy is ongoing. CDC will continue to follow people vaccinated during all trimesters of pregnancy to better understand effects on pregnancy and babies.

- **Data show that receiving an mRNA COVID-19 vaccine during pregnancy reduces the risk for infection and severe illness for people who are pregnant.** Recent studies compared people who were pregnant and received an mRNA COVID-19 vaccine with people who did not. Scientists found that COVID-19 vaccination lowered the risk of infection from the virus that causes COVID-19 and was even more effective at reducing the risk of getting very sick from COVID-19.[6-10]
- **Vaccination during pregnancy builds antibodies that might protect the baby.** When people receive an mRNA COVID-19 vaccine during pregnancy, their bodies build antibodies against COVID-19, similar to people who are not pregnant. Antibodies made after a pregnant person received an mRNA COVID-19 vaccine have been found in umbilical cord blood. This means COVID-19 vaccination during pregnancy might help protect babies against COVID-19. More data are needed to determine how these antibodies, similar to those produced with other vaccines, may provide protection to the baby.[11-13]
  - A recent small study found that at 6 months old, the majority (57%) of infants born to pregnant people who were vaccinated during pregnancy **had detectable antibodies against COVID-19**, compared to 8% of infants born to pregnant people who had COVID-19 during pregnancy.[14]
- **New data show that completing a two-dose primary mRNA COVID-19 vaccine series during pregnancy can help protect babies younger than 6 months old from hospitalization due to COVID-19.** In this report, the majority (84%) of babies hospitalized with COVID-19 were born to pregnant people who were not vaccinated during pregnancy.[15]
- **No safety concerns were found in animal studies.** Studies in animals receiving a Moderna, Pfizer-BioNTech, or Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccine before or during pregnancy found no safety concerns in pregnant animals or their babies.
- **No adverse pregnancy-related outcomes occurred in previous clinical trials that used the same vaccine platform as the J&J/Janssen COVID-19 vaccine.** Vaccines that use the same viral vector as the J&J/Janssen COVID-19 vaccine have been given to people in all trimesters of pregnancy, including in a large-scale Ebola vaccination trial. No adverse pregnancy-related outcomes, including adverse outcomes affecting the baby, were associated with vaccination in these trials. Learn more about how viral vector vaccines work.

More clinical trials on the safety of COVID-19 vaccines and how well they work in people who are pregnant are underway or planned. Vaccine manufacturers are also collecting and reviewing data from people in the completed clinical trials who received a vaccine and became pregnant during the trial.

> V-safe provides quick and confidential health check-ins via text messages and web surveys so you can quickly and easily share with CDC how you or your dependent feel after getting a COVID-19 vaccine.

People who are Pregnant

CDC recommends that people who are pregnant get vaccinated and stay up to date with their COVID-19 vaccines, including getting a COVID-19 booster shot when it's time to get one. CDC recommendations align with those from professional medical organizations serving people who are pregnant, including the American College of Obstetricians and Gynecologists, Society for Maternal Fetal Medicine, and the American Society for Reproductive Medicine, along with many other professional medical organizations.

Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) are preferred over the J&J/Janssen COVID-19 vaccine for primary and booster vaccination, but the J&J/Janssen COVID-19 vaccine may be considered in some situations.

Getting a COVID-19 vaccine can protect you from getting very sick from COVID-19, and keeping you as healthy as possible during pregnancy is important for the health of your baby. If you are pregnant, consider having a conversation with your healthcare professional about COVID-19 vaccination. While such a conversation might be helpful, it is not required before vaccination. You can receive a COVID-19 vaccine, including a booster shot, without any additional documentation from your healthcare professional.

Common Questions about Vaccination during Pregnancy

What are the long-term effects on the baby when a person gets a COVID-19 vaccine during pregnancy?

Scientific studies to date have shown no safety concerns for babies born to people who were vaccinated against COVID-19 during pregnancy.[1,5] Based on how these vaccines work in the body, experts believe they are unlikely to pose a risk for long-term health effects. CDC continues to monitor, analyze, and disseminate information from people vaccinated during all trimesters of pregnancy to better understand effects on pregnancy and babies.

