Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

COVID-19 Vaccine Effectiveness by Product and Timing in New York State

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Supplementary Appendix

Contents

Supplementary Methods

Cohort definitions

All cohorts in the study were *closed*, with no movement allowed in or out, and thus had a fixed sample size beginning on May 1 and lasting through the entire analytic period. The vaccinated cohorts were defined from persons who became fully-vaccinated in the months of January through April (further split out by age group and product received), based on the statewide immunization databases (NYSIIS/CIR). The unvaccinated cohorts were conceptualized as persons who were never vaccinated until the data were frozen on September 23, per the Census population minus persons partially or fully vaccinated on September 23 (and further split out by age group).

Fully vaccinated cohorts were defined from individuals who were fully vaccinated as of May 1, 2021 (≥14 days after receipt of the final dose). The final, series-completing dose was defined as second dose a Pfizer-BioNTech or Moderna or one dose Janssen. Any individuals that were NOT fully vaccinated as of May 1, 2021 (including partially vaccinated as of May 1, 2021 *or* fully vaccinated after May 1, 2021) were excluded from these cohorts (closed cohort) and all aspects of the analysis. We specifically defined 24 closed, fully-vaccinated cohorts at the valid combinations of the 3 age-groups (18-49, 50-64, ≥65 years), 3 vaccines (Pfizer-BioNTech, Moderna, Janssen), and 3 month groups of fully-vaccination (January/February, March, April). We note, because of its approval date, Janssen full-vaccination was not possible in January/February.

Never vaccinated ('unvaccinated') cohorts were based on the estimated number of adults in the population who were not fully or partially vaccinated as of September 23, 2021 (date of data extraction). This was estimated separately for each of the 3 age groups (and region, in Sensitivity Analysis #5, described below), by computing the Census population minus the total persons partially or fully vaccinated on September 23. We illustrate this the calculation for the *total* adult population in New York State (NYS): The 2018 Census population estimate for NYS persons ≥18 years was 15,474,107. On

September 23, 2021, the fully or partially vaccinated 18 plus population was 12,187,667 . Thus, the never vaccinated population as of September 23, 2021 was 3,286,440 (=15,474,107-12,187,667). Unlike for vaccinated cohorts, who were exclusively represented as individual-level records, the total population denominators for the unvaccinated cohorts were calculated as aggregate counts (although numerator events of unvaccinated cases and hospitalizations were based on individual records, per below). For the life-table method applied to cases, individual level data lines were created for the portion of the unvaccinated cohorts that had no incident case (illustrated as the green group 'D' and discussed more below). The incidence-rates based hospitalization analysis was performed at the aggregate count level.

We note that for both fully vaccinated and unvaccinated cohorts, in the primary analysis, persons with a positive laboratory result within 90 days before May 1 were considered not susceptible for either outcome and excluded, per the CDC case-definition.[1] Between February 1 to April 30, 2021, 233,757 cases occurred among persons not vaccinated as of September 23, 2021. Thus, continuing the example for the statewide adult population the total susceptible population was 3,052,683 (= 3,286,440 - 233,757; the sum of the 3 age-specific unvaccinated cohorts in Table 1).

Outcomes

Incident laboratory-confirmed COVID-19 cases were defined as a positive SARS-CoV-2 NAAT or antigen test result (based on collection date) between May 1, 2021 and August 28, 2021, reported to ECLRS. For individuals with multiple positive results during this period, collection date associated with the first positive was used. ECLRS was matched to NYSIIS/CIR to determine vaccination status for all positive results. Those that matched to vaccinated persons in the above closed cohorts were used to classify incident cases among those vaccinated persons (cell A in the figure below). Positive results that did not match to anybody vaccinated (fully or partially) as of September 23, were records considered associated with persons in the unvaccinated cohorts. These individual records are represented as cell C in the figure below.

Incident laboratory-confirmed COVID-19 hospitalizations were defined as a new admission with a laboratory-confirmed positive COVID-19 result, between May 1 and August 28, 2021, reported in HERDS. These were matched with the NYSIIS/CIR in a process just as above to determine incident hospital admissions among the cohorts of fully-vaccinated and unvaccinated persons.

Summary of cohort approach

To summarize these concepts, in the figure below, we illustrate conceptually how incident cases were identified for this study among closed vaccinated and unvaccinated cohorts, through the linkage of the statewide vaccination (NYSIIS/CIR) and laboratory testing (ECLRS) datasets. The orange cells A-C indicate individual-level matches to determine individual-level vaccination and case status, whereas the green cell D indicates non-matches in both databases and calculated as an aggregate count. The sums A + B represents the fully-vaccinated, closed cohorts studied, which were further defined at each combination of product, age, and month of receipt. Incident cases A were the subject of weekly estimation of the hazard function (see next section).

Closed cohorts of persons never vaccinated by September 23 (“unvaccinated”) are represented as C + D, and were a hybrid of individual-level matching (C) and aggregate calculation (D). The total for D was estimated as the starting census-based cohort defined above minus the total persons in cell C (for each age group). Because the life-table analysis performed is done on individual-level records, lines of data were created to represent each member of cell D and appended to the dataset containing records for A-C. For the analysis of incident hospitalizations between May 1 – August 31, the identical process was conducted between the vaccination and hospitalization (HERDS) databases.

Schematic for classification of incident cases among closed vaccinated and unvaccinated cohorts

		New laboratory-confirmed infection during weeks of May 1 – August 28, in laboratory testing database? Yes	No
Received dose of COVID-19 vaccine, in the registry, as of September 23?	***Yes, fully-vaccinated between January & April***	**A.** Vaccinated person with incident case	**B.** Vaccinated person without incident case
	Yes, but not fully-vaccinated between January & April	*Excluded from analysis*	*Excluded from analysis*
	Not in vaccine registry	**C.** Unvaccinated person with incident case	**D.** Unvaccinated persons without incident case, determined by subtraction

Life-table analysis for COVID-19 cases

For every vaccinated cohort (defined by age, vaccine product, and/or time of full-vaccination as per above), we applied the life-table approach to estimate the weekly hazard function *h(t)*, using SAS v9.4 (Cary, NC), PROC LIFETEST.[2] This was compared to the analogous life-table for the unvaccinated cohort of the same age group, with the HR estimated weekly as *h(t)* for the vaccinated cohort / *h(t)* for the unvaccinated cohort.

In the table below, we illustrate this approach for the first 3 weeks of May for the cohort of persons 18-49 years, fully-vaccinated with Pfizer-BioNTech in January or February. In the first week, the entire cohort of 217,159 (found in Table 1) is at-risk. In that week, from the record-linkage between NYS immunization registries (NYSIIS/CIR) and laboratory testing (ECLRS), 56 incident laboratory-confirmed infections were identified among these vaccinated persons, and assumed to have occurred uniformly, or on-average at the midpoint of the week. Thus, per the life-table method, weekly $h(t) = \frac{56}{217{,}159 - \left(\frac{56}{2}\right)} = 0.000258$. Converted to an average daily rate per 100,000, *h(t) = 3.68* (found in Table S2). In the same week among 2,074,191 unvaccinated persons, defined using the census denominator approach above, 5,191 incident laboratory-confirmed infections were identified (determined as infections not linked to an immunization record). For this group, the average daily *h(t) = 35.80.* Comparing the vaccinated vs. unvaccinated group, we find *HR = 3.68/35.80 = 0.103* and *VE = 1 – HR = 89.7%* (found in Table 2 and Figure 1). The number of cases in the first week is then subtracted from the risk set for the second week, and the process is repeated for the second week onwards.

Sample calculation of hazard function and VE estimates for first 3 weeks of May, 2021

					Weekly estimates	Avg. daily estimates (weekly / 7)			
	Start	***End***	***n at risk***	***Cases***	***h(t)***	***h(t)***	***h(t) per 100,000***	***HR***	***VE***
18-49 years, Pfizer-BioNTech, January/February									
Week 1	5/1/2021	5/7/2021	217,159	56	0.000258	0.0000368	3.68	0.103	**89.7%**
Week 2	5/8/2021	5/14/2021	217,103	38	0.000175	0.0000250	2.50	0.094	**90.6%**
Week 3	5/15/2021	5/21/2021	217,065	35	0.000161	0.0000230	2.30	0.115	**88.5%**
18-49 years, Unvaccinated									
Week 1	5/1/2021	5/7/2021	2,074,191	5,191	0.002506	0.0003575	35.80	*ref.*	*ref.*
Week 2	5/8/2021	5/14/2021	2,069,000	3,840	0.001858	0.0002651	26.54	*ref.*	*ref.*
Week 3	5/15/2021	5/21/2021	2,065,160	2,908	0.001409	0.0002012	20.13	*ref.*	*ref.*

Primary and sensitivity analyses

In the primary analysis, persons with a positive laboratory result within 90 days before May 1 were considered not susceptible for either outcome and excluded, per the CDC case-definition.[1] Sensitivity analyses #1-4 considered variations in the cohort construction and outcomes considered. Sensitivity analysis #5 stratified the data to adjust for urbanicity, and sensitivity analysis #6 considered the potential for unmeasured confounding to influence our VE estimates.

Sensitivity analyses #1 -4 to probe the impact of variations in the cohort definitions:

1. The primary analysis used the 2018 Vintage Census file for defining the unvaccinated population, consistent with previous COVID-19 surveillance practice. The intercensal estimates for 2020 projected a 0.8% decrease in the NYS adult population relative to 2018, however the Decennial 2020

estimates projected a 3.9% increase, although age-specific estimates are unavailable.[3] To assess the potential impact of these added persons on the calculated unvaccinated population sizes, we distributed the estimated additional 606,000 adults to each age group, proportional to their 2018 representation.

2. Cases within 90 days of May 1 unmatched with the immunization registry were classified unvaccinated; a false non-match could potentially deflate the unvaccinated population. This analysis did not exclude unvaccinated persons with cases within 90 days.
3. About half of hospitalized patients in HERDS were reported admitted "for COVID-19", using non-standardized definitions.[4] The hospitalization analysis was repeated restricted to such hospitalizations, as opposed to those "with COVID-19" in the primary analysis.
4. The primary analysis defined the susceptible population size identically for both cases and hospitalizations, using a case-based definition. Because no such susceptibility definition exists for hospitalizations, the hospitalization analyses were repeated for the entire time-defined cohort sizes without exclusions applied.

Urbanicity-stratified analyses (sensitivity analysis #5)

In this analysis, we stratified our life-table analysis for cases and our incidence rates analysis hospitalizations, within levels of urbanicity, to add additional control for geographic differences in vaccination and COVID-19 outcomes. Levels of urbanicity vs. rurality were defined according to the 2013 CDC National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties, which are classified for New York State as follows.[5]

NCHS Urbanization Level	State population in region	Core-Based Statistical Areas (CBSA) Included	Counties
1) Large central metro	51%	New York City, Buffalo and Rochester CBSA urban core	Bronx, Erie, Kings, Monroe, New York, Queens, Richmond
2) Large fringe metro	28%	New York City, Buffalo and Rochester CBSA suburbs	Dutchess, Livingston, Nassau, Niagara, Ontario, Orange, Orleans, Putnam, Rockland, Suffolk, Wayne, Westchester, Yates
3) Medium metro	9%	Albany, Utica, Syracuse CBSA	Albany, Herkimer, Madison, Oneida, Onondaga, Oswego, Rensselaer, Saratoga, Schenectady, Schoharie
4) Small metro	4%	Binghamton, Elmira, Watertown-Fort Drum, Glens Falls, Kingston, Ithaca CBSA	Broome, Chemung, Jefferson, Tioga, Tompkins, Ulster, Warren, Washington
5) Micropolitan	5%	Other CBSA	Cattaraugus, Cayuga, Chautauqua, Clinton, Columbia, Cortland, Franklin, Fulton, Genesee, Montgomery, Otsego, Seneca, St. Lawrence, Steuben
6) Noncore	2%	Outside of CBSA	Allegany, Chenango, Delaware, Essex, Greene, Hamilton, Lewis, Schuyler, Sullivan, Wyoming

Determination of county was based on residential address. For persons with a COVID-19 diagnosis in ECLRS this address was utilized, and for those admitted to the hospital, the address provided in HERDS was used (since more recent than the address at time of vaccination provided in NYSIIS/CIR). For all others vaccinated, the address in NYSIIS/CIR was used. Denominator estimates for those unvaccinated were based on county populations from the same 2018 Census Vintage file.

