

SYNTHESIS

SARS-CoV-2 Infections after Vaccination – What We Know So Far

07/05/2021

Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

Key Findings

- The COVID-19 vaccines produced by AstraZeneca/COVISHIELD, Moderna, and Pfizer-BioNTech are highly effective at preventing SARS-CoV-2 infection and severe COVID-19 disease, and breakthrough infections are rare.
- Vaccinated individuals represent a small proportion of those who test positive with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Additionally, only a small proportion of vaccinated individuals go on to become infected with SARS-CoV-2.
- In most publications, the majority of cases after vaccination were asymptomatic.
- A relatively small proportion of COVID-19 cases with infections following vaccination were hospitalized (<10%); between 0 to 5% of infections after vaccination resulted in death.
- In studies that reported multiple time points for infection after first and second dose vaccination, the percentage of post-vaccination infections decreased as time from vaccination increased. Most infections occurred up to 14 days after the first dose of a two-dose series, when an individual is considered not yet protected from vaccination.

Background

Protection from COVID-19 vaccination does not occur immediately and immunity develops over time. Vaccine effectiveness is about 60-80% for preventing symptomatic COVID-19 infection 3-4 weeks after receiving a single dose of Pfizer-BioNTech, Moderna and 60-70% for preventing symptomatic COVID-19 after a single dose of the AstraZeneca vaccine; however, this varies by population.¹ The effectiveness increases to greater than 85% after a second dose of mRNA vaccine. The vaccine effectiveness for the Janssen/Johnson & Johnson vaccine is 77%. The vaccine effectiveness for preventing severe disease and COVID-19-related hospitalization ranges from 70% to 90% for the Pfizer-BioNTech, Moderna and AstraZeneca vaccines, and from 70% to greater than 90% for preventing mortality (in terms of reducing deaths attributable to COVID-19).¹

For the general population in Ontario, COVID-19 vaccine effectiveness is 60% for preventing symptomatic disease and 70% for preventing severe outcomes (hospitalization or death) two weeks or more after a first dose of mRNA vaccine; this increases to 91% and 98%, respectively, after a second dose.¹

The effectiveness of vaccines may be impacted by variants of concern (VOCs). Evidence from real-world studies suggests that, for the VOCs currently circulating in Canada, the Alpha (B.1.1.7, first identified in United Kingdom [UK]), Gamma (P.1, first identified in Brazil) and Delta (B.1.617.2, first identified in India) variants may not have a significant impact on VE (particularly after full vaccination/two doses).¹

Vaccines are not 100% effective in preventing disease; therefore infections after vaccination, which include ‘vaccine breakthrough cases’, are possible.² This What We Know So Far (WWKSF) aims to describe SARS-CoV-2 infections after vaccination in relation to: case definitions and prevalence, with data on timeline since vaccination, disease severity, partial and full vaccination, and VOCs where it is reported.

Methods

Searches for peer-reviewed and pre-print literature were conducted between May 12, 2021 and May 14, 2021 by PHO Library Services. Searches conducted used the following databases: MEDLINE, Embase, Global Health, BIOSIS Previews, CINAHL, Scopus and NIH COVID-19 Portfolio. Search terms included but were not limited to: ‘COVID-19/SARS-CoV-2/coronavirus’, ‘vaccination’, ‘breakthrough infection’, or ‘vaccine failure/escape’.

Grey literature searches were conducted between May 9 to 11, 2021 using Google as well as custom search engines for Ontario’s Public Health Units, Canadian Health Departments and Agencies, International Public Health Resources. Search queries were provided by PHO’s Library services and includes search terms such as ‘COVID-19/SARS-CoV-2/coronavirus’, ‘breakthrough infection’, or ‘vaccine failure/escape’. The first 100 responses for each query were screened by a single reviewer. On July 5, 2021, the Findings were updated using the most recent PHO report on COVID-19 cases after vaccination.

For the purposes of this synthesis, we included reports of SARS-CoV-2 infection any time after dose one of a one- or two-dose series.

As the scientific evidence is expanding rapidly, the information provided in this document is only current as of the date of respective literature searches.

Findings

The findings below describe definitions of ‘breakthrough cases’ (i.e., fully vaccinated cases), followed by tables summarizing the proportion of COVID-19 cases that are vaccinated and the proportion of vaccinated individuals that become infected with SARS-CoV-2. We then describe COVID-19 cases among individuals who have been vaccinated in terms of age, severity, whether individuals were asymptomatic or symptomatic, and the time interval between vaccination(s) and infection. Lastly, we provide summaries of studies that report SARS-CoV-2 infections after vaccination using additional outcome measures.

What is a breakthrough case?

Some jurisdictions are monitoring and reporting on infections after vaccination.³⁻⁵ The definition of 'breakthrough cases' varies across jurisdictions.

CANADA

- The Public Health Agency of Canada (PHAC) defines breakthrough infections as “infections that occur > 14 days after completing the primary series of a COVID-19 vaccine where a person has SARS-CoV-2 RNA or antigen detected on a respiratory specimen.”⁶
- PHO defines a breakthrough case as “cases with a symptom onset date that was 7 or more days following receipt of the second dose of a 2-dose series COVID-19 vaccine or 14 or more days following the first dose of a 1-dose series COVID-19 vaccine.”³

UNITED STATES (US)

- The US Centers For Disease Control and Prevention (CDC) defines a breakthrough case as “a person who has SARS-CoV-2 RNA or antigen detected on a respiratory specimen collected \geq 14 days after completing the primary series of a U.S. Food and Drug Administration (FDA)-authorized COVID-19 vaccine.”⁴

UNITED KINGDOM (UK)

- Public Health England (PHE) defines breakthrough cases as “individuals with a SARS-CoV-2 polymerase chain reaction (PCR) positive sample with symptom onset date at least seven days after their second dose of vaccine (this includes any cases who develop symptoms after a second dose of vaccine).”⁵

What Proportion of COVID-19 Cases are Vaccinated?

- Vaccinated individuals represent a small proportion of SARS-CoV-2-positive cases.
- In most of the publications we identified, vaccinated individuals represented < 5% of COVID-19 cases. The few exceptions included an outbreak and a setting in which the Alpha variant was just emerging and thus, increasing the incidence of COVID-19 locally.
- **Table 1** summarizes studies examining the proportion of SARS-CoV-2 cases that were either partially or fully vaccinated. More detailed descriptions of each study can be found in Appendix A.

What Proportion of Individuals Become SARS-CoV-2 Positive After Vaccination?

- A small proportion of vaccinated individuals go on to become infected with SARS-CoV-2.
- In most of the publications we identified, < 5% of individuals vaccinated with one or two doses went on to become SARS-CoV-2-positive, and in most of these reports, the proportion that became infected was < 2%. The highest proportion of post-vaccination infection was reported during an outbreak.

- **Table 2** summarizes studies examining the proportion of individuals who get COVID-19 after being either partially or fully vaccinated. More detailed descriptions of each study can be found in Appendix A.

Table 1. Proportion of COVID-19 cases that are vaccinated

Jurisdiction	Population	Proportion of cases that are vaccinated (N [%]), time since vaccination	Vaccines products	Variant of concern (VOC) and/or outbreak
Canada ⁷	General	2,274 (1.3%) ≥ 14 days after first dose	Pfizer-BioNTech, Moderna, AstraZeneca	NR
Ontario, Canada ³	General	14,293/396,076 (3.6%) ≥ 14 days after first dose or 0 to < 7 days after second dose 1,648/396,076 (0.4%) ≥ 7 days after second dose	Pfizer-BioNTech, Moderna, AstraZeneca	The most frequently reported VOC among partially vaccinated and breakthrough cases was Alpha (8,561 cases, 53.7 %), which was the dominant circulating SARS-CoV-2 virus from late March 2021 to mid-June 2021. Additionally, there were cases of the Beta variant (B.1.351, first identified in South Africa) among partially vaccinated and breakthrough cases, and cases of the Gamma variant among breakthrough cases.
Chicago, US ⁸	Nursing facility residents /staff	22/627 (3.5%) ≥ 14 days after second dose	Mostly Moderna, very little Pfizer-BioNTech	NR
Kentucky, US ⁹	Nursing facility residents/staff	2/46 (4.3%) < 14 days after second dose 20/46 (47.8%) ≥ 14 days after second dose	Pfizer-BioNTech	During an outbreak
California, US ¹⁰	General population	1,379 (0.1%), time following vaccine administration not reported	Pfizer-BioNTech, Moderna, Janssen/Johnson & Johnson	NR

Jurisdiction	Population	Proportion of cases that are vaccinated (N [%]), time since vaccination	Vaccines products	Variant of concern (VOC) and/or outbreak
UK ¹¹	General population	238/12,525 (2%) 0-7 days after first dose 421/12,525 (3%) 8-20 days after first dose 417/12,525 (3%) ≥ 21 after first dose 72/12,525 (1%) after two doses, time not reported	AstraZeneca, Pfizer-BioNTech	During the study period, the Alpha variant became dominant.
England, UK ¹²	Hospital admissions	27/174 (16%) vaccinated, time following vaccination not defined and first or second dose not specified, but mean duration between vaccination and positive test was 18.19 days (interquartile range [IQR] 13.25)	AstraZeneca, Pfizer-BioNTech*	NR
Italy ¹³	HCWs	40/92 (43%) after two doses, time not reported	Pfizer-BioNTech	During the study period, the dominant SARS-CoV-2 variant was Alpha.
Europe ¹⁴	Geriatric rehab centre	5/16 (0.3%) “fully vaccinated” not defined	Pfizer-BioNTech	During the study period, there was an outbreak of Alpha cases at the facility.