When during pregnancy should a person get a COVID-19 vaccine?

CDC and professional medical organizations, including the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine, recommend COVID-19 vaccination at any point in pregnancy, as well as booster doses for those eligible. COVID-19 vaccination can protect you from getting very sick from COVID-19, and keeping you as healthy as possible during pregnancy is important for the health of your baby.

Which COVID-19 vaccine should pregnant people receive?

In most situations, including for people who are pregnant and people who are breastfeeding, Pfizer-BioNTech or Moderna COVID-19 vaccines (mRNA COVID-19 vaccines) are preferred over the J&J/Janssen COVID-19 vaccine for primary and booster vaccination due to the risk of serious adverse events. Thrombosis with thrombocytopenia syndrome (TTS) is a rare but serious adverse event that causes blood clots in large blood vessels and low platelets (blood cells that help form clots) and is associated with the J&J/Janssen COVID-19 vaccine. Vaccine recipients must be informed of the risks and benefits of J&J/Janssen COVID-19 vaccination. The J&J/Janssen COVID-19 vaccine may be considered in some situations, including for persons who

- Had a severe reaction after an mRNA vaccine dose or who have a severe allergy to an ingredient of Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines),
- Would otherwise remain unvaccinated for COVID-19 due to limited access to Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines); or
- Wants to get the J&J/Janssen COVID-19 vaccine despite the safety concerns.

Learn more about the considerations for J&J/Janssen COVID-19 vaccine.

If you are pregnant and have questions about COVID-19 vaccine

If you would like to speak to someone about COVID-19 vaccination during pregnancy, you can contact MotherToBaby whose experts are available to answer questions in English or Spanish by phone or chat. The free and confidential service is available Monday–Friday, 8am–5pm (local time). To reach MotherToBaby:

- Call 1-866-626-6847
- Chat live or send an email MotherToBaby

People who are Breastfeeding

CDC recommends that people who are breastfeeding get vaccinated and stay up to date with their COVID-19 vaccines, including getting a COVID-19 booster shot when it's time to get one. Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) are preferred over the J&J/Janssen COVID-19 vaccine for primary and booster vaccination, but the J&J/Janssen COVID-19 vaccine may be considered in some situations. Clinical trials for the COVID-19 vaccines currently used in the United States did not include people who were breastfeeding. Therefore, there are limited data available on the

- Safety of COVID-19 vaccines in people who are breastfeeding
- Effects of vaccination on the breastfed baby
- Effects on milk production or excretion

COVID-19 vaccines cannot cause COVID-19 infection in anyone, including the mother or the baby. None of the COVID-19 vaccines contain live virus. Vaccines are effective at preventing COVID-19 in people who are breastfeeding. Recent reports have shown that breastfeeding people who have received mRNA COVID-19 vaccines have antibodies in their breastmilk, which could help protect their babies. More data are needed to determine what level of protection these antibodies may provide to the baby.[13, 16-20]

Vaccine Side Effects

Side effects can occur after receiving any of the available COVID-19 vaccines, especially after the second dose for vaccines that require two doses or a booster. People who are pregnant have not reported different side effects from people who are not pregnant after vaccination with mRNA COVID-19 vaccines (Moderna and Pfizer-BioNTech vaccines). [1] Fever, for any reason, has been associated with adverse pregnancy outcomes. Fever in pregnancy may be treated with acetaminophen as needed, in moderation, and in consultation with a healthcare provider. Learn more at Possible Side Effects After Getting a COVID-19 Vaccine.

Although rare, some people have had severe allergic reactions after receiving a COVID-19 vaccine. Talk with your healthcare provider if you have a history of allergic reaction to any other vaccine or injectable therapy (intramuscular, intravenous, or subcutaneous).

Key considerations you can discuss with your healthcare provider include:

- The benefits of vaccination
- The unknown risks of developing a severe allergic reaction
- If you have an allergic reaction after receiving a COVID-19 vaccine during pregnancy, you can receive treatment for it.