For the cases analysis, data were analyzed in 3 strata: 1) large central metro and large fringe metro, 2) medium metro, and 3) small metro, micropolitan, noncore. This is was due to regional cohesion of the first two levels and sparseness of outcomes in the other levels. Because of this sparseness, the analysis interval for strata 2-3 was changed from 7 days to 14 days. For the hospital analysis, data were sufficient to permit the analysis restricted to stratum 1 only.

Bias analysis for potential impacts of unmeasured confounding on observed vaccine effectiveness estimates (sensitivity analysis #6)

Beyond potential confounding for age and region, addressed in the current analyses, there exists the potential for unmeasured confounding in multiple directions. For example:

- Persons vaccinated may be more likely to experience testing and thus have increased case detection relative to unvaccinated persons (*decreasing* observed VE relative to reality).
- Persons vaccinated may be less likely to wear masks than unvaccinated persons, which would correspond to public health recommendations at particular times, as noted in the manuscript. This could in turn increase viral exposure and the occurrence of both COVID-19 diagnosis and hospitalization among vaccinated persons versus those unvaccinated. Thus, this might *decrease* the observed VE relative to reality. This is a mechanism for behavioral effects noted in the manuscript.
- Persons unvaccinated may also face higher risk in terms of less mask usage, distancing, or other factors that increase their exposure. This could in turn increase the occurrence of both COVID-19 diagnosis and hospitalization among unvaccinated persons versus those vaccinated and thus, this might *increase* the observed VE relative to reality.

To explore the potential for unmeasured confounding in both directions to impact our estimates, we have applied the "bounding factor" approach by Ping and VanderWeele.[6] This is a flexible method to assesses how much an unmeasured confounder *U*, of varying strength associations with each of the exposure and outcome, could influence the observed exposure-outcome association in the study, relative to truth. The bounding factor, *B*, is the underlying basis for VanderWeele and Ping's *E-value*, which answers how extreme this factor would need to be to have an observed association be truly a null association.[7] This factor is calculated as $B = RR_{UD} + RR_{EU}/(RR_{UD} + RR_{EU} - 1)$, where RR_{UD} represents the risk-ratio between *U* and the disease outcome *D* (e.g. COVID-19 cases and hospitalizations) and RR_{EU} represents the risk-ratio between the exposure *E* (e.g. vaccination) and *U*. We assessed, for plausible ranges of RR_{UD} and RR_{EU}, and in different directions as hypothesized above, the impact of confounding due to *U* on observed *HR* or *IRR,* and thus *VE*, relative to underlying reality.

Figure S1: Weekly hazard rates for Laboratory-confirmed COVID-19 cases by Vaccine Receipt, Age, and Timing of Vaccination

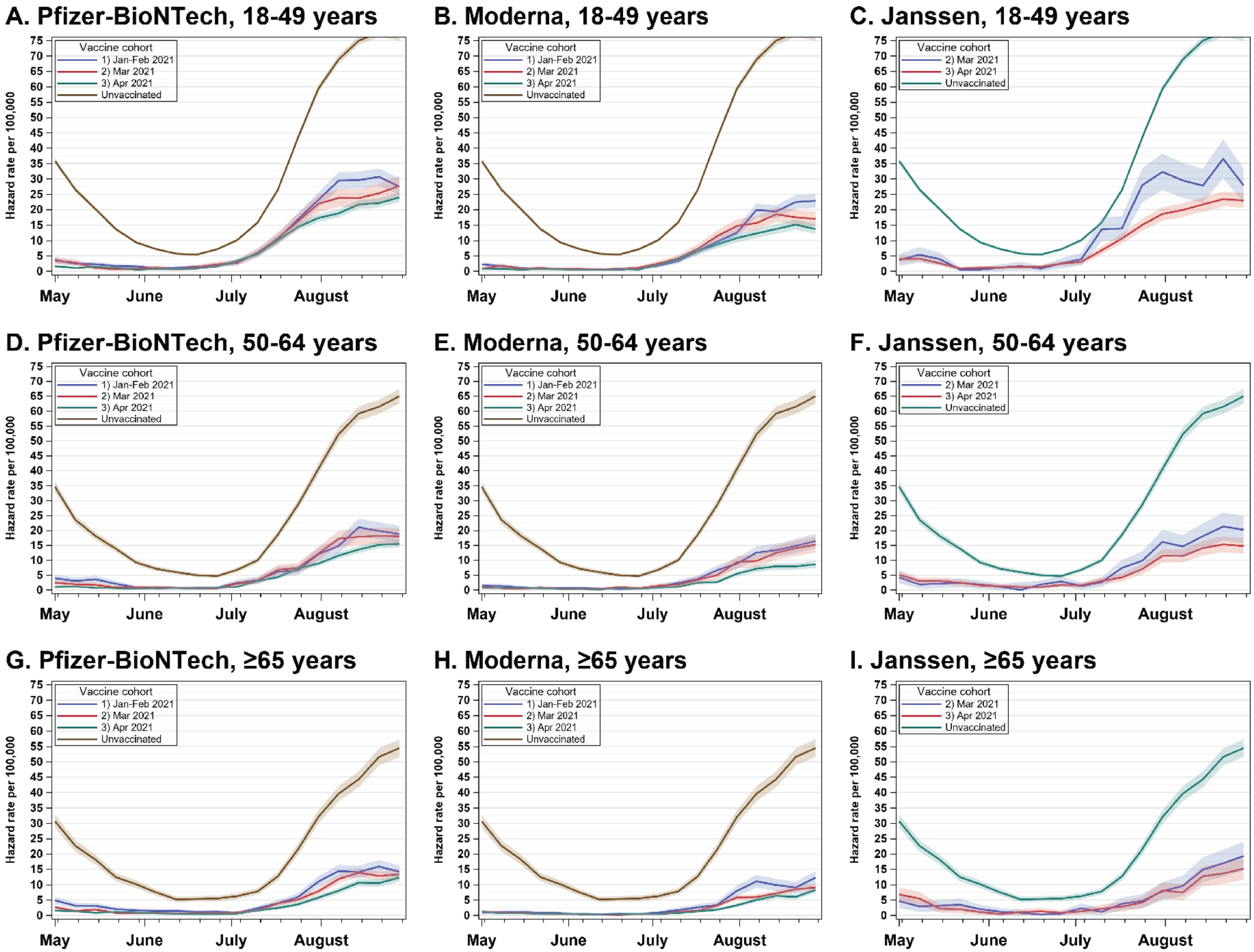

Figure S2: Monthly incidence rates for laboratory-confirmed COVID-19 hospitalization by Vaccine Receipt, Age, and Timing of Vaccination

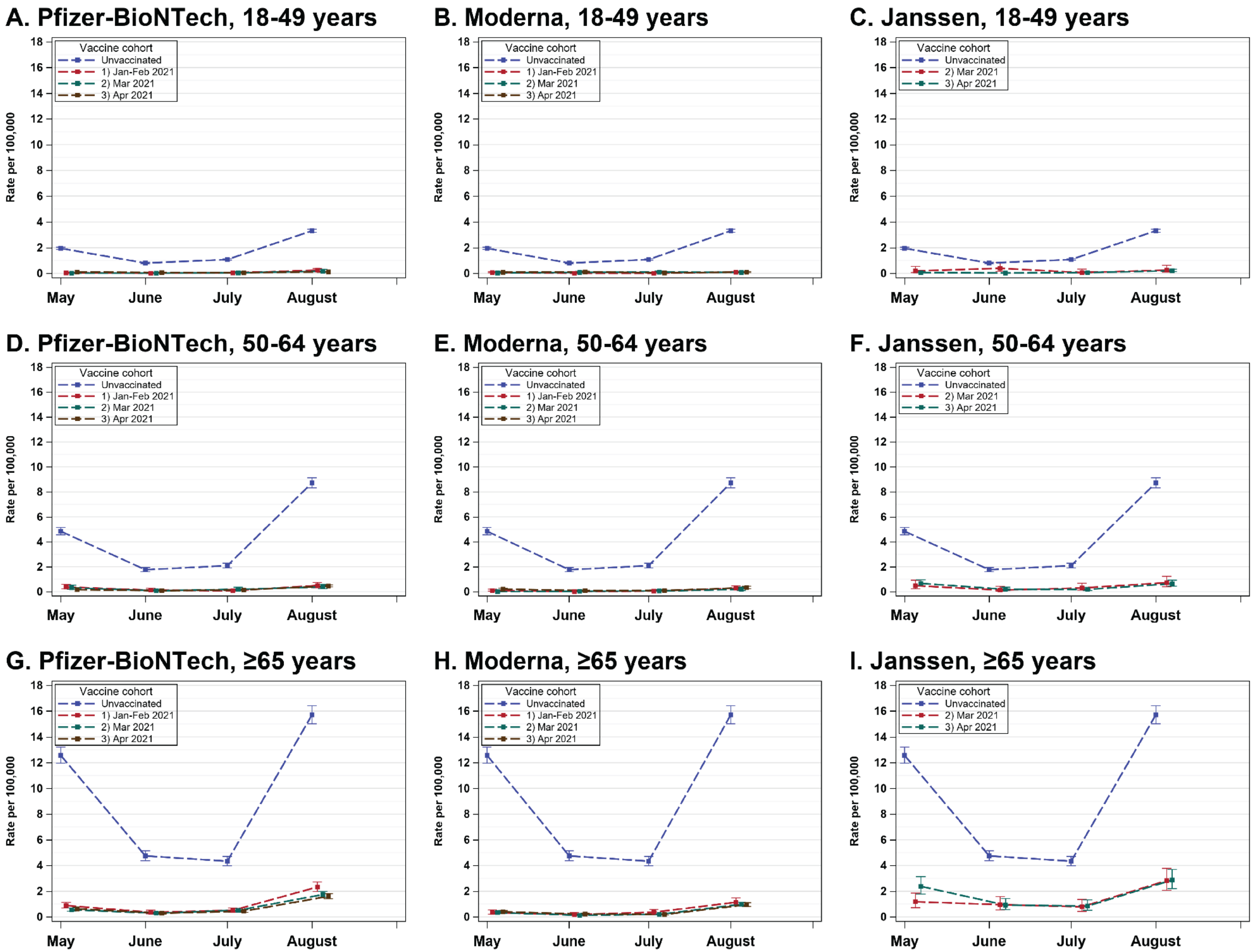

Figure S3. Estimated Vaccine Effectiveness against Laboratory-confirmed COVID-19 Cases, by Vaccine Product, Age, and Timing of Vaccination: Large Central Metro and Large Fringe Metro Counties