NR - Not reported; *Not reported in the publication but the UK has been using AstraZeneca and Pfizer-BioNTech COVID-19 vaccines for their COVID-19 Immunization Program.¹⁵

Table 2. Proportion of individuals that get COVID-19 after vaccination

Jurisdiction	Population	Proportion of individuals that get COVID-19 after vaccination (N [%]), time since vaccination	Vaccine products	VOC
Ontario, Canada ³	General population	Of 9,413,440 people who received ≥ 1 dose: 14,293/9,413,440 (0.15%) tested positive ≥ 14 days after first dose or 0 to < 7 days after the second dose 1,648/9,413,440 (0.02%) tested positive ≥ 7 days after second dose	Pfizer-BioNTech, Moderna, AstraZeneca	The most frequently reported VOC among partially vaccinated and breakthrough cases was Alpha (8,561 cases, 53.7%), which was the dominant circulating SARS-CoV-2 virus from late March 2021 to mid-June 2021. Sixty-eight (< 1%) cases of the Beta variant (1%) and 217 cases of Gamma (1.3%) were detected.
British Columbia, Canada ⁷	General population	618 (0.14%) tested positive > 14 days after at least a first dose No denominator reported Of those 618 cases, 42 (7%) were ≥ 7 days after second dose	Pfizer-BioNTech, Moderna, AstraZeneca	NR
Manitoba, Canada ⁷	General population	195 (0.06%) tested positive > 14 days after first dose No denominator reported	Pfizer-BioNTech, Moderna, AstraZeneca	NR
US ^{4,16}	General population	Out of approximately 95 million people vaccinated with two doses: 9,245 (0.01%) tested positive > 14 days after second dose	NR	NR
US ¹⁷	HCWs	51/3,052 (1.7%) tested positive after one or two doses (time frame not reported)	Pfizer-BioNTech	NR
US ¹⁸	HCWs	379/36,659 (1.03%) tested positive after first dose (time frame not reported but 70% tested positive ≤ 14 days after first dose)	Pfizer-BioNTech, Moderna	NR

Jurisdiction	Population	Proportion of individuals that get COVID-19 after vaccination (N [%]), time since vaccination	Vaccine products	VOC
		37/28,184 (0.13%) tested positive after second dose (time frame not reported but 59% within days 1 to 7 after second dose)		
Oregon, US ¹⁹	General population	Of > 700,000 people vaccinated with two doses: 168 (0.024%) tested positive ≥ 14 days after second dose	NR	NR
Minnesota, US ²⁰	General population	Of 800,000 people vaccinated with two doses: 89/800,000 (0.01%) tested positive > 14 days after second dose	NR	NR
Washington, US ²¹	General population	Of more than 1.7 million people vaccinated with two doses: 217 (0.01%) tested positive ≥ 14 days after second dose	NR	NR
California, US ²²	General population	Of 100,532 people vaccinated with two doses: 21/100,532 (0.02%) tested positive > 14 days after second dose	Pfizer-BioNTech, Moderna, Janssen/Johnson & Johnson	NR
Sacramento, US ²³	General population	271/559,268 (0.05%) of those fully vaccinated (time frame not reported) tested positive	NR	NR
New York, US ²⁴	Individuals at a New York university	2/417 (0.48%) tested positive > 14 days after second dose	Pfizer-BioNTech, Moderna	NR

Jurisdiction	Population	Proportion of individuals that get COVID-19 after vaccination (N [%]), time since vaccination	Vaccine products	VOC
South Carolina, US ²⁵	General population	141 (< 0.5%) tested positive \geq 14 days after second dose No denominator reported	NR	NR
South Carolina, US ²⁶	General population	155/950,000 (0.02%) of fully vaccinated individuals tested positive (time frame not reported)	NR	NR
Kentucky, US ⁹	Nursing facility residents/staff	18/71 (25.4%) residents tested positive \geq 14 days after second dose 4/56 (7.1%) HCWs tested positive \geq 14 days after second dose	Pfizer-BioNTech	Study took place during an outbreak at a nursing facility. An R.1 lineage variant was detected with whole genome sequencing (WGS).
UK ²⁷	General population	3106/103,622 (3%) tested positive after first dose (time frame not reported)	Pfizer-BioNTech, AstraZeneca	The Alpha variant was dominant during study period.
Wales, UK ²⁸	General population	148/14,104 (1.05%) vaccinated individuals tested positive	Pfizer-BioNTech, AstraZeneca	NR
England, UK ²⁹	HCWs	4/1358 (0.3%) tested positive \geq 14 days after first dose	Pfizer-BioNTech	The Alpha variant was dominant during study period.
Israel ³⁰	Staff at a medical centre	32/725 (4.4%) tested positive 15-35 days after first dose 3/725 (0.41%) tested positive after second dose (and 41-65 days after first dose)	Pfizer-BioNTech	NR
Israel ³¹	HCWs	8/5,517 (0.1%) (symptomatic) tested positive > 7 days after second dose	Pfizer-BioNTech	NR

Jurisdiction	Population	Proportion of individuals that get COVID-19 after vaccination (N [%]), time since vaccination	Vaccine products	VOC
		19/5,517 (0.3%) (asymptomatic) tested positive > 7 days after second dose)		
Israel ³²	HCWs	22/4,081 (0.54%) tested positive 1 to 10 days after first dose	Pfizer-BioNTech	NR
Israel ³³	HCWs	78/7214 (1.08%) tested positive after first dose (time frame not reported) 3/6818 (0.04%) tested positive after second dose (time frame not reported)	Pfizer-BioNTech	NR
Israel ³⁴	General population	2484 (0.57%) tested positive 1 to 12 days after first dose 614 (0.27%) tested positive 13 to 24 days after first dose	Pfizer-BioNTech	NR
India ³⁵	General population	Covaxin: 4,208/11 million (0.04%) tested positive after first dose (time frame not reported) and 695/11 million (0.006%) tested positive after second dose (time frame not reported) COVISHIELD: 17,145/116 million (0.014%) tested positive after first dose (time frame not reported), and 5,014/116 million (0.004%) after second dose (time frame not reported)	Covaxin, COVISHIELD	NR

NR - Not reported

What Age Groups Get COVID-19 Infections After Vaccination?

It is important to note that most vaccination programs initially prioritized older adults and therefore, breakthrough cases among this population may be overrepresented in the findings below. Additionally, vaccines may be less effective in older adults.³⁶ The distribution of breakthrough cases may change as vaccine eligibility expands.

CANADA

- PHO reported that when examining infections that occurred after partial or full vaccination between December 14, 2020 and June 12, 2021, the proportions of partially vaccinated and breakthrough cases increased with age, and were highest among cases 80 years of age and older.³ Among individuals 80 years and older who received ≥ 1 dose of vaccine and later contracted COVID-19, 1,959/599,693 (0.33%) were ≥ 14 days after first the dose or 0 to < 7 days after second dose, and 310/599,693 (0.05%) were ≥ 7 days after the second dose.