People Who Would Like to Have a Baby

CDC recommends that people who are trying to get pregnant now or might become pregnant in the future, as well as their partners, get vaccinated and stay up to date with their COVID-19 vaccines, including getting a COVID-19 booster shot when it's time to get one. Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) are preferred over the J&J/Janssen COVID-19 vaccine for primary and booster vaccination, but the J&J/Janssen COVID-19 vaccine may be considered in some situations. In addition, everyone who is trying to get pregnant now, or might become pregnant in the future, should get a booster shot if eligible.

> **Find a COVID-19 vaccine or booster:** Search vaccines.gov, text your ZIP code to 438829, or call 1-800-232-0233 to find locations near you.

Related Pages

- Allergic Reactions
- People Who Would Like to Have a Baby

For Healthcare and Public Health

- Considerations for the Use of COVID-19 Vaccines Currently Available in the U.S.
- COVID-19 Vaccination among Pregnant People
- Management of Anaphylaxis after COVID-19 Vaccination
- ACOG Recommendations for Vaccinating Pregnant People
- ACOG Practice Advisory: COVID-19 Vaccination Considerations for Obstetric-Gynecologic Care
  - ACOG video about COVID-19 vaccines for people who are pregnant
- COVID-19 Clinical and Professional Resources
- Clinic Poster: Protect yourself and your baby from COVID-19
- Clinic Poster: Protect yourself and your baby from COVID-19 (Español)

More Information

Mother to Baby: Information for people who are pregnant of breastfeeding

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Last Updated Mar. 3, 2022

Hunterdon Healthcare
Your full circle of care.
(https://www.hunterdonhealthcare.org/)

Insurance Information

Hunterdon Healthcare System participates with many different insurance companies, each having individual rules. Please present your insurance card at the beginning of each appointment and let us know if there have been any changes in your coverage. We will help you with your plan as it relates to benefits, referrals, and billing; but ultimately it is your responsibility to understand your insurance.

We are currently accepting from the following providers:

- Aetna (http://www.aetna.com/)
- Aetna Better Health (https://www.aetnabetterhealth.com/)
- Aetna Medicare Solutions (https://www.aetnamedicare.com/)
- Aetna Medicare Advantage (All plans)
- AmeriHealth (http://www.amerihealth.com/)
- Beech Street (http://www.beechstreet.com/)
- Cigna (http://www.cigna.com/)
- Community Care Network (CCN)
- Consumer Health Network (CHN) (https://www.chn.com/)
- Coventry (https://member.cvty.com/memberPortalWeb/appmanager/memberPortal/member)
- Devon Health (http://www.devonhealth.com/)
- First Health (https://providerlocator.firsthealth.com/home/index)
- HMC Patient Assistance Program
- Horizon Blue Cross Blue Shield of New Jersey (http://www.horizonblue.com/)
- All Blue Cross Plans through Blue Card Program
- Horizon Blue Cross Blue Shield Indemnity
- Horizon Blue Cross Blue Shield Direct Access (All product types)
- Horizon Blue Cross Blue Shield EPO (All product types)
- Horizon Blue Cross Blue Shield HMO (All product types)
- Horizon Blue Cross Blue Shield OMNIA (All product types)

- Horizon Blue Cross Blue Shield POS (All product types)
- Horizon Blue Cross Blue Shield PPO (All product types)
- Horizon Blue Cross Blue Shield Medicare Advantage (All product types)
- Horizon Casualty (http://horizoncasualty.com/)
- Horizon NJ Health (http://www.horizonnjhealth.com/)
- Horizon NJ TotalCare
- MagnaCare (http://www.magnacare.com)
- Magellan Behavioral Health
- Medicare (http://www.medicare.gov/)
- NJ State Medicaid (http://www.medicaid.gov/)
- Oxford Health Plan PPO (http://www.oxhp.com/)
- Oxford Health Plan HMO
- Oxford Medicare Advantage Plans
- Physician Healthcare Systems (PHCS) (http://www.multiplan.com/)
- QualCare PPO (https://www.qualcareinc.com/Login/Login.aspx)
- United Healthcare (http://www.uhc.com/)
- United Healthcare Community Plan (NJFAMCAR & NJDUALCM) (http://www.uhccommunityplan.com/)
- United Medicare Advantage Plans
- United Medicare Advantage Private Fee for Service Plans (PFFS)

It is also important to have a good understanding of your healthcare benefits. Please call your managed healthcare provider directly with any questions.