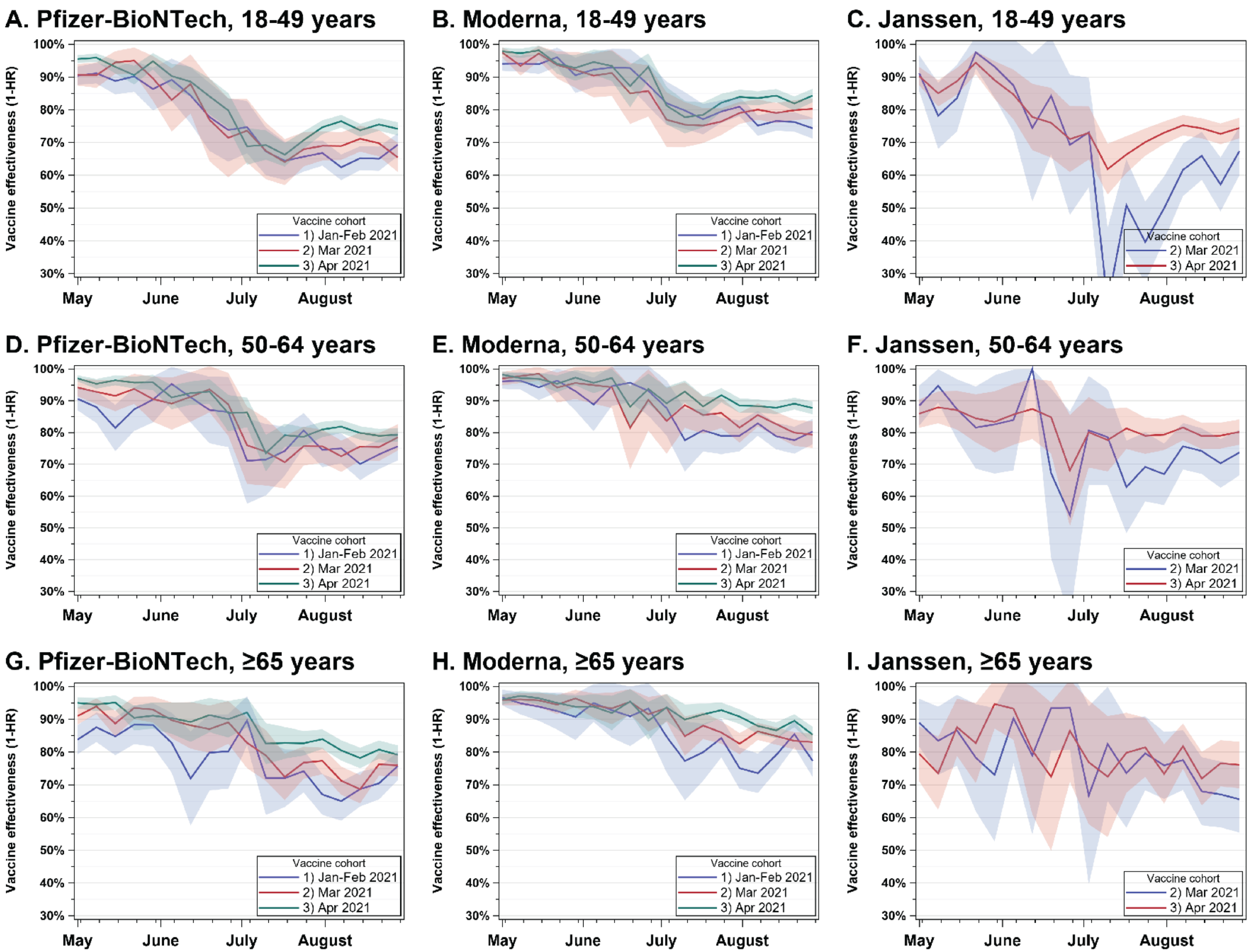

Figure S4. Estimated Vaccine Effectiveness against Laboratory-confirmed COVID-19 Cases, by Vaccine Product, Age, and Timing of Vaccination: Medium Metro Counties

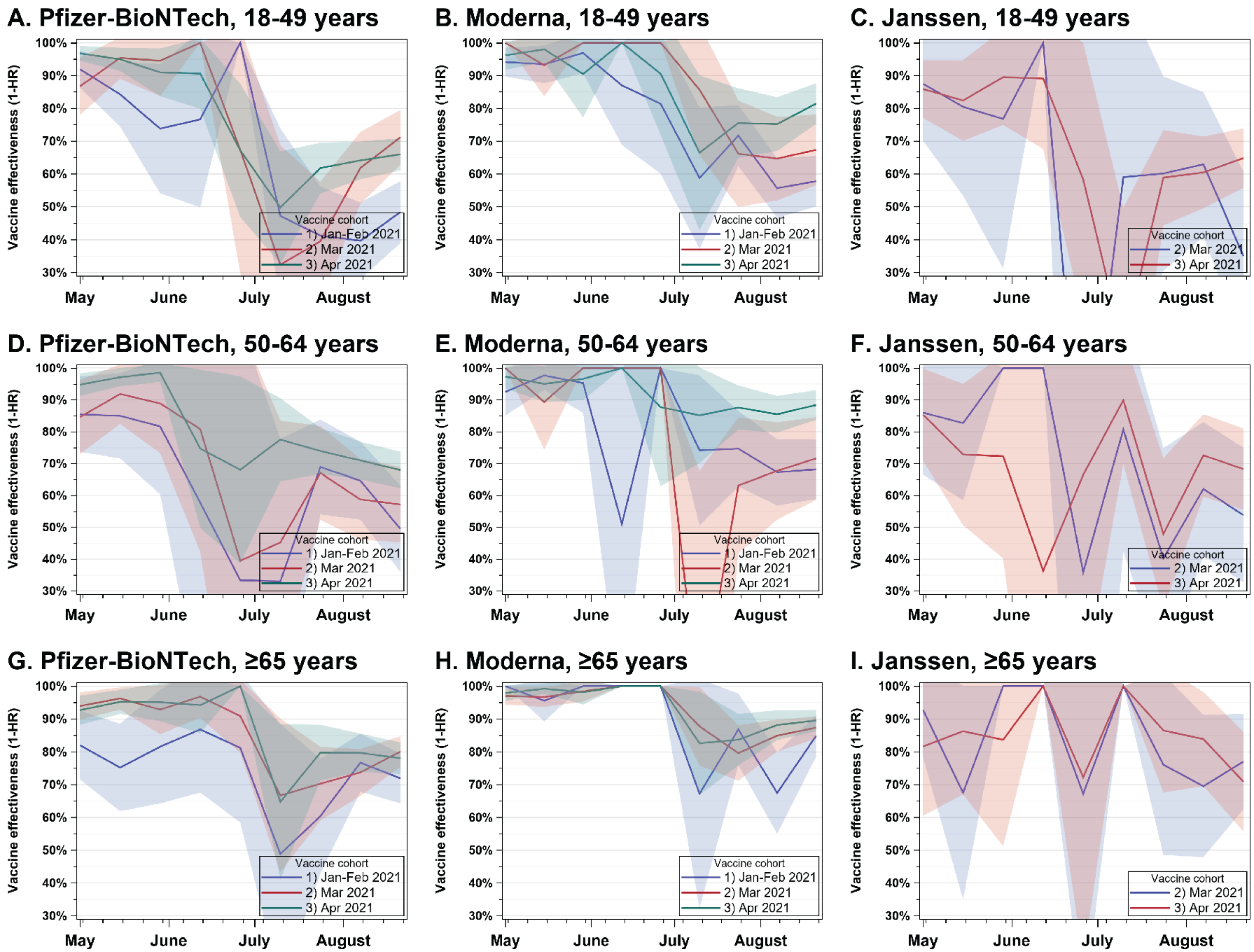

Figure S5. Estimated Vaccine Effectiveness against Laboratory-confirmed COVID-19 Cases, by Vaccine Product, Age, and Timing of Vaccination: Small Metro, Micropolitan, and Noncore Counties

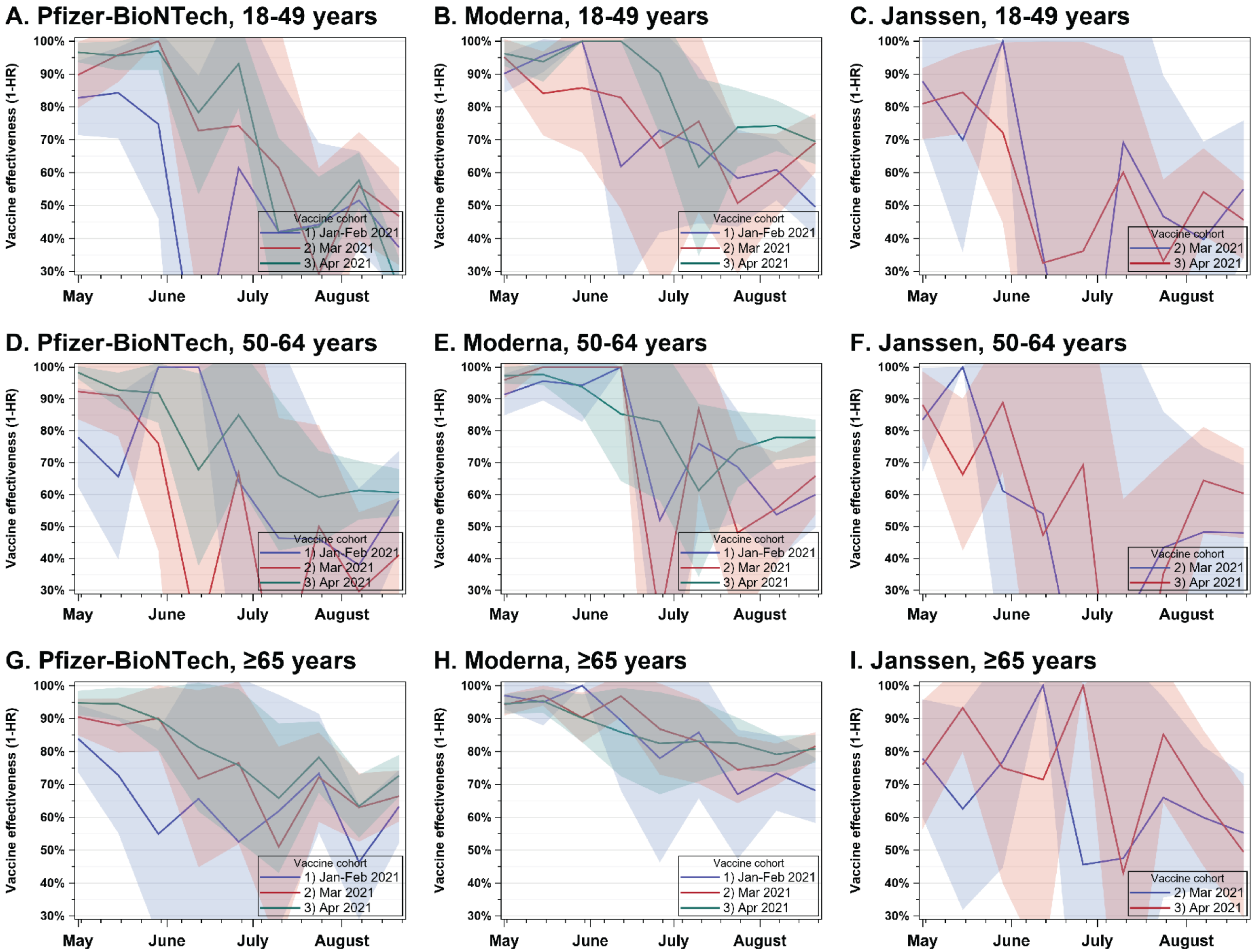

Figure S6. Estimated Vaccine Effectiveness against Laboratory-confirmed COVID-19 Hospitalizations, by Vaccine Product, Age, and Timing of Vaccination: Large Central Metro and Large Fringe Metro Counties