US

- As of April 26, 2021 in US, of the 9,245 vaccine breakthrough cases (fully vaccinated individuals), 63% were females, and 45% were ≥ 60 years of age.⁴
- A prospective cohort study of HCWs at an urban academic medical center during a high community prevalence period reported that SARS-CoV-2 cases in HCWs that occurred > 14 days from initial dose of Pfizer-BioNTech or Moderna, compared to within 14 days, were more often older (46 versus 38 years of age, $p=0.007$).³⁷
- As of April 3, 2021, in Washington State, the median age of cases with confirmed vaccine breakthrough had shifted downward since the first cases were reported, with more cases in the 40 to 59 year old age group compared to previous weeks.²¹
- As of April 13, 2021, 70 of the 200,000 individuals in Delaware who had been fully vaccinated had tested positive for COVID-19. Of these 70 individuals, three were “of advanced age” with underlying conditions and needed to be hospitalized, with one death.³⁸ In Delaware, Pfizer-BioNTech, Moderna, and Janssen/Johnson & Johnson vaccines were administered.
- The Oregon Health Authority reported 168 breakthrough cases (≥ 14 days after final dose) among the approximately 700,000 individuals in Oregon who were fully vaccinated.¹⁹ Many of these individuals had asymptomatic infection. Three of the 168 breakthrough cases died. Most of the cases occurred in individuals > 65 years of age with underlying health conditions. None of the cases were associated with a COVID-19 variant of concern.

UK

- A cross-sectional audit of COVID-19 positive admissions (excluding intensive care) to a UK hospital over one weekend found 27 (16%) of the 174 COVID-19 inpatients had been vaccinated.¹² The mean age of the inpatients was 82.3 years (IQR 11.75).

What is the Severity of COVID-19 Disease in Vaccinated Individuals?

- In most of the identified publications, the majority of cases after vaccination were asymptomatic. A relatively small proportion of COVID-19 cases with infections following vaccination were hospitalized ($< 10\%$); between 0 to 5% of infections after vaccination resulted in death.

- **Table 3** summarizes studies examining the proportion of COVID-19 cases after vaccination that were symptomatic and/or asymptomatic, as well as hospitalization and death from COVID-19 in vaccinated individuals. More detailed descriptions of each study can be found in Appendix A.

When Do Infections After Vaccination Occur?

- In publications that reported multiple time points for infection after first and second dose vaccination, the percentage of post-vaccination infections decreased as time from vaccination increased. Most infections occurred up to 14 days after the first dose of a two-dose series, when an individual is considered not yet protected from vaccination.
- **Table 4** describes the time frame at which SARS-CoV-2 infections occurred following vaccination. Detailed descriptions of each study can be found in Appendix A.

Table 3. Severity and symptoms of COVID-19 disease in vaccinated individuals

Jurisdiction		Asymptomatic	Symptomatic	Hospitalizations	Deaths
Canada ⁷		NR	NR	Of 2,274 infections \geq 14 days after one dose, 203 (9%) were admitted to hospital	Of 2,274 infections \geq 14 days after one dose, 53 (2%) died
Ontario, Canada ³		Of all infections \geq 14 days after first dose or 0 to < 7 days after second dose, 4,408/14,293 (30.84%) were asymptomatic Of all infections \geq 7 days after second dose, 860/1,648 (52.18%) were asymptomatic	Of all infections \geq 14 days after first dose or 0 to < 7 days after second dose, 9,885/14,293 (69.16%) were symptomatic Of all infections \geq 7 days after second dose, 788/1,648 (47.82%) were symptomatic	The proportion of age-specific hospital admissions and intensive care unit (ICU) admissions for both partially vaccinated (\geq 14 days after first dose to < 7 days after second dose) and breakthrough (\geq 7 days after second dose) cases was lower than the proportion of hospital and ICU admissions among unvaccinated COVID-19 cases.	The proportion of age-specific deaths for both partially vaccinated (\geq 14 days after first dose or 0 to < 7 days after second dose) and breakthrough (\geq 7 days after second dose), cases was lower than the proportion of fatalities among unvaccinated COVID-19 cases. Of the 32 deaths among cases that were \geq 7 days after second dose, one was 50-59 years of age, three were 60-69 years of age, three were 70-79 years of age and the remainder (25/32 deaths) were 80+ years of age.
British Columbia, Canada ⁷		NR	NR	NR	Of 618 infections > 14 days after at least a first dose, 18 (3%) of those individuals died
Manitoba, Canada ⁷		NR	NR	NR	Of 195 infections after vaccination (> 14 days after first dose), 7 (3.6%) died, all seniors
US ⁴		Of 9,245 infections (fully vaccinated, not defined), 27% were asymptomatic	NR	Of 9,245 infections (fully vaccinated, not defined), 9% were hospitalized	Of 9,245 infections (fully vaccinated individuals, not defined), 1% died

Jurisdiction		Asymptomatic	Symptomatic	Hospitalizations	Deaths
US ⁸		Of 22 infections among residents/staff in a nursing facility ≥ 14 days after second dose: 14 (64%) were asymptomatic	NR	Of 22 infections among residents/staff in a nursing facility ≥ 14 days after second dose: 2 (9%) were hospitalized	Of 22 infections among residents/staff in a nursing facility ≥ 14 days after second dose: 1 (5%) died
US ¹⁷		Of 51 infections among vaccinated (any time after first dose) HCWs, 29 (57%) were asymptomatic	Of 51 infections among vaccinated HCWs, 22 (43%) were either symptomatic or were tested because of an exposure	NR	NR
Washington, US ²⁶		NR	NR	Of 102 infections after vaccination, most were mild; however, 8 (8%) individuals were hospitalized	Of 102 infections after vaccination, 2 (2%) individuals died
Washington, US ²¹		NR	NR	Of infections that occurred after vaccination (with hospitalization information available), 12% required hospitalization (Note: hospitalization data for about half of breakthrough cases was missing)	Of 217 infections after vaccination (> 14 days after receiving their final dose), 5 died
California, US ²²		NR	Of 21 infections > 14 days after receiving the final dose: Majority of cases were mild	Of 21 infections > 14 days after receiving the final dose: None were hospitalized	Of 21 infections > 14 days after receiving the final dose: None died

Jurisdiction		Asymptomatic	Symptomatic	Hospitalizations	Deaths
Kentucky, US ⁹		NR	Of 22 infections ≥ 14 days after second dose: 8 people were symptomatic	Of 22 infections ≥ 14 days after second dose: 2 people were hospitalized	Of 22 infections ≥ 14 days since second dose: 1 person died
Oregon, US ¹⁹		Of 168 infections ≥ 14 days after the second dose, many were asymptomatic	NR	NR	Of 168 infections ≥ 14 days after the final dose, 3 cases died
UK ¹¹		Of the 421 infections among individuals vaccinated with a first dose 8 to 20 days before their positive test, 234 (56%) were asymptomatic Of the 417 infections among individuals vaccinated with one dose ≥ 21 days before their positive test, 260 (62%) were asymptomatic Of the 72 infections among those who were positive after their second vaccine dose (days not reported), 60 (83%) were asymptomatic	NR	NR	NR

Jurisdiction		Asymptomatic	Symptomatic	Hospitalizations	Deaths
UK ³⁹		Of the 71 infections that occurred \geq 21 day after first dose, and the 9 infections that occurred 7 days after the second dose: 10 (13%) were asymptomatic	Of the 71 infections that occurred \geq 21 day after first dose, and the 9 infections that occurred 7 days after the second dose: 32 (40%) were symptomatic and had typical COVID-19 symptoms 13 (16%) were symptomatic and had other symptoms 25 (31%) did not complete the questionnaire	NR	NR
England, UK ⁴⁰		No symptomatic infections were observed following two vaccine doses (timeline not specified)	NR	None of the HCWs that were vaccinated with two doses (timeline not specified) were admitted to hospital	NR
England, UK ⁴¹		NR	NR	Of the cases that attended the hospital, 5.3 per 100,000 of the vaccinated cohort (not defined) were hospitalized	NR
France ¹⁴		NR	A case series in a geriatric rehabilitation ward during an outbreak reported that out of 16 cases, 5 had been fully vaccinated	NR	NR

Jurisdiction		Asymptomatic	Symptomatic	Hospitalizations	Deaths
			(not defined), and only 1/5 was symptomatic (they were immunocompromised). In contrast, 7/11 unvaccinated cases were symptomatic.		
Italy ¹³		Of infections among workers ≥ 7 days after second dose, 25 (63%) were asymptomatic (compared to workers who were not fully vaccinated, of whom 20 [38%] were asymptomatic)	Of infections among workers ≥ 7 days after second dose, 15 (37%) were symptomatic (compared to workers who were not fully vaccinated, of whom 32 [62%] were symptomatic)	NR	NR
Israel ⁴²		Of infections ≥ 14 days after second dose, the incidence rate for asymptomatic infection was 1.2 per 100,000 person-days (versus 40.9 per 100,000 person-days for unvaccinated individuals)	Of infections ≥ 14 days after second dose, the incidence rate for symptomatic infection was 0.6 per 100,000 person-days (versus 32.5 per 100,000 person-days for unvaccinated individuals)	Of infections ≥ 14 days after second dose, the incidence rate for hospitalization was 0.1 per 100,000 person-days (versus 2.7 per 100,000 person-days for unvaccinated individuals)	Of infections ≥ 14 days after second dose, the incidence rate for COVID-19-related death was < 0.1 per 100,000 person-days (versus 0.6 per 100,000 person-days for unvaccinated individuals)