If your insurance requires a referral or authorization, please contact our office. Please note that we request 2 business days to process referrals.

Please click here for: Out of Network Insurance (http://www.hunterdonhealthcare.org/for-patients/out-of-network-insurance/)

Centers for Medicare and Medicaid Services for Comprehensive Joint Replacement

Hunterdon Medical Center is participating in the Comprehensive Care for Joint Replacement (CJR) model. Medicare designed this model to encourage higher quality and greater financial accountability from hospitals when Medicare beneficiaries receive lower-extremity joint replacement procedures (LEJR), typically hip and knee replacements. Hunterdon Medical Center 's participation in the CJR model should not restrict your access to care for your medical condition or your freedom to choose your health care providers and services. All existing Medicare beneficiary protections continue to be available to you. Medicare is using the CJR model to encourage

Hunterdon Medical Center to work more closely with your doctors and other healthcare providers that help patients recover after discharge from the hospital including, but not limited to, nursing homes, skilled nursing facilities, home health agencies, inpatient rehabilitation facilities, and long-term care hospitals.

The following list of physicians includes healthcare providers and suppliers that have established a financial arrangement with Hunterdon Medical Center in order to share in financial rewards and/or losses in the CJR model. This group of physicians all practice with MidJersey Orthopaedics and bill under TIN # 22-2175464.

Suneel K. Basra, DPM
Scott T. Bleazey, DPM
Richard Chang, MD
Patrick M. Collalto, MD
Philip J. Glassner, MD
Eric Gordon, MD
Robert C. More, MD
Michael E. Pollack, MD
Thomas A. St. John, MD

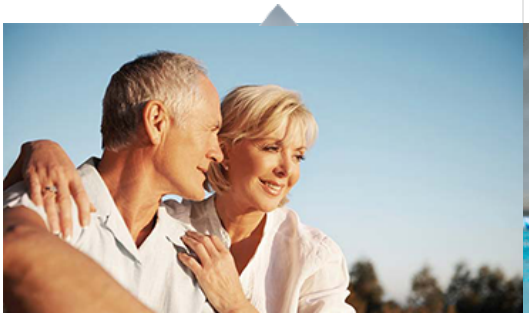
To review the HMC Policy for Selecting Collaborators for the CJR Program, please click here (https://www.hunterdonhealthcare.org/wp-content/uploads/2019/06/HMC-Policy-for-Selecting-Collaborators-for-the-CJR-Program-2019.pdf).

Hunterdon Healthcare Practices Financial Policy (http://www.hunterdonhealthcare.org/for-patients/financial-policy/)

Event Calendar

Hunterdon Healthcare offers an array of educational events, including childbirth, healthy living and fitness classes.

LEARN MORE (/CALENDAR)



Health and Wellness Centers

Where health and fitness meet to help you stay healthy at every age.

LEARN MORE (HTTP://WELLNESS.HUNTERDONHEALTHCARE.ORG/)

Primary and Specialty Care Services

The Hunterdon Healthcare network consists of over 30 primary and specialty practices.