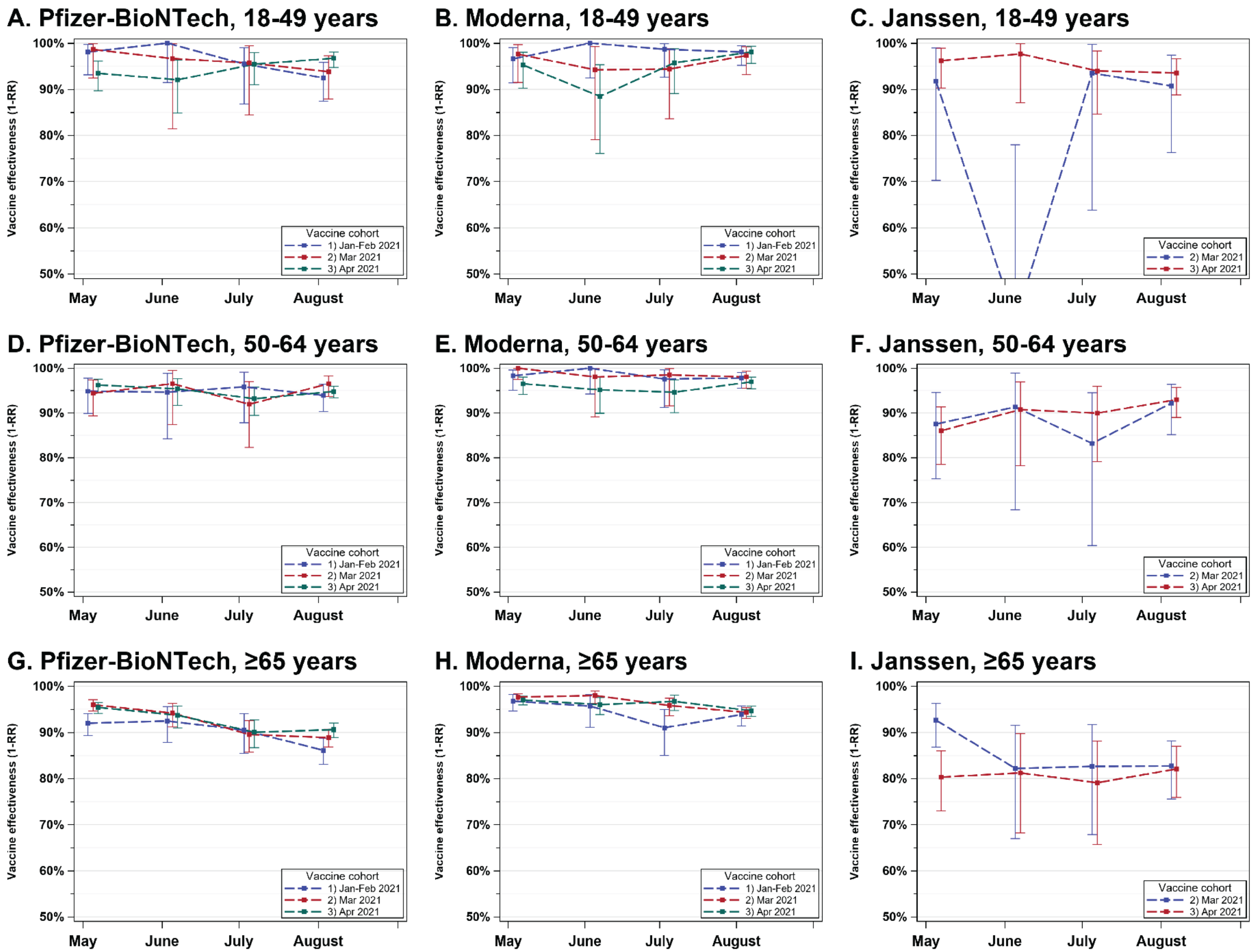

Table S1: Overview of phased vaccine eligibility in New York State

Effective Date	**Eligible Population**
December 14, 2020	High-risk hospital staff, affiliates, volunteers and contract staff, following the clinical risk assessment guidance
December 21, 2020	- High-risk hospital staff including State-operated OMH psychiatric centers - Emergency Medical Services (EMS) Personnel - Medical Examiners and Coroners - Funeral workers who have direct contact with infectious material and bodily fluids - Health care or other high-risk direct care essential staff working in LTCFs and long-term, congregate settings overseen by Office of People with Developmental Disabilities (OPWDD) the Office of Mental Health (OMH) and the Office of Addiction Services and Supports (OASAS). - Persons living in LTCFs and in long-term congregate settings overseen by OPWDD and OMH
December 28, 2020	- High-risk hospital and FQHC staff, including OMH psychiatric centers - Emergency Medical Services (EMS) Personnel - Medical Examiners and Coroners - Agency staff and residents in congregate living situations run by OPWDD, OMH and OASAS. - Urgent Care providers - Any staff administering COVID-19 Vaccinations
January 4, 2021	- All Outpatient/Ambulatory front line, high risk health care providers who provide direct in-person patient care or other staff in a position where they have direct contact with patients, such as receptionists, of any age. - All front line, high risk public health workers who have direct contact with patients, including those conducting COVID-19 Tests
January 12, 2021	- Age 65 and older - First Responder or Support Staff for First Responder Agency o Fire - State Fire Service, including firefighters and investigators (professional and volunteer) o Local Fire Service, including firefighters and investigators (professional and volunteer) - Police and Investigations - State Police, including Troopers - State Park Police, DEC Police, Forest Rangers - SUNY Police - Sheriffs' Offices - County Police Departments and Police Districts - City, Town, and Village Police Departments - Transit of other Public Authority Police Departments

Effective Date	**Eligible Population**
January 12, 2021 *continued*	- State Field Investigations, including DMV, SCOC, Justice Center, DFS, IG, Tax, OCFS, SLA o Public Safety Communications - Emergency Communication and PSAP Personnel, including dispatchers and technicians o Other Sworn and Civilian Personnel - Court Officer - Other Police or Peace Officer - Support or Civilian Staff for Any of the Above Services, Agencies, or Facilities - Corrections o State DOCCS Personnel, including correction and parole officers o Local Correctional Facilities, including correction officers o Local Probation Departments, including probation officers o State Juvenile Detention and Rehabilitation Facilities o Local Juvenile Detention and Rehabilitation Facilities - P-12 Schools o P-12 school (public or non-public) or school district faculty or staff (includes all teachers, substitute teachers, student teachers, school administrators, paraprofessional staff, and support staff including bus drivers) o Contractor working in a P-12 school (public or non-public) or school district (including contracted bus drivers) o Licensed, registered, approved or legally exempt group childcare - In-Person College Faculty and Instructors - Employees or Support Staff of Licensed, Registered, Approved or Legally Exempt Group Childcare Settings - Licensed, Registered, approved or legally exempt group Childcare Provider - Public Transit o Airline and airport employee o Passenger railroad employee o Subway and mass transit employee (i.e., MTA, LIRR, Metro North, NYC Transit, Upstate transit) o Ferry employee o Port Authority employee o Public bus employee - Public Facing Grocery Store Workers - Individual living in a homeless shelter where sleeping, bathing or eating accommodations must be shared with individuals and families who are not part of your household. - Individual working (paid or unpaid) in a homeless shelter where sleeping, bathing or eating accommodations must be shared by individuals and families who are not part of the same household, in a position where there is potential for interaction with shelter residents.

Effective Date	Eligible Population
February 8, 2021	- Restaurant employees, - Restaurant delivery workers, and - For-hire vehicle drivers, including taxi, livery, black car, and transportation network company drivers
February 15, 2021	**Individuals with comorbidities and underlying conditions are eligible to receive COVID-19 vaccine.** The list is subject to change as additional scientific evidence is published and as New York State obtains and analyzes additional state-specific data. Adults over the age of 16 with the following conditions due to increased risk of moderate or severe illness or death from the virus that causes COVID-19 are eligible: • Cancer (current or in remission, including 9/11-related cancers); • Chronic kidney disease; • Pulmonary Disease, including but not limited to, COPD (chronic obstructive pulmonary disease), asthma (moderate-to-severe), pulmonary fibrosis, cystic fibrosis, and 9/11 related pulmonary diseases; • Intellectual and Developmental Disabilities including Down Syndrome; • Heart conditions, including but not limited to heart failure, coronary artery disease, cardiomyopathies, or hypertension (high blood pressure); • Immunocompromised state (weakened immune system) including but not limited to solid organ transplant or from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, use of other immune weakening medicines, or other causes; • Severe Obesity (BMI 40 kg/m2), Obesity (body mass index [BMI] of 30 kg/m2 or higher but < 40 kg/m2); • Pregnancy; • Sickle cell disease or Thalassemia; • Type 1 or 2 diabetes mellitus; • Cerebrovascular disease (affects blood vessels and blood supply to the brain); • Neurologic conditions, including but not limited to Alzheimer's Disease or dementia; and • Liver disease.
March 1, 2021	- Public-facing hotel workers.
March 17, 2021	- Public-facing government and public employees, - Not-for-profit workers who provide public-facing services to New Yorkers in need, and - Essential in-person public-facing building service workers and providers of essential building services.
March 23, 2021	- New York Residents age 50 and older.
March 30, 2021	- New York Residents age 30 to 50.
April 6, 2021	- All New York State residents age 16 and older, including individuals studying in New York, or individuals employed in the State of New York
May 6, 2021	- All individuals 16 years of age and older that reside in the United States
May 13, 2021	- All individuals **12 years of age and older** that reside in the United States

Table S2: Weekly Hazard Rates for Laboratory-confirmed COVID-19 Cases by Vaccine Receipt, Age, and Timing of Vaccination