NR - Not reported

Table 4. Time between vaccination and infection

Jurisdiction	≤ 14 days after first dose	≥ 14 days after first dose	≤ 14 days after second dose	≥ 14 days after second dose
Ontario, Canada ³	Of 34,014 post-vaccination infections of COVID-19: 18,073 (53.1%) occurred 0 to 13 days after first dose	Of 34,014 post-vaccination infections of COVID-19: 7,315 (21.5%) occurred at ≥ 28 days after first dose	Of 34,014 post-vaccination infections of COVID-19: 145 (0.4%) occurred 7 to 13 days after second dose	Of 34,014 post-vaccination infections of COVID-19: 1,503 (4.4%) occurred ≥ 14 days after second dose
Chicago ⁸	NR	NR	NR	The median interval from second vaccine dose to infection was 29 days (IQR 23 – 42 days).
California, US ¹⁸	Of 36,659 HCWs that received the first dose of vaccine: 145 (0.39%) infections occurred 1 to 7 days after first dose 125 (0.34%) infections occurred 8 to 14 days after first dose	Of 36,659 HCWs that received the first dose of vaccine: 57 (0.16%) infections occurred 15 to 21 days after first dose 15 (0.04) infections occurred ≥ 22 days after first dose	Of 28,184 HCWs that received two doses of vaccine: 22 (0.08%) infections occurred 1 to 7 days after second dose 8 (0.03%) infections occurred 8 to 14 days after second dose	Of 28,184 HCWs that received two doses of vaccine: 7 (0.02%) infections occurred ≥ 15 days after second dose
California, US ⁴³	Of 22,729 HCWs with ≥ 1 dose of COVID-19 vaccine: 114 (60.3%) infections occurred ≤ 14 days after first dose	NR	Of 22,729 HCWs with ≥ 1 dose of COVID-19 vaccine: 49 (25.9%) infections occurred ≤ 14 days after second dose	Of 22,729 HCWs with ≥ 1 dose of COVID-19 vaccine: 26 (13.8%) infections occurred > 14 days after second dose
England, UK ⁴¹	NR	Infections peaked 14 days after the first dose, and hospitalizations peaked between days 23 and 26. Rate of positive COVID-19 tests (at 14 – 20 days after first dose): 28.2 per 100,000 people per day (22.9 to 34.3)	NR	NR

Jurisdiction	≤ 14 days after first dose	≥ 14 days after first dose	≤ 14 days after second dose	≥ 14 days after second dose
England, UK ⁴⁴	Infection rate per 10,000 person days for the first dose was 22.06 at 0-6 days, 25.98 at 7-13 days	Infection rate per 10,000 person days for the first dose was 26.21 at 14-20 days, 19.99 at 21-27 days, 9.74 at 29-34 days, and 14.55 at ≥ 49 days	NR	NR
Wales, UK ²⁸	From 148 infections after vaccination, 40% occurred within 7 days, 60% within 14 days	From 148 infections after vaccination, 85% occurred within 21 days, 90% within 28 days, and over 95% within 35 days	NR	NR
France ¹⁴	NR	NR	NR	A case series of 5 SARS-CoV-2 positive patients in geriatric rehabilitation ward found that the time from their second dose to infection ranged from 8 to 29 days.
Israel ⁴⁵	Among individuals ages 60+: 7,438 infections occurred between 1 to 13 days after first dose	Among individuals ages 60+: 5,262 infections occurred 14 to 20 days after first dose	Among individuals ages 60+: 1,199 infections occurred 0 to 6 days after second dose 1,202 infections occurred 7 to 13 days after second dose	Among individuals ages 60+: 295 infections occurred more than 14 days after second dose

NR - Not reported

Studies Reporting Infections after Vaccination Using Other Outcomes

US

- A health surveillance study of HCWs at a US hospital from December 17, 2020 to March 20, 2021, reported that of 3,052 workers who received one or two doses of the Pfizer-BioNTech COVID-19 vaccine, the incident rate ratio (IRR) for a positive COVID-19 test decreased with the time since the first dose and continued to decrease from the first dose to ≥ 7 days after the second dose (i.e., 0-11 days after first dose IRR: 0.59 (95% CI 0.39-0.91); ≥ 12 days after first dose and before second dose IRR: 0.42 (95% CI 0.26-0.70); 0-6 days after second dose IRR: 0.2 (95% CI 0.07-0.53); ≥ 7 days after second dose IRR: 0.04 (95% CI 0.02-0.09)).¹⁷ Of the 51 vaccinated SARS-CoV-2-positive workers, 29 (57%) were asymptomatic and 22 (43%) were either symptomatic or were tested because of an exposure, compared to 185 unvaccinated SARS-CoV-2-positive workers, of whom 79 (43%) were asymptomatic and 106 (57%) were symptomatic or tested because of a known exposure.
- A prospective cohort study of HCWs at an urban academic medical center in Boston during a high community prevalence period reported an adjusted SARS-CoV-2 infection rate ratio of 0.18 (95% CI 0.10 to 0.32) (> 14 days after first dose of Pfizer-BioNTech or Moderna) (and 0.73 [95% CI 0.53-1.00] for 1 to 14 days after first dose).³⁷ HCWs were screened daily for COVID-19 symptoms and tested if symptomatic, with asymptomatic testing for workplace exposures, following out-of-state travel, and when requested; however, routine asymptomatic serial screening was not performed during this period.
- A prospective cohort study of HCWs, first responders, and other essential and frontline workers was conducted in eight US locations from December 14, 2020 to March 13, 2021, using weekly routine testing and symptomatic testing. They reported 0.04 infections per 1,000 person-days among individuals ≥ 14 days after the second dose with an mRNA vaccine (i.e., Pfizer-BioNTech or Moderna), and 0.19 infections per 1,000 person-days among those partially immunized (≥ 14 days after first dose and before second dose).⁴⁶

UK

- The Coronavirus Clinical Characterisation Consortium (ISARIC4C/CO-CIN) analyzed a quarter of all hospital patients in England, Scotland and Wales between early December 2020 and early April 2021.⁴⁷ They found that 1% of hospital admissions between December and April were of people with COVID-19 who had already had one vaccine dose.
- A cross-sectional audit of COVID-19 positive admissions (excluding intensive care) to a UK hospital over one weekend found 27 of the 174 (16%) COVID-19 inpatients had been vaccinated.¹² Of the 27 vaccinated patients, 11 (41%) had their positive COVID-19 test within 14 days of vaccination (first or second dose not clearly specified), suggesting possible infection close to the time of vaccination.
- A longitudinal cohort study of HCWs in Oxfordshire, UK who were screened routinely from March 2020 to February 2021 reported that compared to unvaccinated seronegative HCWs, the incidence of symptomatic SARS-CoV-2 infections was 67% lower for previously seronegative HCWs with one dose (adjusted IRR (aIRR): 0.33 [95% CI 0.21-0.52; $p < 0.001$]), and no symptomatic infections were reported after a second dose.⁴⁰ Rates of any SARS-CoV-2 positive result, irrespective of symptoms, were highest in unvaccinated seronegative HCWs (635 cases),

and incidence was reduced by 64% in seronegative HCWs with one dose of vaccine (64 cases, aIRR: 0.36 [95% CI 0.26-0.50; $p < 0.001$]), reduced by 90% in HCWs with two doses of vaccine (2 cases, aIRR: 0.10 [95% CI 0.02-0.38; $p < 0.001$]), and reduced by 96% in vaccinated previously seropositive HCWs (1 case, aIRR: 0.04 [0.01-0.27; $p = 0.001$]). Over the study period, the Alpha variant became the dominant strain before decreasing in prevalence. HCWs were offered the AstraZeneca or Pfizer-BioNTech COVID-19 vaccines.