LEARN MORE (/SERVICE/PRIMARYCARE/)

(https://www.facebook.com/HunterdonHealthcare) (https://twitter.com/hunterdonhealth) (https://www.pinterest.com/hunterdonhealth/) (https://www.instagram.com/hunterdonhealthcare/) (https://www.youtube.com/user/hunterdonhealth) (rss)

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- DAILY HEALTH QUESTIONNAIRE (HTTPS://FORMS.GLE/UBND9AL5M6QA4EZQ6)

Hunterdon Healthcare
Your full circle of care.
(https://www.hunterdonhealthcare.org/)

Clinical Quality

Overview

Clinical Quality (Https://Www.Hunterdonhealthcare.Org/About-Us/Quality-Safety/Clinical-Quality/)
Patient Advocacy (Https://Www.Hunterdonhealthcare.Org/About-Us/Quality-Safety/Patient-Advocacy/)
Patient Experience (Https://Www.Hunterdonhealthcare.Org/About-Us/Quality-Safety/Patient-Experience/)
Patient Safety (Https://Www.Hunterdonhealthcare.Org/About-Us/Quality-Safety/Patient-Safety/)
HRO – Higher Reliability Organization (Https://Www.Hunterdonhealthcare.Org/About-Us-2/Hro-Higher-Reliability-Organization/)

Hunterdon Medical Center leads hospitals in New Jersey and the U.S. for many leading performance indicators of quality healthcare. These quality measures are gathered by three leading organizations:

- **The Centers for Medicare and Medicaid Services (CMS)** — CMS is a federal agency within the U.S. Department of Health and Human Services (http://www.hhs.gov/) that oversees Medicare (http://www.medicare.gov/default.aspx) and works with state governments to administer Medicaid (http://www.state.nj.us/humanservices/dmahs/clients/medicaid/).
- **The Joint Commission for the Accreditation of Healthcare Organizations (TJC)** —The Joint Commission for the Accreditation of Healthcare Organizations is an independent, not-for-profit organization that accredits and certifies over 17,000 healthcare organizations and programs in the United States.
- **The New Jersey Department of Health and Senior Services** — This state agency oversees public health services, senior services and health systems as well as healthcare management and administration in New Jersey.

We encourage our patients to visit the following resources to compare our quality of service to other healthcare systems across the state and nation.

- The Leapfrog Group (http://www.leapfroggroup.org/)
- Hospital Compare (https://www.medicare.gov/hospitalcompare/?AspxAutoDetectCookieSupport=1)

Quality Indicators – Hunterdon Medical Center measures quality based on its response to the following situations:

- Heart Attack Care
- Treatment for Heart Failure
- Pneumonia
- Surgical Care
- Rapid Response
- Infection Prevention

Hunterdon Medical Center Heart Attack Care

Hunterdon Medical Center provides fast treatment for heart attacks. Hunterdon Medical Center's door-to-balloon time (the time a patient enters the Emergency Department until the time a balloon is inserted to open up the artery) averages less than 60 minutes, which is faster than national guidelines (which are about 90 minutes).

Heart Attack Measures

A heart attack (also called an acute myocardial infarction or AMI) occurs when arteries leading to the heart become blocked and cause the supply of blood to be slowed or stopped. When this happens, heart muscle doesn't get the oxygen and nutrients it needs. As a result, any heart tissue that is affected may die.

Due to the urgent nature of a suspected heart attack or AMI, it is vital to recognize symptoms provide heart care quickly, particularly for patients who may have previously experienced cardiac arrest. The longer the heart muscle is deprived of oxygen by coronary artery disease or a sudden heart attack, the more damage to the heart muscle occurs.

The most crucial element that affects the survival of patients having a heart attack is how quickly the arteries of the heart can be reopened. All elements of heart attack care are important, yet receiving medication or a procedure to unblock blood vessels sooner translates into higher survival rates.

Heart Failure Care

Hunterdon Medical Center provides expert care to help diagnose and manage heart failure. Our goal is to improve heart function for all heart failure patients.

Our success in treating people for heart failure (also called congestive heart failure) is measured by the percentage of patients that receive appropriate treatment. The goal of Hunterdon Medical Center is to provide all appropriate measures for treating heart failure 100% of the time.