Vaccine cohort	**May 1 week** *Hazard rate[1] (95% CI)*	**July 10 week** *Hazard rate[1] (95% CI)*	**August 28 week** *Hazard rate[1] (95% CI)*
18-49 years			
Pfizer-BioNTech	2.4 (2.0, 2.8)	5.7 (5.2, 6.3)	25.4 (24.2, 26.6)
January/February	3.7 (2.7, 4.6)	6.1 (4.8, 7.3)	27.5 (24.9, 30.2)
March	3.5 (2.4, 4.6)	5.9 (4.5, 7.4)	27.7 (24.6, 30.9)
April	1.6 (1.2, 2.0)	5.6 (4.8, 6.3)	24.0 (22.5, 25.5)
Moderna	1.3 (1.0, 1.7)	3.8 (3.3, 4.3)	17.6 (16.4, 18.8)
January/February	2.3 (1.6, 3.0)	3.3 (2.5, 4.2)	22.9 (20.6, 25.1)
March	0.8 (0.3, 1.3)	4.2 (3.0, 5.3)	17.0 (14.6, 19.3)
April	0.9 (0.5, 1.3)	4.0 (3.1, 4.8)	13.8 (12.2, 15.3)
Janssen	3.9 (3.0, 4.8)	8.1 (6.8, 9.4)	23.9 (21.7, 26.2)
March	3.7 (1.7, 5.7)	13.6 (9.8, 17.5)	27.9 (22.4, 33.5)
April	4.0 (3.0, 5.0)	6.8 (5.5, 8.2)	23.0 (20.6, 25.4)
Unvaccinated	35.8 (34.8, 36.8)	15.8 (15.2, 16.5)	76.4 (75.0, 77.9)
50-64 years			
Pfizer-BioNTech	1.7 (1.4, 2.1)	3.1 (2.6, 3.5)	16.4 (15.4, 17.5)
January/February	3.9 (2.6, 5.2)	3.3 (2.1, 4.4)	18.8 (16.0, 21.6)
March	2.4 (1.4, 3.4)	3.1 (2.0, 4.2)	18.0 (15.3, 20.7)
April	1.0 (0.7, 1.4)	3.0 (2.5, 3.6)	15.5 (14.3, 16.8)
Moderna	0.9 (0.6, 1.2)	1.5 (1.2, 1.9)	11.8 (10.8, 12.9)
January/February	1.4 (0.7, 2.2)	2.4 (1.5, 3.3)	16.4 (14.0, 18.9)
March	1.1 (0.4, 1.8)	1.8 (0.9, 2.7)	15.2 (12.6, 17.9)
April	0.7 (0.3, 1.0)	1.1 (0.6, 1.5)	8.6 (7.4, 9.8)
Janssen	4.8 (3.6, 6.0)	2.9 (2.0, 3.9)	16.4 (14.2, 18.6)
March	4.2 (2.2, 6.3)	2.6 (1.0, 4.3)	20.3 (15.7, 24.8)
April	5.1 (3.6, 6.6)	3.1 (1.9, 4.2)	14.8 (12.2, 17.3)
Unvaccinated	34.6 (32.8, 36.4)	10.0 (9.0, 10.9)	64.9 (62.5, 67.4)
≥65 years			
Pfizer-BioNTech	2.6 (2.2, 3.0)	1.8 (1.4, 2.1)	13.0 (12.2, 13.9)
January/February	4.9 (3.7, 6.0)	2.3 (1.5, 3.1)	14.2 (12.2, 16.2)
March	2.7 (2.0, 3.3)	1.6 (1.1, 2.1)	13.4 (11.9, 14.8)
April	1.6 (1.1, 2.0)	1.6 (1.1, 2.1)	12.2 (11.0, 13.5)
Moderna	1.2 (1.0, 1.5)	1.1 (0.8, 1.3)	9.2 (8.5, 9.9)
January/February	0.9 (0.3, 1.5)	1.7 (0.9, 2.5)	12.2 (10.1, 14.4)
March	1.3 (0.9, 1.7)	1.2 (0.8, 1.6)	9.1 (8.0, 10.2)
April	1.3 (0.9, 1.7)	0.8 (0.5, 1.1)	8.3 (7.3, 9.3)
Janssen	5.9 (4.2, 7.6)	1.8 (0.8, 2.7)	17.0 (14.1, 19.8)
March	4.7 (2.4, 6.9)	1.2 (0.0, 2.3)	19.3 (14.7, 24.0)
April	6.8 (4.4, 9.2)	2.2 (0.8, 3.6)	15.2 (11.6, 18.8)
Unvaccinated	30.6 (28.5, 32.8)	7.8 (6.7, 8.9)	54.4 (51.5, 57.3)

1. Hazard rate represents average daily cases per 100,000 person-days in the given week

Table S3: Estimated percentage of specimens with the Delta variant from the CDC national SARS-CoV-2 genomic surveillance program, HHS Region 2 (New York, New Jersey, Puerto Rico, US Virgin Islands)

Week beginning	**Percent of specimens Delta variant**
5/1/2021	1.8%
5/8/2021	3.0%
5/15/2021	3.9%
5/22/2021	7.2%
5/29/2021	12.9%
6/5/2021	27.1%
6/12/2021	36.3%
6/19/2021	54.1%
6/26/2021	69.8%
7/3/2021	81.3%
7/10/2021	85.3%
7/17/2021	95.5%
7/24/2021	96.8%
7/31/2021	97.7%
8/7/2021	99.1%
8/14/2021	99.4%
8/21/2021	99.6%
8/28/2021	99.6%

Data were extracted on 9/14/2021, from https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Table S4: Estimated correlation coefficients between weekly paired logit[vaccine effectiveness against cases] and logit[estimated percentage of specimens with the Delta variant]

Vaccine cohort	**Estimated correlation coefficient**
18-49 years	
Pfizer-BioNTech	-0.92
Moderna	-0.94
Janssen	-0.77
50-64 years	
Pfizer-BioNTech	-0.93
Moderna	-0.95
Janssen	-0.68
≥65 years	
Pfizer-BioNTech	-0.95
Moderna	-0.97
Janssen	-0.67

Table S5: Weekly Incidence Rates for Laboratory-confirmed COVID-19 Hospitalizations by Vaccine Receipt, Age, and Timing of Vaccination

Vaccine cohort	**May 2021** *Rate [1] (95% CI)*	**June 2021** *Rate [1] (95% CI)*	**July 2021** *Rate [1] (95% CI)*	**August 2021** *Rate [1] (95% CI)*
18-49 years				
Pfizer-BioNTech	**0.08 (0.05, 0.11)**	**0.05 (0.02, 0.08)**	**0.05 (0.03, 0.08)**	**0.16 (0.12, 0.21)**
January/February	0.04 (0.01, 0.13)	0.02 (0.00, 0.09)	0.04 (0.01, 0.13)	0.25 (0.15, 0.40)
March	0.02 (0.00, 0.12)	0.02 (0.00, 0.12)	0.04 (0.01, 0.15)	0.17 (0.07, 0.34)
April	0.10 (0.06, 0.16)	0.06 (0.03, 0.11)	0.05 (0.02, 0.10)	0.12 (0.07, 0.18)
Moderna	**0.07 (0.04, 0.11)**	**0.07 (0.04, 0.11)**	**0.04 (0.02, 0.08)**	**0.09 (0.05, 0.14)**
January/February	0.07 (0.02, 0.15)	0.01 (0.00, 0.08)	0.01 (0.00, 0.07)	0.09 (0.04, 0.19)
March	0.04 (0.00, 0.13)	0.08 (0.02, 0.20)	0.09 (0.03, 0.22)	0.07 (0.02, 0.19)
April	0.08 (0.04, 0.17)	0.11 (0.05, 0.20)	0.04 (0.01, 0.11)	0.09 (0.04, 0.18)
Janssen	**0.08 (0.03, 0.17)**	**0.10 (0.04, 0.20)**	**0.06 (0.02, 0.14)**	**0.22 (0.13, 0.34)**
March	0.19 (0.04, 0.56)	0.40 (0.15, 0.86)	0.06 (0.00, 0.36)	0.26 (0.07, 0.66)
April	0.06 (0.02, 0.15)	0.03 (0.00, 0.11)	0.06 (0.02, 0.15)	0.21 (0.11, 0.35)
Unvaccinated	**1.95 (1.84, 2.06)**	**0.80 (0.73, 0.88)**	**1.08 (1.00, 1.16)**	**3.31 (3.17, 3.46)**
50-64 years				
Pfizer-BioNTech	**0.21 (0.16, 0.28)**	**0.09 (0.06, 0.13)**	**0.14 (0.10, 0.19)**	**0.45 (0.37, 0.54)**
January/February	0.37 (0.21, 0.61)	0.13 (0.04, 0.30)	0.07 (0.02, 0.22)	0.49 (0.30, 0.76)
March	0.31 (0.17, 0.53)	0.07 (0.02, 0.22)	0.19 (0.08, 0.38)	0.38 (0.22, 0.62)
April	0.16 (0.10, 0.23)	0.08 (0.05, 0.14)	0.14 (0.09, 0.21)	0.46 (0.36, 0.57)
Moderna	**0.13 (0.09, 0.20)**	**0.05 (0.03, 0.10)**	**0.07 (0.04, 0.12)**	**0.29 (0.22, 0.37)**
January/February	0.09 (0.02, 0.22)	0.00 (0.00, 0.08)	0.04 (0.01, 0.16)	0.28 (0.15, 0.48)
March	0.00 (0.00, 0.10)	0.03 (0.00, 0.15)	0.05 (0.01, 0.19)	0.19 (0.08, 0.39)
April	0.20 (0.12, 0.31)	0.09 (0.04, 0.17)	0.10 (0.05, 0.18)	0.32 (0.22, 0.45)
Janssen	**0.61 (0.42, 0.85)**	**0.17 (0.08, 0.32)**	**0.21 (0.11, 0.37)**	**0.66 (0.46, 0.91)**
March	0.48 (0.21, 0.94)	0.12 (0.01, 0.45)	0.30 (0.10, 0.70)	0.72 (0.37, 1.25)
April	0.66 (0.43, 0.97)	0.18 (0.07, 0.38)	0.18 (0.07, 0.37)	0.64 (0.41, 0.94)
Unvaccinated	**4.85 (4.54, 5.17)**	**1.76 (1.57, 1.96)**	**2.09 (1.88, 2.30)**	**8.73 (8.31, 9.16)**
≥65 years				
Pfizer-BioNTech	**0.65 (0.56, 0.75)**	**0.30 (0.24, 0.37)**	**0.48 (0.41, 0.57)**	**1.80 (1.65, 1.95)**
January/February	0.89 (0.66, 1.15)	0.36 (0.22, 0.54)	0.51 (0.35, 0.72)	2.33 (1.96, 2.74)
March	0.55 (0.42, 0.71)	0.29 (0.20, 0.42)	0.52 (0.39, 0.67)	1.74 (1.50, 2.01)
April	0.63 (0.50, 0.78)	0.29 (0.20, 0.40)	0.44 (0.34, 0.57)	1.60 (1.39, 1.83)
Moderna	**0.36 (0.30, 0.44)**	**0.18 (0.13, 0.23)**	**0.22 (0.17, 0.28)**	**0.99 (0.88, 1.11)**
January/February	0.34 (0.19, 0.56)	0.19 (0.08, 0.37)	0.36 (0.21, 0.59)	1.14 (0.84, 1.50)
March	0.33 (0.24, 0.45)	0.12 (0.07, 0.20)	0.20 (0.13, 0.29)	0.98 (0.82, 1.17)
April	0.40 (0.30, 0.52)	0.22 (0.15, 0.32)	0.19 (0.13, 0.28)	0.95 (0.79, 1.13)
Janssen	**1.86 (1.44, 2.37)**	**0.93 (0.64, 1.32)**	**0.82 (0.55, 1.17)**	**2.85 (2.32, 3.46)**
March	1.18 (0.70, 1.87)	0.95 (0.52, 1.59)	0.79 (0.41, 1.38)	2.82 (2.04, 3.80)
April	2.38 (1.75, 3.15)	0.92 (0.55, 1.45)	0.84 (0.49, 1.35)	2.87 (2.18, 3.71)
Unvaccinated	**12.57 (11.93, 13.24)**	**4.75 (4.35, 5.17)**	**4.33 (3.96, 4.73)**	**15.70 (14.99, 16.45)**

1. Incidence rate represents average daily hospitalizations per 100,000 person-days in the given week

Table S6: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 cases, adjusted for census uncertainty (sensitivity analysis #1)