- A study in England from November 2020 to February 2021 matched older (aged 80-83 years) Pfizer-BioNTech vaccine recipients with younger (aged 76-79 years) persons not yet eligible to receive the vaccine.⁴¹ The authors reported an average of 13.7 per 100,000 SARS-CoV-2 infections per day in vaccinated individuals (78.8% had received dose two within 26 days of dose 1) compared to 23.2 per 100,000 in unvaccinated controls. Focussing on different time points following first dose, the rate of positive COVID-19 tests per 100,000 people per day was 28.2 (95% CI 22.9 to 34.3) at 14 to 20 days, 13.4 (95% CI 10.7 to 16.2) at 21 to 27 days, 9.7 (95% CI 7.6 to 11.9) at 28 to 34 days, 4.6 (95% CI 3.3 to 6.1) at 35 to 41 days.
- A prospective cohort study of frail older adults living in long-term care facilities in England and undergoing routine asymptomatic testing from December 2020 to March 2021 reported that the adjusted hazard ratio (aHR) for SARS-CoV-2 infection 28 to 34 days after the AstraZeneca vaccine was 0.33 (95%CI 0.16, 0.68), and 0.32 (95% CI 0.15, 0.66) at 35 to 48 days post-vaccination, while the aHR for infection after Pfizer-BioNTech vaccination were 0.47 (95% CI 0.20, 1.06) at 28 to 34 days, and 0.35 (95% CI 0.17, 0.71) at 35-48 days post-vaccination. A reduced risk of PCR-positive infection was seen in the early post-vaccination period (0-13 days) in residents who received the AstraZeneca COVID-19 vaccine (0-6 days: aHR 0.51, 95% CI 0.6-0.99; 7-13 days: aHR 0.58, 95%CI 0.35, 0.96) but not with Pfizer-BioNTech.⁴⁴ The infection rate per 10,000 person days for the first dose of either vaccine was 22.06 at 0 to 6 days, 25.98 at seven to 13 days, 26.21 at 14 to 20 days, 19.99 at 21 to 27 days, 9.74 at 29-34 days, and 14.55 at ≥ 49 days.
- An interim analysis of the SIREN prospective cohort study of workers in publicly-funded hospitals in the UK reported that 21 days or more after the first dose of Pfizer-BioNTech, there were 71 new infections (incidence density of 8 per 10000 person-days of follow-up) and nine new infections seven days after the second dose (incidence density of 4 per 10000 person-days of follow-up).³⁹ Within 14 days before and after the date of a positive SARS-CoV-2 test, 10 (13%) of the vaccinated cases were asymptomatic, 32 (40%) had typical COVID-19 symptoms, 13 (16%) had other symptoms, and 25 (31%) did not complete the questionnaire. The Alpha variant was dominant at the time of the study.

ISRAEL

- In Israel, a real-world effectiveness study using a national surveillance system was conducted to examine the effectiveness of two doses of the Pfizer-BioNTech vaccine.⁴² The study was conducted between January 24 and April 3, 2021. They compared the incidence rates of COVID-19 infection in unvaccinated individuals to individuals seven days after receiving the second dose of vaccine (fully vaccinated). The SARS-CoV-2 incidence rate was 91.5 per 100,000 person-days in unvaccinated compared to 3.1 per 100,000 person-days in fully vaccinated individuals. For asymptomatic SARS-CoV-2 infection, the incidence rate was 40.9 versus 1.8 per 100,000 person-days for unvaccinated and fully vaccinated individuals, respectively. For symptomatic infection, the incidence rate was 4.6 versus 0.3 per 100,000 person-days, respectively. For COVID-19-related hospitalization, the incidence rates was 2.7 versus 0.2 per 100,000 person-

days respectively, and 0.6 versus 0.1 per 100,000 person-days for COVID-19-related death, respectively.

- A case-control study conducted in Israel examined the distribution of SARS-CoV-2 variants observed in infections of vaccinated individuals and matched infections of unvaccinated individuals (i.e., controls).⁴⁸ They found those who tested positive at least one week after their second dose of the Pfizer-BioNTech vaccine were disproportionately infected with the Beta variant, compared with unvaccinated individuals (odds ratio of 8:1). Additionally, those who tested positive between two weeks after their first dose and one week after their second dose (i.e., partially vaccinated) were disproportionately infected with the Alpha variant compared to controls (odds ratio of 26:10).⁴⁸ These results demonstrate that there is an increased incidence of the Beta variant in vaccine breakthrough infections in fully vaccinated individuals, and increased incidence of Alpha in partially vaccinated individuals. At the time of the study, Alpha was the dominant strain of the virus, while the Beta variant was less prevalent (< 1% of cases in the sample).
- A retrospective cohort study was conducted between December 20, 2020 and February 25, 2021 in Israel with 6,710 HCWs who underwent periodic testing for symptomatic and asymptomatic SARS-CoV-2 infection, as per workplace screening protocols.³¹ 5,517 (82.2%) received two doses, and 757 (11.3%) were not vaccinated. Symptomatic SARS-CoV-2 infection occurred in eight fully vaccinated HCWs (> 7 days after second dose) versus 38 unvaccinated HCWs (4.7 vs 149.8 per 100 000 person-days). Asymptomatic SARS-CoV-2 infection occurred in 19 fully vaccinated versus 17 unvaccinated HCWs (11.3 vs 67.0 per 100 000 person-days).

Limitations

- The type of surveillance or study design used to identify infections after vaccination may over or underestimate the incidence of cases post-vaccination (e.g., a passive surveillance system used by the CDC to track infections after vaccination versus routine testing of staff and residents in congregate living settings).
- Differences in the local incidence of COVID-19 at the time of each study could also impact the rate of infections after vaccination. If a study reported that it was conducted during an outbreak or at the peak in the pandemic, we reported that information in the Appendix.
- Differences in circulating VOCs and potential impact on VE could result in some studies reporting higher or lower rates of infections after vaccination. To address this, if a study reported on VOCs, we reported that information.
- The role of previous SARS-CoV-2 infection was out of scope and therefore not considered if it was reported in a study. Therefore, the role of natural immunity in post-vaccination infections, which might be particularly relevant for highly exposed HCWs, could contribute to a lower rate of infections after vaccination. The corollary of vaccinated HCWs having higher rates of infections after vaccination due to frequent exposure also limits the generalizability of these types of studies. The same limitation applies to residents and staff in congregate living settings.
- Due to immunization programs prioritizing certain populations (e.g., HCWs, older individuals, individuals with co-morbidities etc.), it is challenging to make inferences into who gets infections after vaccination, at least across studies. Additionally, because many vaccination programs

prioritize older individuals, breakthrough cases among this populations may be overrepresented in our findings.

Conclusions

- The COVID-19 vaccines produced by AstraZeneca/COVISHIELD, Moderna, and Pfizer-BioNTech are highly effective at preventing SARS-CoV-2 infection and severe COVID-19 disease, and breakthrough infections are exceptionally rare.
- Most infections after vaccination occur before partial or full immunity have had time to develop.
- The duration of protection conferred by full vaccination, as well as the protection against newly circulating VOCs merits further study.

References

1. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 real-world vaccine effectiveness – what we know so far [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Jun 25]. Available from: <https://www.publichealthontario.ca/-/media/documents/ncov/covid-wwksf/2021/04/wwksf-vaccine-effectiveness.pdf?la=en>
2. Centres for Disease Control and Prevention. What you should know about the possibility of COVID-19 illness after vaccination [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2021 [cited 2021 Jun 8]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html>
3. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Enhanced epidemiological summary: confirmed cases of COVID-19 following vaccination in Ontario: December 14, 2020 to June 12, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Jul 5]. Available from: <https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-epi-confirmed-cases-post-vaccination.pdf?la=en>
4. Centers for Disease Control and Prevention. COVID-19 vaccine breakthrough case investigation and reporting [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2021 [cited 2021 Jun 28]. Available from: <https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html>
5. Public Health England. Reporting to the enhanced surveillance of COVID-19 cases in vaccinated individuals [Internet]. London: Crown Copyright; 2021 [cited 2021 Jun 28]. Available from: <https://www.gov.uk/government/publications/covid-19-enhanced-surveillance-of-cases-in-vaccinated-individuals/reporting-to-the-enhanced-surveillance-of-covid-19-cases-in-vaccinated-individuals>
6. Public Health Agency of Canada. Emerging evidence on COVID-19: rapid review on protective immunity, update 1. Ottawa, ON: Public Health Agency of Canada; 2021 [cited 2021 Jun 04].
7. Grant K. Relatively few COVID-19 cases reported after receiving first vaccine dose, data show. Globe and Mail [Internet], 2021 May 3 [cited 2021 Jun 8]; Toronto. Available from:

<https://www.theglobeandmail.com/canada/article-relatively-few-covid-19-cases-reported-after-receiving-first-vaccine/>

8. Teran RA, Walblay KA, Shane EL, Xydis S, Gretsch S, Gagner A, et al. Postvaccination SARS-CoV-2 infections among skilled nursing facility residents and staff members — Chicago, Illinois, December 2020–March 2021. *MMWR Morbid Mortal Wkly Rep.* 2020;70(17):632-8. Available from:

https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e1.htm?s_cid=mm7017e1_w

9. Centers for Disease Control and Prevention. COVID-19 outbreak associated with a SARS-CoV-2 R.1 lineage variant in a skilled nursing facility after vaccination program — Kentucky, March 2021 [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2021 [cited 2021 Jun 08]. Available from:

<https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e2.htm>

10. Allday E. State has about 1,400 ‘breakthrough’ COVID cases in fully vaccinated people [Internet]. *San Francisco Chronicle* [Internet], 2021 Apr 27 [cited 2021 Jun 04]. Available from:

<https://www.msn.com/en-us/health/medical/state-has-about-1400-breakthrough-covid-cases-in-fully-vaccinated-people/ar-BB1g6LzI>

11. Pritchard E, Matthews PC, Stoesser N, Eyre DW, Gethings O, Vihta KD, et al. Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study using the UK’s COVID-19 Infection Survey. *medRxiv* 21255913 [Preprint]. 2021 Apr 23 [cited 2021 Jun 08]. Available from:

<https://www.medrxiv.org/content/10.1101/2021.04.22.21255913v1.full.pdf>

12. Robbins T, Baitule S, Kyrou I, Ray P, Morgan N, Berry L, et al. SARS-CoV-2 infection despite vaccination: an under-reported COVID-19 cohort. *Clin Med.* 2021;21(2):e243. Available from:

<https://doi.org/10.7861/clinmed.Let.21.2.6>

13. Sansone E, Tiraboschi M, Sala E, Albin E, Lombardo M, Castelli F, et al. Effectiveness of BNT162b2 vaccine against the B.1.1.7 variant of SARS-CoV-2 among healthcare workers in Brescia, Italy. *J Infect.* 2021;83(1):e17-8. Available from:

<https://doi.org/10.1016/j.jinf.2021.04.038>

14. Donadio C, Rainone A, Gouronne A, Belmin J, Lafuente-Lafuente C. Asymptomatic COVID-19 cases among older patients despite BNT162b2 vaccination: a case series in a geriatric rehabilitation ward during an outbreak. *J Infect.* 2021;83(1):119-45. Available from:

<https://doi.org/10.1016/j.jinf.2021.04.004>

15. Public Health England. COVID-19 vaccination: information for healthcare practitioners [Internet]. London: Crown Copyright; 2020 [cited 2021 Jun 28]. Available from:

<https://www.gov.uk/government/publications/covid-19-vaccination-programme-guidance-for-healthcare-practitioners>

16. Chen E. CDC limits review of vaccinated but infected; draws concern. *Bloomberg* [Internet], 2021 May 9 [cited 2021 Jun 04]; Prognosis. Available from: <https://www.bloomberg.com/news/articles/2021-05-09/cdc-limits-reviews-of-vaccinated-but-infected-spurring-concerns>

17. Tang TL, Hijano DR, Gaur AH, Geiger TL, Neufeld EJ, Hoffman JM, et al. Asymptomatic and symptomatic SARS-CoV-2 infections after BNT162b2 vaccination in a routinely screened workforce. JAMA. 2021;325(24):2500-2. Available from: <https://doi.org/10.1001/jama.2021.6564>
18. Keehner J, Horton LE, Pfeffer MA, Longhurst CA, Schooley RT, Currier JS, et al. SARS-CoV-2 infection after vaccination in health care workers in California. N Engl J Med. 2021;384(18):1774-5. <https://doi.org/10.1056/NEJMc2101927>
19. Haas R. Oregon reports small number of COVID cases in vaccinated people. OPB [Internet], 2021 Apr 8 [cited 2021 Jun 04]; Health. Available from: <https://www.opb.org/article/2021/04/08/oregon-reports-small-number-of-covid-cases-in-vaccinated-people/>
20. Fiore K. 'Breakthrough' COVID infection rates as expected. MedPage Today [Internet], 2021 Apr 21 [cited 2021 Jun 29]. Available from: <https://www.medpagetoday.com/special-reports/exclusives/92071>
21. Washington State Department of Health. News release: update on vaccine breakthrough cases in Washington State [Internet]. Kent, WA: Washington State Department of Health; 2021 [cited 2021 Jun 04]. Available from: <https://www.doh.wa.gov/Newsroom/Articles/ID/2740/Update-on-vaccine-breakthrough-cases-in-Washington-state>
22. Pera M. Marin records 21 'breakthrough' infections after COVID-19 vaccines. Mercury News [Internet], 2021 Apr 19 [cited 2021 Jun 04]; Health. Available from: <https://www.mercurynews.com/2021/04/19/cdc-reports-5800-covid-19-infections-74-deaths-in-fully-vaccinated-people-2/>
23. Sacramento County Public Health. Sacramento County public health epidemiology COVID-19 dashboards [Internet]. Sacramento, CA: Sacramento County Public Health; 2021 [cited 2021 May 28]. Available from: <https://sac-epidemiology.maps.arcgis.com/apps/MapSeries/index.html?appid=e11bc926165742ab99f834079f618dad>
24. Hacisuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, et al. Vaccine breakthrough infections with SARS-CoV-2 variants. N Engl J Med. 2021;384(23):2212. Available from: <https://doi.org/10.1056/NEJMoa2105000>
25. Blomquist R, Dickerson B. DHEC: S.C. sees over 100 COVID-19 'breakthrough cases' in fully vaccinated people. WMBF News [Internet]; 2021 Apr 6 [cited 2021 Jun 04]. Available from: <https://www.wmbfnews.com/2021/04/06/dhec-sc-sees-over-covid-breakthrough-cases-fully-vaccinated-people/>
26. Schimpff, S. Coronavirus breakthrough infections are not common [Internet]. San Francisco, CA: Medium; 2021 [cited 2021 Jun 04]. Available from: <https://medium.com/beingwell/coronavirus-breakthrough-infections-are-not-common-334bb0c84b43>

27. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infect Dis*. 2021;21(7):939-49. Available from: [https://doi.org/10.1016/S1473-3099\(21\)00224-3](https://doi.org/10.1016/S1473-3099(21)00224-3)
28. Hollinghurst J, North L, Perry M, Akbari A, Gravenor MB, Lyons RA, et al. COVID-19 infection risk amongst 14,104 vaccinated care home residents: a national observational longitudinal cohort study in Wales, United Kingdom, December 2020 to March 2021. *medRxiv* 21253940 [Preprint]. 2021 Jan 1 [cited 2021 Jun 08]. Available from: <https://www.medrxiv.org/content/10.1101/2021.03.19.21253940v1.full.pdf>
29. Azamgarhi T, Hodgkinson M, Shah A, Skinner J, Briggs T, Hauptmannova I, et al. Experience of COVID-19 vaccination of healthcare workers in a hospital setting. *ResearchSquare* [Preprint]. 2021 Mar 09 [cited 2021 Jun 08]. Available from: <https://assets.researchsquare.com/files/rs-257937/v1/28400b2e-76d1-49a4-9be8-b93bd1a45f64.pdf>
30. Jabal KA, Amram HB, Beiruti K, Brimat I, Saada AA, Bathish Y, et al. SARS-CoV-2 immunogenicity in individuals infected before and after COVID-19 vaccination: Israel, January-March 2021: implications for vaccination policy. *medRxiv* 21255273 [Preprint]. 2021 Apr 16 [cited 2021 Jul 14]. Available from: <https://doi.org/10.1101/2021.04.11.21255273>
31. Angel Y, Spitzer A, Henig O, Saiag E, Sprecher E, Padova H, et al. Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers. *JAMA*. 2021;325(24):2457-65. Available from: <https://doi.org/10.1001/jama.2021.7152>
32. Centers for Disease Control and Prevention. Postvaccination COVID-19 among healthcare workers, Israel [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2021 [cited 2021 Jun 17]. Available from: https://wwwnc.cdc.gov/eid/article/27/4/21-0016_article
33. Amit S, Regev-Yochay G, Afek A, Kreiss Y, Leshem E. Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients. *Lancet*. 2021;397(10277):875-7. Available from: [https://doi.org/10.1016/S0140-6736\(21\)00448-7](https://doi.org/10.1016/S0140-6736(21)00448-7)
34. Chodick G, Tene L, Patalon T, Gazit S, Ben-Tov A, Cohen D, et al. The effectiveness of the first dose of BNT162 b 2 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world evidence. *medRxiv* 21250612 [Preprint]. 2021 Jan 29 [cited 2021 Jul 14]. Available from: <https://doi.org/10.1101/2021.01.27.21250612>
35. TWC India Edit Team. COVID-19 vaccine breakthrough infections: what they are and why we must still get inoculated. *The Weather Channel* [Internet], 2021 Apr 27 [cited 2021 Jun 04]; Coronavirus. Available from: <https://weather.com/en-IN/india/coronavirus/news/2021-04-28-covid-vaccine-breakthrough-infections>
36. Chung H, He S, Nasreen S, Sundaram M, Buchan SA, Wilson SE, et al. Effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines against symptomatic SARS-CoV-2 infection and severe COVID-19 outcomes in Ontario, Canada. *medRxiv* 21257744 [Preprint]. 2021 May 28 [cited 2021 May 28]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.05.24.21257744>