Heart failure means the heart can't pump enough blood to meet the body's needs. "Congestive" refers to a buildup of fluid. This condition can cause shortness of breath, swelling of limbs and other symptoms. Underlying problems such as coronary artery disease and high blood pressure can contribute to this problem.

The goal of Hunterdon Medical Center when treating heart failure is to provide specific tests and medication to improve heart function. Additionally, Hunterdon Medical Center provides lifestyle counseling to help our patients embrace ways to improve their health after being discharged from the hospital.

Hunterdon Medical Center Pneumonia Prevention and Care

When a patient arrives at Hunterdon Medical Center with signs and symptoms of pneumonia, our expert staff provides quality care to diagnose and treat.

Pneumonia is a lung disease caused by a viral or bacterial infection. It can spread to the blood, lungs, middle ear or nervous system. Pneumonia can fill the lungs with mucus, causing lower blood oxygen levels. It mainly causes illness in children younger than age 2 and adults over age 65, and can lead to death in these populations. About 2 million people in the U.S. develop pneumonia each year.

Providing appropriate antibiotics in a timely manner and giving oxygen as needed are treatments that improve the outcomes of pneumonia patients. Preventive measures such as flu and pneumococcal vaccines, as well as smoking cessation counseling, also help reduce the incidence of pneumonia.

Hunterdon Medical Center Surgical care

Hunterdon Medical Center is a participant in the Surgical Care Improvement Project, a national campaign aimed at reducing surgical complications.

Hunterdon Medical Center has consistently provided quality surgical care by embracing nationally recommended treatments or best practices. Our success in treating surgical patients is measured by the percentage of patients who receive appropriate treatment. The hospital's goal is to provide all appropriate measures for avoiding post-surgical complications 100% of the time.

The Surgical Care Improvement Project (SCIP) within the Hunterdon Healthcare System consists of quality measures that examine a defined set of treatments for our surgical patients. These measures are reviewed monthly and help reduce the incidence of four types of post-surgical complications: surgical site infection, adverse cardiac events, deep vein thrombosis and postoperative pneumonia.

Hunterdon Medical Center Rapid Response Teams

In the event of a concerning change in the patient's condition, a Rapid Response Team intervenes as quickly as possible to stabilize the patient's condition to prevent a more serious outcome.

Hunterdon Medical Center's Rapid Response Teams may be called to assess patients for:

- Chest pain
- Change in heart rate
- Change in systolic blood pressure
- Change in respiratory rate
- Closing airway
- Change in mental status
- Seizure
- Failure to respond to treatment

A Rapid Response Team is comprised of a nursing supervisor, critical care nurse, respiratory therapist, intensivist, resident and the patient's nurse. The team can be at a patient's bedside in under a minute, bringing the expertise of a critical care unit to every unit in the hospital. The teams are available
24 hours a day, seven days a week.

The goal of all Rapid Response Teams at Hunterdon Medical Center is to prevent the need for more intensive treatment and refer the patient to a critical care unit if necessary. Our Rapid Response Teams have helped cut down on the number of calls for immediate assistance after a patient's heart or breathing has stopped.

Hunterdon Medical Center Surgical Infection and Operative Complications Prevention

Many post-operative infections and post-operative complications can be prevented by using proficient surgical and operating room procedures.

The most critical factors in the prevention or post operative infections, although difficult to quantify, are the sound judgment and proper technique of the surgeon and surgical team as well as the general health and disease state of the patient.

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Centers for Disease Control and Prevention

COVID-19

Safety of COVID-19 Vaccines

Updated May 3, 2022

What You Need to Know

- COVID-19 vaccines are **safe and effective**.
- Millions of people in the United States have received COVID-19 vaccines under the most intense safety monitoring in US history.
- CDC recommends you get a COVID-19 vaccine as soon as possible.

Hundreds of Millions of People Have Safely Received a COVID-19 Vaccine

More than 576 million doses of COVID-19 vaccine had been given in the United States from December 14, 2020, through May 2, 2022. To view the current total number of COVID-19 vaccinations that have been administered in the United States, please visit the CDC COVID Data Tracker.