Vaccine cohort	**May 1 week** *% VE (95% CI)*	**July 10 week** % VE (95% CI)	**August 28 week** % VE (95% CI)
18-49 years			
Pfizer-BioNTech	**92.0 (90.7, 93.2)**	**56.4 (51.6, 61.1)**	**59.9 (57.8, 62.0)**
January/February	87.7 (84.4, 90.9)	54.0 (44.4, 63.6)	56.6 (52.3, 60.9)
March	88.3 (84.5, 92.1)	54.9 (43.6, 66.2)	56.2 (51.1, 61.3)
April	94.6 (93.2, 95.9)	57.7 (51.9, 63.5)	62.1 (59.6, 64.7)
Moderna	**95.5 (94.5, 96.6)**	**71.2 (67.0, 75.4)**	**72.2 (70.3, 74.1)**
January/February	92.4 (90.0, 94.8)	74.8 (68.2, 81.4)	63.9 (60.3, 67.6)
March	97.3 (95.6, 99.0)	68.4 (59.6, 77.1)	73.2 (69.5, 76.9)
April	97.0 (95.7, 98.4)	69.9 (63.4, 76.4)	78.3 (75.8, 80.8)
Janssen	**86.8 (83.8, 89.8)**	**38.4 (28.3, 48.5)**	**62.2 (58.6, 65.8)**
March	87.6 (80.9, 94.4)	-3.5 (-33.1, 26.1)	55.9 (47.1, 64.7)
April	86.6 (83.2, 90.0)	48.1 (37.9, 58.3)	63.7 (59.8, 67.6)
50-64 years			
Pfizer-BioNTech	**94.0 (92.8, 95.2)**	**63.1 (56.6, 69.6)**	**69.5 (67.2, 71.8)**
January/February	86.4 (81.9, 90.9)	60.6 (46.0, 75.2)	65.2 (59.8, 70.6)
March	91.6 (88.1, 95.0)	63.0 (49.1, 76.9)	66.6 (61.4, 71.8)
April	96.4 (95.2, 97.5)	63.7 (56.2, 71.1)	71.2 (68.7, 73.8)
Moderna	**96.7 (95.7, 97.8)**	**81.6 (76.8, 86.4)**	**78.0 (75.9, 80.1)**
January/February	95.0 (92.5, 97.6)	71.2 (59.5, 82.8)	69.5 (64.8, 74.2)
March	96.3 (93.9, 98.7)	78.6 (67.6, 89.6)	71.7 (66.7, 76.8)
April	97.7 (96.5, 98.8)	87.3 (82.1, 92.4)	84.0 (81.8, 86.3)
Janssen	**83.3 (79.0, 87.6)**	**64.7 (52.8, 76.6)**	**69.6 (65.3, 73.9)**
March	85.3 (78.1, 92.6)	68.1 (48.1, 88.1)	62.4 (53.9, 71.0)
April	82.4 (77.2, 87.6)	63.2 (48.9, 77.5)	72.6 (67.8, 77.4)
≥65 years			
Pfizer-BioNTech	**89.7 (88.0, 91.4)**	**73.0 (66.9, 79.1)**	**71.1 (68.7, 73.6)**
January/February	81.0 (76.2, 85.7)	64.3 (50.9, 77.6)	68.5 (63.8, 73.2)
March	89.6 (86.9, 92.2)	75.1 (66.5, 83.6)	70.4 (66.8, 74.0)
April	93.9 (92.1, 95.7)	75.4 (67.6, 83.1)	72.9 (69.8, 76.1)
Moderna	**95.2 (94.1, 96.2)**	**83.4 (79.0, 87.8)**	**79.7 (77.8, 81.6)**
January/February	96.5 (94.1, 98.8)	73.7 (60.6, 86.7)	72.9 (67.9, 78.0)
March	95.0 (93.4, 96.6)	82.0 (75.5, 88.5)	79.9 (77.3, 82.5)
April	94.9 (93.3, 96.5)	88.0 (82.9, 93.1)	81.7 (79.2, 84.1)
Janssen	**77.0 (70.2, 83.8)**	**73.1 (58.5, 87.7)**	**62.5 (55.8, 69.1)**
March	81.8 (72.8, 90.8)	82.1 (64.4, 99.8)	57.3 (46.7, 67.8)
April	73.4 (63.9, 82.9)	66.3 (44.9, 87.7)	66.4 (58.2, 74.5)

Table S7: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 cases, using the entire unvaccinated population size (sensitivity analysis #2)

Vaccine cohort	**May 1 week** *% VE (95% CI)*	**July 10 week** % VE (95% CI)	**August 28 week** % VE (95% CI)
<u>18-49 years</u>			
Pfizer-BioNTech	**92.8 (91.7, 93.9)**	**60.9 (56.7, 65.2)**	**64.2 (62.3, 66.0)**
January/February	88.9 (86.0, 91.8)	58.8 (50.2, 67.4)	61.2 (57.4, 65.0)
March	89.5 (86.1, 92.9)	59.6 (49.5, 69.7)	60.9 (56.3, 65.4)
April	95.1 (93.9, 96.3)	62.1 (56.9, 67.3)	66.2 (63.9, 68.4)
Moderna	**96.0 (95.0, 96.9)**	**74.2 (70.4, 78.0)**	**75.2 (73.5, 76.9)**
January/February	93.2 (91.0, 95.3)	77.4 (71.5, 83.4)	67.7 (64.5, 71.0)
March	97.5 (96.0, 99.1)	71.7 (63.8, 79.5)	76.1 (72.8, 79.4)
April	97.3 (96.1, 98.5)	73.0 (67.2, 78.9)	80.6 (78.4, 82.9)
Janssen	**88.2 (85.4, 90.9)**	**44.8 (35.8, 53.9)**	**66.3 (63.1, 69.5)**
March	88.9 (82.9, 95.0)	7.2 (-19.3, 33.8)	60.6 (52.7, 68.5)
April	88.0 (84.9, 91.0)	53.5 (44.4, 62.7)	67.6 (64.1, 71.0)
<u>50-64 years</u>			
Pfizer-BioNTech	**94.6 (93.5, 95.7)**	**66.7 (60.9, 72.6)**	**72.6 (70.5, 74.6)**
January/February	87.7 (83.7, 91.8)	64.5 (51.3, 77.6)	68.7 (63.8, 73.5)
March	92.4 (89.3, 95.5)	66.7 (54.2, 79.2)	70.0 (65.3, 74.6)
April	96.7 (95.7, 97.7)	67.3 (60.6, 73.9)	74.1 (71.8, 76.4)
Moderna	**97.1 (96.1, 98.0)**	**83.4 (79.1, 87.8)**	**80.3 (78.4, 82.1)**
January/February	95.5 (93.2, 97.8)	74.0 (63.6, 84.5)	72.6 (68.3, 76.8)
March	96.7 (94.5, 98.9)	80.7 (70.8, 90.6)	74.6 (70.1, 79.1)
April	97.9 (96.8, 98.9)	88.5 (83.9, 93.2)	85.7 (83.6, 87.7)
Janssen	**84.9 (81.1, 88.8)**	**68.2 (57.5, 78.9)**	**72.6 (68.7, 76.5)**
March	86.8 (80.3, 93.3)	71.3 (53.3, 89.3)	66.2 (58.5, 73.9)
April	84.1 (79.4, 88.8)	66.9 (54.0, 79.8)	75.4 (71.0, 79.7)
<u>≥65 years</u>			
Pfizer-BioNTech	**90.7 (89.2, 92.2)**	**75.7 (70.2, 81.2)**	**74.1 (71.9, 76.3)**
January/February	**82.9 (78.6, 87.1)**	**67.9 (55.9, 79.8)**	**71.7 (67.4, 75.9)**
March	90.6 (88.2, 93.0)	77.6 (69.9, 85.3)	73.4 (70.2, 76.6)
April	94.5 (92.8, 96.1)	77.8 (70.9, 84.8)	75.7 (72.9, 78.5)
Moderna	**95.6 (94.7, 96.6)**	**85.1 (81.1, 89.0)**	**81.7 (80.0, 83.5)**
January/February	96.8 (94.7, 98.9)	76.3 (64.6, 88.0)	75.7 (71.2, 80.2)
March	95.5 (94.1, 97.0)	83.8 (78.0, 89.6)	81.9 (79.6, 84.3)
April	95.4 (93.9, 96.9)	89.2 (84.6, 93.8)	83.5 (81.3, 85.8)
Janssen	**79.3 (73.2, 85.4)**	**75.8 (62.7, 88.9)**	**66.3 (60.3, 72.2)**
March	83.6 (75.5, 91.7)	83.9 (68.0, 99.8)	61.6 (52.1, 71.1)
April	76.1 (67.5, 84.6)	69.7 (50.4, 88.9)	69.8 (62.5, 77.1)

Table S8: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 hospitalizations, adjusted for census uncertainty (sensitivity analysis #1)

Vaccine cohort	**May 2021** *% VE (95% CI)*	**June 2021** % VE (95% CI)	**July 2021** % VE (95% CI)	**August 2021** % VE (95% CI)
18-49 years				
Pfizer-BioNTech	**95.4 (92.9, 97.1)**	**93.1 (88.1, 96.4)**	**94.7 (91.0, 97.1)**	**94.3 (92.4, 95.8)**
January/February	97.3 (92.0, 99.4)	97.7 (87.2, 99.9)	95.0 (85.5, 99.0)	90.9 (85.3, 94.7)
March	98.7 (92.7, 100.0)	96.7 (81.6, 99.9)	95.3 (82.8, 99.4)	93.8 (87.8, 97.3)
April	93.8 (90.1, 96.3)	90.4 (82.7, 95.2)	94.4 (89.2, 97.4)	95.7 (93.4, 97.4)
Moderna	**95.9 (93.2, 97.7)**	**89.7 (82.9, 94.3)**	**95.1 (90.9, 97.6)**	**96.8 (95.0, 98.0)**
January/February	96.0 (90.5, 98.7)	98.0 (88.6, 99.9)	98.5 (91.8, 100.0)	96.7 (93.1, 98.7)
March	97.7 (91.8, 99.7)	88.6 (70.6, 96.9)	89.7 (75.9, 96.7)	97.3 (93.2, 99.3)
April	94.8 (89.8, 97.8)	83.7 (69.8, 92.2)	95.3 (87.9, 98.7)	96.6 (93.5, 98.4)
Janssen	**94.8 (89.3, 97.9)**	**85.1 (70.5, 93.6)**	**93.3 (84.3, 97.8)**	**92.2 (87.6, 95.4)**
March	88.2 (65.4, 97.6)	40.6 (-30.1, 78.3)	92.9 (60.2, 99.8)	90.7 (76.2, 97.5)
April	96.4 (90.6, 99.0)	95.4 (83.4, 99.4)	93.4 (83.0, 98.2)	92.5 (87.4, 95.9)
50-64 years				
Pfizer-BioNTech	**94.7 (93.0, 96.0)**	**94.0 (90.7, 96.3)**	**92.1 (88.9, 94.6)**	**93.8 (92.5, 94.9)**
January/February	90.9 (84.9, 94.9)	91.3 (79.6, 97.2)	95.8 (87.5, 99.1)	93.2 (89.5, 95.9)
March	92.3 (86.8, 95.9)	95.0 (85.1, 99.0)	89.0 (78.2, 95.3)	94.8 (91.5, 97.0)
April	96.1 (94.4, 97.5)	94.3 (90.3, 96.9)	92.0 (88.0, 95.0)	93.7 (92.2, 95.1)
Moderna	**96.7 (95.1, 97.9)**	**96.3 (93.1, 98.2)**	**95.7 (92.8, 97.7)**	**96.1 (94.8, 97.1)**
January/February	97.9 (94.5, 99.4)	100.0 (94.4, 100.0)	97.5 (91.0, 99.7)	96.1 (93.4, 98.0)
March	100.0 (97.6, 100.0)	98.1 (89.4, 100.0)	96.9 (88.8, 99.6)	97.4 (94.7, 99.0)
April	95.0 (92.4, 96.9)	94.0 (88.4, 97.3)	94.5 (89.8, 97.4)	95.5 (93.8, 96.9)
Janssen	**85.0 (78.9, 89.7)**	**88.7 (78.3, 94.9)**	**87.7 (78.3, 93.7)**	**90.9 (87.4, 93.6)**
March	88.2 (76.6, 94.9)	91.6 (69.4, 99.0)	82.9 (59.7, 94.5)	90.2 (82.8, 94.9)
April	83.6 (75.8, 89.4)	87.5 (73.9, 95.0)	89.8 (78.7, 95.9)	91.3 (87.0, 94.4)
≥65 years				
Pfizer-BioNTech	**93.8 (92.8, 94.7)**	**92.4 (90.4, 94.0)**	**86.6 (83.9, 89.0)**	**86.3 (84.9, 87.6)**
January/February	91.6 (88.9, 93.7)	91.0 (86.1, 94.5)	85.9 (79.8, 90.6)	82.2 (78.9, 85.1)
March	94.7 (93.1, 96.0)	92.6 (89.4, 95.1)	85.7 (81.1, 89.4)	86.7 (84.6, 88.7)
April	94.0 (92.6, 95.3)	92.7 (89.8, 94.9)	87.7 (83.9, 90.8)	87.8 (85.9, 89.5)
Moderna	**96.5 (95.8, 97.2)**	**95.6 (94.1, 96.7)**	**94.0 (92.2, 95.4)**	**92.4 (91.5, 93.3)**
January/February	96.7 (94.6, 98.2)	95.3 (90.6, 98.0)	89.9 (83.5, 94.3)	91.3 (88.5, 93.6)
March	96.8 (95.7, 97.7)	96.8 (94.8, 98.2)	94.6 (91.9, 96.5)	92.5 (91.0, 93.8)
April	96.2 (95.0, 97.2)	94.4 (91.9, 96.3)	94.7 (92.1, 96.6)	92.7 (91.3, 94.0)
Janssen	**82.3 (77.3, 86.4)**	**76.5 (66.4, 84.1)**	**77.4 (67.1, 85.0)**	**78.3 (73.4, 82.4)**
March	88.7 (82.1, 93.3)	76.0 (59.4, 87.0)	78.2 (61.6, 88.8)	78.4 (70.8, 84.5)
April	77.4 (69.8, 83.4)	76.8 (62.9, 86.3)	76.7 (62.4, 86.6)	78.1 (71.5, 83.4)