37. Bouton TC, Lodi S, Turcinovic J, Weber SE, Quinn E, Korn C, et al. COVID-19 vaccine impact on rates of SARS-CoV-2 cases and post vaccination strain sequences among healthcare workers at an urban academic medical center: a prospective cohort study. medRxiv 21254655 [Preprint]. 2021 Apr 27 [cited 2021 Jul 14]. Available from: <https://doi.org/10.1101/2021.03.30.21254655>
38. Barrish C. 70 fully vaccinated Delawareans have contracted COVID-19, and one death. WHY [Internet], 2021 Apr 13 [cited 2021 Jun 04]; Coronavirus pandemic. Available from: <https://whyy.org/articles/70-fully-vaccinated-delawareans-have-contracted-covid-19-and-one-death/>
39. Hall VJ, Foulkes S, Saei A, Andrews N, Oguti B, Charlett A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. Lancet. 2021;397(10286):1725-35. Available from: [https://doi.org/10.1016/S0140-6736\(21\)00790-X](https://doi.org/10.1016/S0140-6736(21)00790-X)
40. Lumley SF, Rodger G, Constantinides B, Sanderson N, Chau KK, Street TL, et al. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. medRxiv 21253218 [Preprint]. 2021 Mar 12 [cited 2021 Jun 8]. Available from: <https://www.medrxiv.org/content/10.1101/2021.03.09.21253218v1.full.pdf>
41. Mason T, Whitston M, Hodgson J, Watkinson RE, Lau YS, Abdulrazeg O, et al. Effects of BNT162b2 mRNA vaccine on Covid-19 infection and hospitalisation among older people: matched case control study for England medRxiv 21255461 [Preprint]. 2021 Apr 22 [cited 2021 Jun 8]. Available from: <https://www.medrxiv.org/content/10.1101/2021.04.19.21255461v1.full.pdf>
42. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet. 2021;397(10287):1819-29. Available from: [https://doi.org/10.1016/S0140-6736\(21\)00947-8](https://doi.org/10.1016/S0140-6736(21)00947-8)
43. Jacobson KB, Pinsky BA, Rath MEM, Wang H, Miller JA, Skhiri M, et al. Post-vaccination SARS-CoV-2 infections and incidence of the B.1.427/B.1.429 variant among healthcare personnel at a northern California academic medical center. medRxiv 21255431 [Preprint]. 2021 Apr 24 [cited 2021 Jul 14]. Available from: <https://www.medrxiv.org/content/10.1101/2021.04.14.21255431v2>
44. Shrotri M, Krutikov M, Palmer T, Giddings R, Azmi B, Subbarao S, et al. Vaccine effectiveness of the first dose of ChAdox1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long term care facilities (VIVALDI Study). medRxiv 21254391 [Preprint]. 2021 Mar 26 [cited 2021 Jun 8]. Available from: <https://www.medrxiv.org/content/10.1101/2021.03.26.21254391v1>
45. Aran D. Estimating real-world COVID-19 vaccine effectiveness in Israel using aggregated counts. medRxiv 21251139 [Preprint]. 2021 Feb 23 [cited 2021 Jul 14]. Available from: <https://doi.org/10.1101/2021.02.05.21251139>
46. Thompson MG, Burgess JL, Naleway AL, Tyner HL, Yoon SK, Meece J, et al. Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2

infection among health care personnel, first responders, and other essential and frontline workers - eight U.S. locations, December 2020-March 2021. MMWR Morb Mortal Wkly Rep. 2021;70(13):495-500. Available from: <https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e3.htm>

47. BBC News. Hospital Covid admissions after jab 'very, very small'. BBC [Internet]. 2021 Apr 30 [cited 2021 Jun 9]. Available from: <https://www.bbc.com/news/health-56933756>

48. Kustin T, Harel N, Finkel U, Perchik S, Harari S, Tahor M, et al. Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2 mRNA vaccinated individuals. medRxiv 21254882 [Preprint]. 2021 Apr 16 [cited 2021 Jul 14]. Available from: <https://doi.org/10.1101/2021.04.06.21254882>

49. Maya C. Breakthrough infections emerge new concern. The Hindu [Internet], 2021 Apr 24 [cited 2021 Jun 04]; Kerala. Available from: <https://www.thehindu.com/news/national/kerala/breakthrough-infections-emerge-new-concern/article34403512.ece>

50. Bharat Biotech. COVAXIN® - India's first indigenous COVID-19 vaccine [Internet]. India: Bharat Biotech; 2021 [cited 2021 Jun 21]. Available from: <https://www.bharatbiotech.com/covaxin.html>

51. Government of Canada. AstraZeneca COVID-19 vaccine: what you should know [Internet]. Ottawa, ON: Government of Canada; 2021 [cited 2021 Jun 21]. Available from: <https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/astrazeneca.html>

Appendix A: Detailed Study Findings

Canada

- PHAC reported 2,274 breakthrough infections (≥ 14 days after one dose) as of April 26, 2021. This represents 1.3% of all COVID-19 cases reported to PHAC since vaccines began being administered.⁷ Of these 2,274 cases reported, 203 (9%) were admitted to hospital and 53 (2%) died.⁷
- The BC Centre for Disease Control (BCCDC) reported that as of April 7, 2021, there were 618 breakthrough infections (> 14 days after at least a first dose), which is the equivalent to 0.14% of vaccinated individuals.⁷ Of those 618 cases, 42 were ≥ 7 days past their second dose. Of those 618 vaccine breakthrough cases, 18 (3%) died.⁷ Two of the 18 deaths were in people who had received both doses. Most of the partly or fully vaccinated people who died of COVID-19 were over 80 years of age.
- As of April 26, 2021, Manitoba reported 195 cases after vaccination (> 14 days after first dose), which represents about 0.06% of first-dose recipients. Seven of them died (3.6%), all of them seniors.⁷
- PHO reported that of the almost 9.4 million vaccinated individuals in Ontario from December 14, 2020 to June 12, 2021, only 0.15% (14,293) became infected ≥ 14 days after the first dose or 0 to < 7 after the second dose, and only 0.02% (1,648) became infected ≥ 7 days after their second dose.³ The majority (53.1%) of post-vaccination cases occurred ≤ 14 days after first dose, and therefore were not yet protected from vaccination when they acquired their infection. Pfizer-BioNTech, Moderna and AstraZeneca vaccines were administered during this time frame. Partially vaccinated (≥ 14 days after first dose or 0 to < 7 after the second dose) and breakthrough (≥ 7 days after the second dose) cases comprise a very small proportion of the total number of COVID-19 cases reported from December 14, 2020 to June 12, 2021. Of the 396,076 COVID-19 cases reported in this time period, 3.6% were partially vaccinated and 0.4% were breakthrough cases. The proportion of partially vaccinated and breakthrough cases increased with age, and was highest among cases ≥ 80 years of age. The proportion of age-specific hospital admissions, ICU admissions, and deaths for both partially vaccinated and breakthrough cases was lower than the proportion of hospital, ICU admissions and deaths among unvaccinated COVID-19 cases. The most frequently reported VOC among partially vaccinated and breakthrough cases was Alpha (8,561 cases, 53.7%), which was the dominant circulating SARS-CoV-2 virus from late March 2021 to mid-June 2021. Sixty-eight cases of the Beta variant and 217 Gamma variants were detected.

US

- As of April 26, 2021, more than 95 million Americans were fully vaccinated against SARS-CoV-2 and the CDC had reported 9,245 breakthrough infections (≥ 14 days after final dose) (representing a rate of 0.0001%) based on data from 46 states and territories.⁴ Of the 9,245 vaccine breakthrough cases, 27% were asymptomatic, 9% were hospitalized, and 1% had died.⁴

TENNESSEE

- A health surveillance study of HCWs at a US hospital from December 17, 2020 to March 20, 2021, reported that out of 3,052 workers who received one or two doses of the Pfizer-BioNTech COVID-19 vaccine, the IRR for a positive COVID-19 test decreased with the time since dose one and continued to decrease from dose one to ≥ 7 days after the second dose.¹⁷ Of the 51 vaccinated SARS-CoV-2-positive workers, 29 (57%) were asymptomatic and 22 (43%) were either symptomatic or were tested because of an exposure, compared to 185 unvaccinated SARS-CoV-2-positive workers, of whom 79 (43%) were asymptomatic and 106 (57%) were symptomatic or tested because of a known exposure.