COVID-19 vaccines are **safe and effective**. COVID-19 vaccines were evaluated in tens of thousands of participants in clinical trials. The vaccines met the Food and Drug Administration's (FDA's) rigorous scientific standards for safety, effectiveness, and manufacturing quality needed to support emergency use authorization (EUA). Learn more about EUAs in this video.

The Pfizer-BioNTech, Moderna, and Johnson & Johnson/Janssen COVID-19 vaccines will continue to undergo the most intensive safety monitoring in US history. This monitoring includes using both established and new safety monitoring systems to make sure that COVID-19 vaccines are safe.

Common Side Effects

Some people have side effects after getting their COVID-19 vaccine, while others might have no side effects. Side effects may affect the ability to do daily activities, but they should go away within a few days. Learn more about common side effects after COVID-19 vaccination.

Serious Safety Problems Are Rare

In rare cases, people have experienced serious health events after COVID-19 vaccination. Any health problem that happens after vaccination is considered an adverse event. An adverse event can be caused by the vaccine or can be caused by a coincidental event not related to the vaccine, such as an unrelated fever, that happened following vaccination.

To date, the systems in place to monitor the safety of these vaccines have found four serious types of adverse events following COVID-19 vaccination, with evidence that suggests, although rare, a link to certain types of COVID-19 vaccinations

that were administered. They are:

Anaphylaxis

Anaphylaxis is a severe type of allergic reaction with symptoms such as hives, difficulty breathing, low blood pressure, or significant swelling of the tongue or lips. **Anaphylaxis after COVID-19 vaccination is rare.** Learn more about COVID-19 vaccines and allergic reactions, including anaphylaxis.

Thrombosis with Thrombocytopenia Syndrome (TTS)

Thrombosis with thrombocytopenia syndrome (TTS) is a rare but serious adverse event that causes blood clots or issues with clotting. **TTS after COVID-19 vaccination is rare.** Learn more about COVID-19 vaccines and adverse events, including TTS.

Myocarditis and Pericarditis

Myocarditis is inflammation of the heart muscle, and pericarditis is inflammation of the outer lining of the heart. **Myocarditis and pericarditis after COVID-19 vaccination are rare**. Learn more about COVID-19 vaccines and adverse events, including myocarditis and pericarditis.

Guillain–Barré Syndrome (GBS)

Guillain-Barré Syndrome (GBS) is a rare disorder where the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis. **GBS after COVID-19 vaccination is rare.** Learn more about COVID-19 vaccines and adverse events, including GBS.

Reports of Death Are Rare

Reports of death after COVID-19 vaccination are rare. FDA requires healthcare providers to report any death after COVID-19 vaccination to the Vaccine Adverse Event Reporting System (VAERS) , even if it's unclear whether the vaccine was the cause. **Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem.** CDC and FDA review reports of death following COVID-19 vaccination and update information as it becomes available. Learn more about adverse events, including reports of death, after COVID-19 vaccination.

Benefits of Vaccination Outweigh the Risks

Serious side effects that could cause a long-term health problem are extremely unusual following any vaccination, including COVID-19 vaccination. The benefits of COVID-19 vaccination outweigh the known and potential risks.

CDC continues to closely monitor the safety of COVID-19 vaccines. Everyone who receives a COVID-19 vaccine can also participate in safety monitoring by enrolling themselves, their children ages five years and older, or other dependents in a smartphone-based system called **v-safe** and completing health check-ins after COVID-19 vaccination.

Have you experienced a side effect following COVID-19 vaccination?

Please report it to VAERS . In addition, enrolling yourself or your dependent in **v-safe** allows you to easily report to CDC how you are feeling after getting a COVID-19 vaccine.

More Information

ACIP COVID-19 Vaccines Safety Technical Sub-Group (VaST)

COVID-19 Vaccine Safety Publications

VaST Subgroup Technical Report

v-safe After Vaccination Health Checker

Vaccine Adverse Event Reporting System (VAERS)

Last Updated May 3, 2022