Table S9: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 hospitalizations, using the entire unvaccinated population size (sensitivity analysis #2)

Vaccine cohort	**May 2021** *% VE (95% CI)*	**June 2021** % VE (95% CI)	**July 2021** % VE (95% CI)	**August 2021** % VE (95% CI)
18-49 years				
Pfizer-BioNTech	**95.8 (93.7, 97.4)**	**93.8 (89.3, 96.7)**	**95.2 (91.9, 97.4)**	**94.9 (93.1, 96.3)**
January/February	97.5 (92.8, 99.5)	97.9 (88.5, 99.9)	95.6 (87.0, 99.1)	91.8 (86.9, 95.2)
March	98.8 (93.4, 100.0)	97.1 (83.5, 99.9)	95.8 (84.6, 99.5)	94.5 (89.1, 97.6)
April	94.4 (91.1, 96.7)	91.4 (84.5, 95.7)	94.9 (90.3, 97.7)	96.2 (94.1, 97.6)
Moderna	**96.3 (93.9, 98.0)**	**90.8 (84.6, 94.9)**	**95.6 (91.8, 97.9)**	**97.1 (95.5, 98.2)**
January/February	96.4 (91.5, 98.8)	98.2 (89.8, 100.0)	98.7 (92.7, 100.0)	97.0 (93.8, 98.8)
March	98.0 (92.6, 99.8)	89.8 (73.7, 97.2)	90.8 (78.4, 97.0)	97.6 (93.9, 99.3)
April	95.4 (90.8, 98.0)	85.4 (72.9, 93.0)	95.8 (89.2, 98.9)	96.9 (94.2, 98.6)
Janssen	**95.4 (90.4, 98.1)**	**86.7 (73.5, 94.3)**	**94.0 (85.9, 98.1)**	**93.0 (88.9, 95.8)**
March	89.4 (68.9, 97.8)	46.8 (-16.7, 80.6)	93.6 (64.3, 99.8)	91.7 (78.7, 97.7)
April	96.7 (91.6, 99.1)	95.9 (85.1, 99.5)	94.1 (84.8, 98.4)	93.3 (88.7, 96.3)
50-64 years				
Pfizer-BioNTech	**95.2 (93.7, 96.4)**	**94.5 (91.6, 96.6)**	**92.9 (90.0, 95.1)**	**94.4 (93.3, 95.4)**
January/February	91.8 (86.4, 95.4)	92.2 (81.6, 97.5)	96.2 (88.7, 99.2)	93.9 (90.6, 96.3)
March	93.1 (88.1, 96.3)	95.5 (86.6, 99.1)	90.1 (80.3, 95.8)	95.3 (92.3, 97.3)
April	96.5 (94.9, 97.7)	94.9 (91.3, 97.2)	92.8 (89.2, 95.5)	94.4 (92.9, 95.6)
Moderna	**97.0 (95.6, 98.1)**	**96.6 (93.7, 98.4)**	**96.2 (93.5, 97.9)**	**96.5 (95.3, 97.3)**
January/February	98.1 (95.0, 99.5)	100.0 (94.9, 100.0)	97.8 (91.9, 99.7)	96.5 (94.0, 98.2)
March	100.0 (97.8, 100.0)	98.3 (90.5, 100.0)	97.2 (89.9, 99.7)	97.7 (95.2, 99.1)
April	95.5 (93.1, 97.2)	94.6 (89.5, 97.5)	95.1 (90.8, 97.6)	96.0 (94.4, 97.2)
Janssen	**86.5 (81.0, 90.7)**	**89.8 (80.4, 95.4)**	**88.9 (80.4, 94.3)**	**91.8 (88.7, 94.3)**
March	89.4 (78.9, 95.4)	92.4 (72.4, 99.1)	84.5 (63.6, 95.0)	91.1 (84.5, 95.4)
April	85.2 (78.2, 90.4)	88.7 (76.4, 95.5)	90.8 (80.8, 96.3)	92.1 (88.3, 94.9)
≥65 years				
Pfizer-BioNTech	**94.4 (93.5, 95.2)**	**93.1 (91.4, 94.6)**	**88.0 (85.5, 90.1)**	**87.7 (86.4, 88.8)**
January/February	92.4 (90.0, 94.3)	91.9 (87.5, 95.0)	87.3 (81.8, 91.5)	84.0 (81.0, 86.6)
March	95.2 (93.8, 96.4)	93.4 (90.4, 95.6)	87.1 (83.0, 90.4)	88.1 (86.1, 89.8)
April	94.6 (93.3, 95.7)	93.4 (90.9, 95.4)	88.9 (85.5, 91.7)	89.0 (87.3, 90.5)
Moderna	**96.9 (96.2, 97.5)**	**96.0 (94.7, 97.0)**	**94.6 (93.0, 95.8)**	**93.2 (92.3, 94.0)**
January/February	97.1 (95.2, 98.4)	95.7 (91.5, 98.2)	90.9 (85.1, 94.9)	92.2 (89.6, 94.2)
March	97.1 (96.1, 97.9)	97.2 (95.3, 98.4)	95.1 (92.7, 96.8)	93.2 (91.9, 94.4)
April	96.6 (95.5, 97.4)	95.0 (92.7, 96.7)	95.2 (92.9, 96.9)	93.5 (92.2, 94.6)
Janssen	**84.0 (79.6, 87.7)**	**78.8 (69.7, 85.7)**	**79.6 (70.4, 86.5)**	**80.4 (76.1, 84.1)**
March	89.9 (83.9, 94.0)	78.4 (63.4, 88.3)	80.4 (65.4, 89.9)	80.6 (73.8, 86.0)
April	79.6 (72.8, 85.0)	79.1 (66.6, 87.7)	79.0 (66.1, 87.9)	80.3 (74.4, 85.1)

Table S10: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 hospitalizations, limiting to hospitalizations reported 'for COVID-19' (sensitivity analysis #3) [1]

Vaccine cohort	**May 2021** *% VE (95% CI)*	**June 2021** % VE (95% CI)	**July 2021** % VE (95% CI)	**August 2021** % VE (95% CI)
18-49 years				
Pfizer-BioNTech	**98.9 (97.7, 99.6)**	**97.3 (94.2, 99.0)**	**98.1 (95.8, 99.3)**	**97.9 (96.8, 98.7)**
January/February	100.0 (97.2, 100.0)	100.0 (92.9, 100.0)	97.2 (90.0, 99.7)	96.4 (92.9, 98.5)
March	100.0 (96.0, 100.0)	97.3 (84.6, 99.9)	96.0 (85.7, 99.5)	99.4 (96.4, 100.0)
April	98.3 (96.2, 99.4)	96.4 (91.5, 98.8)	99.0 (96.2, 99.9)	98.1 (96.6, 99.1)
Moderna	**98.9 (97.3, 99.6)**	**97.7 (94.1, 99.4)**	**97.5 (94.6, 99.1)**	**98.9 (97.9, 99.5)**
January/February	99.3 (96.2, 100.0)	100.0 (93.7, 100.0)	98.8 (93.2, 100.0)	99.2 (97.1, 99.9)
March	99.1 (94.7, 100.0)	95.2 (82.7, 99.4)	93.2 (82.4, 98.1)	98.9 (96.0, 99.9)
April	98.4 (95.2, 99.7)	97.3 (90.1, 99.7)	99.0 (94.5, 100.0)	98.7 (96.7, 99.7)
Janssen	**98.1 (94.6, 99.6)**	**95.3 (86.3, 99.0)**	**95.5 (88.5, 98.8)**	**96.0 (92.8, 98.0)**
March	96.7 (81.6, 99.9)	83.5 (40.0, 98.0)	94.1 (66.8, 99.8)	98.1 (89.2, 100.0)
April	98.5 (94.5, 99.8)	98.1 (89.3, 100.0)	95.9 (87.9, 99.2)	95.5 (91.8, 97.9)
50-64 years				
Pfizer-BioNTech	**98.1 (97.1, 98.8)**	**99.3 (98.0, 99.9)**	**95.9 (93.7, 97.4)**	**96.9 (96.1, 97.6)**
January/February	94.4 (90.0, 97.2)	98.6 (91.9, 100.0)	98.8 (93.4, 100.0)	95.5 (92.7, 97.4)
March	97.0 (93.5, 98.9)	100.0 (94.8, 100.0)	93.1 (84.9, 97.5)	97.8 (95.7, 99.1)
April	99.2 (98.3, 99.7)	99.3 (97.5, 99.9)	95.9 (93.1, 97.7)	97.0 (96.0, 97.8)
Moderna	**98.9 (98.0, 99.5)**	**98.8 (96.8, 99.7)**	**98.7 (97.0, 99.6)**	**98.5 (97.8, 99.1)**
January/February	100.0 (98.4, 100.0)	100.0 (95.3, 100.0)	100.0 (96.2, 100.0)	98.5 (96.8, 99.5)
March	100.0 (98.0, 100.0)	100.0 (94.2, 100.0)	98.7 (92.8, 100.0)	99.1 (97.3, 99.8)
April	98.0 (96.4, 99.1)	97.8 (94.2, 99.4)	98.2 (95.3, 99.5)	98.4 (97.3, 99.1)
Janssen	**91.9 (87.7, 94.9)**	**95.8 (89.2, 98.9)**	**90.6 (83.0, 95.3)**	**94.7 (92.2, 96.5)**
March	93.8 (85.6, 98.0)	96.5 (80.3, 99.9)	85.7 (66.3, 95.4)	93.2 (87.4, 96.7)
April	91.1 (85.6, 94.8)	95.5 (86.8, 99.1)	92.7 (83.9, 97.3)	95.3 (92.4, 97.3)
≥65 years				
Pfizer-BioNTech	**97.6 (97.0, 98.1)**	**97.8 (96.9, 98.5)**	**94.3 (92.7, 95.6)**	**93.0 (92.1, 93.8)**
January/February	97.0 (95.5, 98.1)	97.5 (94.8, 99.0)	95.5 (92.0, 97.7)	90.6 (88.4, 92.5)
March	97.9 (97.0, 98.6)	97.1 (95.2, 98.4)	94.1 (91.4, 96.2)	92.8 (91.3, 94.0)
April	97.6 (96.7, 98.3)	98.5 (97.2, 99.3)	93.9 (91.4, 95.8)	94.2 (93.0, 95.2)
Moderna	**98.6 (98.2, 99.0)**	**98.5 (97.7, 99.0)**	**97.3 (96.2, 98.1)**	**95.9 (95.2, 96.5)**
January/February	98.6 (97.1, 99.4)	98.5 (95.6, 99.7)	94.7 (90.3, 97.5)	95.1 (93.1, 96.6)
March	98.6 (97.8, 99.1)	99.0 (97.8, 99.6)	97.0 (95.2, 98.3)	95.6 (94.6, 96.5)
April	98.8 (98.1, 99.2)	97.9 (96.4, 98.9)	98.3 (96.8, 99.2)	96.4 (95.5, 97.2)
Janssen	**91.7 (88.5, 94.2)**	**90.8 (84.7, 94.9)**	**90.2 (83.7, 94.6)**	**88.7 (85.5, 91.3)**
March	93.7 (89.0, 96.8)	92.9 (83.2, 97.7)	89.4 (78.0, 95.8)	87.9 (82.5, 91.9)
April	90.2 (85.4, 93.7)	89.2 (80.0, 94.9)	90.9 (81.9, 96.1)	89.3 (85.0, 92.6)

1. The restriction applied in this scenario reduced the number of events observed. Estimates of 100.0% reflect strata in which 0 hospitalizations among fully-vaccinated persons occurred for a month and should be interpreted both with caution and in conjunction with the lower-bound of the exact 95% confidence interval.

Table S11: Estimated vaccine effectiveness against laboratory-confirmed COVID-19 hospitalizations, using entire time-defined cohorts, without 90-day prior diagnosis exclusion applied (sensitivity analysis #4)

Vaccine cohort	**May 2021** *% VE (95% CI)*	**June 2021** % VE (95% CI)	**July 2021** % VE (95% CI)	**August 2021** % VE (95% CI)
18-49 years				
Pfizer-BioNTech	**95.9 (93.7, 97.4)**	**93.9 (89.5, 96.8)**	**95.3 (92.0, 97.4)**	**94.9 (93.2, 96.3)**
January/February	97.6 (92.8, 99.5)	98.0 (88.6, 99.9)	95.6 (87.0, 99.1)	91.9 (86.9, 95.3)
March	98.8 (93.5, 100.0)	97.1 (83.6, 99.9)	95.8 (84.7, 99.5)	94.5 (89.2, 97.6)
April	94.5 (91.2, 96.7)	91.5 (84.7, 95.8)	95.0 (90.5, 97.7)	96.2 (94.2, 97.7)
Moderna	**96.4 (94.0, 98.0)**	**90.8 (84.8, 94.9)**	**95.6 (91.9, 97.9)**	**97.1 (95.6, 98.3)**
January/February	96.4 (91.5, 98.8)	98.2 (89.8, 100.0)	98.7 (92.7, 100.0)	97.0 (93.9, 98.8)
March	98.0 (92.7, 99.8)	89.8 (73.8, 97.2)	90.9 (78.6, 97.0)	97.6 (93.9, 99.4)
April	95.4 (90.9, 98.0)	85.6 (73.3, 93.1)	95.8 (89.3, 98.9)	97.0 (94.2, 98.6)
Janssen	**95.4 (90.6, 98.2)**	**86.9 (74.1, 94.4)**	**94.1 (86.2, 98.1)**	**93.1 (89.1, 95.9)**
March	89.6 (69.5, 97.9)	47.7 (-14.7, 80.9)	93.7 (64.9, 99.8)	91.8 (79.1, 97.8)
April	96.8 (91.8, 99.1)	96.0 (85.4, 99.5)	94.2 (85.1, 98.4)	93.4 (88.9, 96.4)
50-64 years				
Pfizer-BioNTech	**95.3 (93.8, 96.5)**	**94.6 (91.7, 96.7)**	**93.0 (90.1, 95.2)**	**94.5 (93.3, 95.5)**
January/February	91.8 (86.5, 95.4)	92.3 (81.7, 97.5)	96.2 (88.8, 99.2)	94.0 (90.6, 96.3)
March	93.1 (88.2, 96.4)	95.5 (86.7, 99.1)	90.2 (80.5, 95.8)	95.3 (92.4, 97.3)
April	96.6 (95.0, 97.7)	94.9 (91.4, 97.3)	92.9 (89.3, 95.5)	94.4 (93.0, 95.6)
Moderna	**97.1 (95.6, 98.1)**	**96.7 (93.8, 98.4)**	**96.2 (93.5, 97.9)**	**96.5 (95.4, 97.4)**
January/February	98.1 (95.1, 99.5)	100.0 (94.9, 100.0)	97.8 (91.9, 99.7)	96.5 (94.0, 98.2)
March	100.0 (97.8, 100.0)	98.3 (90.5, 100.0)	97.2 (90.0, 99.7)	97.7 (95.2, 99.1)
April	95.6 (93.2, 97.3)	94.6 (89.6, 97.6)	95.1 (90.9, 97.7)	96.0 (94.4, 97.3)
Janssen	**86.7 (81.3, 90.8)**	**90.0 (80.8, 95.5)**	**89.1 (80.7, 94.4)**	**92.0 (88.9, 94.4)**
March	89.5 (79.2, 95.5)	92.5 (72.8, 99.1)	84.7 (64.1, 95.1)	91.2 (84.7, 95.5)
April	85.5 (78.6, 90.6)	88.9 (76.9, 95.6)	90.9 (81.1, 96.4)	92.3 (88.5, 95.0)
≥65 years				
Pfizer-BioNTech	**94.4 (93.5, 95.2)**	**93.2 (91.4, 94.6)**	**88.0 (85.6, 90.1)**	**87.7 (86.5, 88.9)**
January/February	92.5 (90.1, 94.4)	92.0 (87.6, 95.1)	87.4 (81.9, 91.6)	84.1 (81.2, 86.7)
March	95.3 (93.9, 96.4)	93.4 (90.5, 95.6)	87.2 (83.1, 90.5)	88.1 (86.2, 89.8)
April	94.7 (93.3, 95.8)	93.5 (90.9, 95.5)	89.0 (85.6, 91.8)	89.1 (87.4, 90.6)
Moderna	**96.9 (96.2, 97.5)**	**96.0 (94.7, 97.1)**	**94.6 (93.0, 95.9)**	**93.2 (92.3, 94.0)**
January/February	97.1 (95.2, 98.4)	95.7 (91.5, 98.2)	90.9 (85.1, 94.9)	92.2 (89.7, 94.2)
March	97.2 (96.2, 97.9)	97.2 (95.4, 98.4)	95.1 (92.8, 96.8)	93.3 (91.9, 94.4)
April	96.6 (95.5, 97.5)	95.0 (92.7, 96.7)	95.2 (93.0, 96.9)	93.5 (92.2, 94.6)
Janssen	**84.2 (79.8, 87.9)**	**79.1 (70.1, 85.9)**	**79.9 (70.8, 86.7)**	**80.7 (76.4, 84.4)**
March	90.0 (84.1, 94.1)	78.6 (63.8, 88.4)	80.6 (65.8, 90.0)	80.8 (74.0, 86.2)
April	79.9 (73.3, 85.3)	79.4 (67.1, 87.9)	79.4 (66.7, 88.1)	80.6 (74.8, 85.3)

Table S12: Potential impacts of unmeasured confounding on observed vaccine effectiveness estimates (sensitivity analysis #6)

Assumptions regarding bias due to unmeasured confounding			Impact on hazard ratio or incidence rate ratio		Impact on vaccine effectiveness	
Association of unmeasured confounder with being unvaccinated (risk-ratio)	Association of unmeasured factor with having COVID-19 outcome (risk-ratio)	Bounding (bias) factor	Value observed in study	Expected value in reality	Value observed in study	Expected value in reality
1.25	1.25	1.04	0.100	0.104	90.0%	89.6%
1.50	1.50	1.13	0.100	0.113	90.0%	88.8%
2.00	2.00	1.33	0.100	0.133	90.0%	86.7%
2.50	2.50	1.56	0.100	0.156	90.0%	84.4%
0.75	1.50	0.90	0.100	0.090	90.0%	91.0%
0.75	2.00	0.86	0.100	0.086	90.0%	91.4%
0.50	1.50	0.75	0.100	0.075	90.0%	92.5%
0.50	2.00	0.67	0.100	0.067	90.0%	93.3%
1.25	1.25	1.04	0.150	0.156	85.0%	84.4%
1.50	1.50	1.13	0.150	0.169	85.0%	83.1%
2.00	2.00	1.33	0.150	0.200	85.0%	80.0%
2.50	2.50	1.56	0.150	0.234	85.0%	76.6%
0.75	1.50	0.90	0.150	0.135	85.0%	86.5%
0.75	2.00	0.86	0.150	0.129	85.0%	87.1%
0.50	1.50	0.75	0.150	0.113	85.0%	88.8%
0.50	2.00	0.67	0.150	0.100	85.0%	90.0%
1.25	1.25	1.04	0.200	0.208	80.0%	79.2%
1.50	1.50	1.13	0.200	0.225	80.0%	77.5%
2.00	2.00	1.33	0.200	0.267	80.0%	73.3%
2.50	2.50	1.56	0.200	0.313	80.0%	68.8%
0.75	1.50	0.90	0.200	0.180	80.0%	82.0%
0.75	2.00	0.86	0.200	0.171	80.0%	82.9%
0.50	1.50	0.75	0.200	0.150	80.0%	85.0%
0.50	2.00	0.67	0.200	0.133	80.0%	86.7%
1.25	1.25	1.04	0.250	0.260	75.0%	74.0%
1.50	1.50	1.13	0.250	0.281	75.0%	71.9%
2.00	2.00	1.33	0.250	0.333	75.0%	66.7%
2.50	2.50	1.56	0.250	0.391	75.0%	60.9%
0.75	1.50	0.90	0.250	0.225	75.0%	77.5%
0.75	2.00	0.86	0.250	0.214	75.0%	78.6%
0.50	1.50	0.75	0.250	0.188	75.0%	81.3%
0.50	2.00	0.67	0.250	0.167	75.0%	83.3%

References

1. CDC. Investigative Criteria for Suspected Cases of SARS-CoV-2 Reinfection (ICR). 2020. (Accessed 9/30/2021, at https://www.cdc.gov/coronavirus/2019-ncov/php/invest-criteria.html.)

2. Lee ET, Wang JW. Statistical Methods for Survival Data Analysis. 4 ed. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2013.

3. Bureau UC. 2020 Census. 2021. (Accessed 9/29/2021, at https://www.census.gov/programs-surveys/decennial-census/decade/2020/2020-census-main.html.)

4. Rosenberg ES, Holtgrave DR, Dorabawila V, et al. New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status - New York, May 3-July 25, 2021. MMWR Morbidity and mortality weekly report 2021;70:1306-11. 10.15585/mmwr.mm7037a7

5. CDC. NCHS Urban-Rural Classification Scheme for Counties. 2021. (Accessed 10/19/2021, at https://www.cdc.gov/nchs/data_access/urban_rural.htm.)

6. Ding P, VanderWeele TJ. Sensitivity Analysis Without Assumptions. Epidemiology (Cambridge, Mass) 2016;27:368-77. 10.1097/ede.0000000000000457

7. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. Annals of internal medicine 2017;167:268-74. 10.7326/m16-2607