CHICAGO

- At the start of 2021, the Chicago Department of Public Health (CDPH) routine screening of SARS-CoV-2 infections in skilled nursing facility (SNF) residents and staff reported 22 (3.5%) of 627 SARS-CoV-2 infections were in individuals who had completed two-dose vaccination at least 14 days earlier.⁸ Fourteen of the 22 cases (64%) were asymptomatic; two residents were hospitalized because of COVID-19, and one died. There were facility-associated secondary transmissions. They also reported that the median interval from second vaccine dose to a positive SARS-CoV-2 test was 29 days (IQR 23–42 days).⁸ Moderna COVID-19 vaccination was exclusively administered at Chicago-based SNFs, but six residents and two staff members received Pfizer-BioNTech COVID-19.

KENTUCKY

- The Kentucky Department for Public Health investigated an outbreak detected on March 1, 2021 among residents and HCWs of a skilled nursing facility.⁹ Vaccinated staff and residents were given the Pfizer-BioNTech vaccine. They detected 22 (17%) breakthrough infections among 127 fully vaccinated staff and residents (≥ 14 days since completing second doses of the Pfizer-BioNTech vaccine), and 22 (35%) infections among 62 unvaccinated individuals.⁹ Specifically, of 71 fully vaccinated residents (≥ 14 days after second dose of Pfizer-BioNTech), 18 contracted SARS-CoV-2 (25.4%).⁹ Of 56 fully vaccinated HCWs, four contracted SARS-CoV-2 (7.1%). In comparison, six of eight (75%) unvaccinated residents contracted SARS-CoV-2, as did 16 of 54 (29.6%) unvaccinated HCWs. In terms of severity, 6.3% of breakthrough cases were symptomatic (versus 32.3% of unvaccinated cases); 1.6% of breakthrough cases were hospitalized (versus 6.5% of unvaccinated cases); 0.8% of breakthrough cases died (versus 3.2% of unvaccinated cases died). WGS was performed for 28 specimens which revealed a cluster of the R.1 lineage.

OREGON

- As of April 2, 2021, The Oregon Health Authority reported 168 breakthrough cases (≥ 14 days after final dose).^{19,20} This represents 0.024% of the approximately 700,000 individuals in Oregon who are fully vaccinated. Many of these individual experienced asymptomatic infection; however, three of the 168 breakthrough cases (0.02%) died. Most of the cases occurred in individuals who were older than 65 years of age and who had underlying health conditions. None of the cases were associated with a COVID-19 variant.

SOUTH CAROLINA

- According to the South Carolina Department of Health and Environmental Control, as of April 5, 2021, 141 breakthrough cases (> 14 days after completing vaccination series), had been

identified in South Carolina (representing 0.007% of the 2.1 million vaccine doses that have been administered in South Carolina, or less than 0.5% of the number of people across the state who had completed their vaccine series).²⁵

- Another report noted that as of April 12, 2021, the South Carolina Health Department reported 155 breakthrough infections out of about 950,000 fully vaccinated residents (i.e., rate of about 0.02%).²⁶

MINNESOTA

- As of March 22, 2021, Minnesota had reported 89 breakthrough infections (> 14 days after final dose) among 800,000 people, with no deaths.²⁰

WASHINGTON STATE

- In Washington State as of March 30, 2021, after vaccinating 1.2 million individuals, there were 102 infections after vaccination (risk of 0.01%). Most of these case were mild; however, eight individuals were hospitalized and two died.²⁶
- As of April 3, 2021, Washington State reported a total of 217 COVID-19 cases after vaccination (> 14 days after final dose), or 0.01% of the 1.7 million fully vaccinated population. They reported five deaths of individuals who experienced vaccine breakthrough.²¹ Those who died were between the ages of 67 to 94 years old and all had multiple underlying conditions. Four were residents of long-term care facilities. Information on breakthrough cases is still being analyzed; however, based on the information available, 12% of breakthrough cases required hospitalization.²¹

NEW YORK

- A brief report examined a cohort of 417 individuals at a New York university who were fully vaccinated with either Pfizer–BioNTech or Moderna vaccines.²⁴ There were two vaccine breakthrough infections (> 14 days after final dose). Viral sequencing indicated the potential role of variants in these breakthrough infections; the E484K mutation was identified for one individual and T95I, del142–144, and D614G mutations were identified for both cases.²⁴

CALIFORNIA

- A study of HCWs in California found that 379 individuals tested positive ≥ 1 day after vaccination (note: 36,659 HCWs received the first dose of vaccine, and 28,184 received the second dose).¹⁸ The majority (77%) of these individuals tested positive within the first two weeks after their first dose of the vaccine. Among those receiving the first dose: 145 individuals tested positive during days one to seven, 125 tested positive during days eight to 14, 57 tested positive during days 15 to 21, and 15 tested positive at day 22 or later. Among those receiving two doses: 22 tested positive during days one to seven, eight tested positive during days eight to 14, and seven tested positive at day 15 or later.¹⁸
- A study of HCWs at a northern California academic medical centre reported that of 22,729 HCWs who received at least one dose of Pfizer-BioNTech or Moderna, 189 infections after vaccination were identified.⁴³ Of these cases, 114 (60.3%) occurred ≤ 14 days after first dose, 49 (25.9%) occurred > 14 days after first vaccine dose to ≤ 14 days after the second dose, and 26 (13.8%) > 14 days after the second dose.⁴³ Additionally, 42 cases tested positive for the L452R mutation

(suggesting the B.1.427/B.1.429 lineage), three had the N501Y mutation, and none were found to have the E484K mutation.⁴³

- A media report from Marin County, California reported that of 100,532 residents that were fully vaccinated against COVID-19, 21 tested positive ≥ 14 days after their final dose of vaccine (Pfizer-BioNTech, Moderna or Janssen/Johnson & Johnson), representing 0.02% of those vaccinated.²² The majority of cases were mild and none of them were hospitalized or died. Some positive samples were sent to laboratories for genomic sequencing; no variants of concern were identified.
- According to the Sacramento County Public Health Epidemiology COVID-19 Dashboard, as of May 28, 2021, 559,268 individuals had been fully vaccinated and of those, 271 individuals (or 0.048%) had a positive PCR result after full vaccination (not defined). Of those 271 cases, 75 of them were symptomatic.²³
- From January 1 to April 21, 2021, there were 1379 cases of COVID-19 among individuals who were fully vaccinated (representing 0.1% of the approximately 1.4 million COVID-19 cases reported in California during that period), according to the California Department of Public Health.¹⁰ In California, Pfizer-BioNTech, Moderna vaccine or Janssen/Johnson & Johnson vaccines were administered.

UK

- The UK's Office for National Statistics (ONS) COVID-19 Infection Survey (CIS) is a large household survey with longitudinal follow-up that includes regular screening for SARS-CoV-2.¹¹ From December 2020 to April 2021, CIS reported that 417 (3%) of new positives were ≥ 21 days after a first dose of vaccine, and 72 (1%) of the positives were after a second dose (no time specified). Of the cases vaccinated 8 to 20 days before their positive test, 56% (234/421) were asymptomatic; of the cases vaccinated with one dose ≥ 21 days before their positive, 62% (260/417) were asymptomatic; and of the cases who were positive after their second vaccine dose (days not reported), 83% (60/72) were asymptomatic. The UK has been using the AstraZeneca and Pfizer-BioNTech COVID-19 vaccines. The CIS reported no difference in the odds of new infection between the two vaccine types. Over the study period, the Alpha variant became dominant in the UK.
- A cross-sectional audit of COVID-19 positive admissions (excluding intensive care) to a UK hospital over one weekend found 27 of the 174 (16%) COVID-19 inpatients had been vaccinated.¹² The mean age of the inpatients was 82.3 years (IQR 11.75), with a mean duration between vaccination and positive COVID-19 swab of 18.19 days (IQR 13.25). Of the 27 vaccinated patients, 11 (41%) had their positive COVID-19 test within 14 days of vaccination, suggesting possible infection close to the time of vaccination.
- A UK prospective observational study from December 2020 to March 2021 reported that 3,106/103,622 individuals vaccinated with one dose tested positive for SARS-CoV-2, compared to 50,340/464,356 unvaccinated controls.²⁷ The Alpha variant became dominant over this time. Participants were vaccinated with either the AstraZeneca or Pfizer-BioNTech COVID-19 vaccines.
- An interim analysis of the SIREN prospective cohort study of workers in publicly-funded hospitals in the UK reported that there were 71 new infections ≥ 21 days after first dose of Pfizer-

BioNTech (incidence density of eight per 10000 person-days of follow-up) and nine new infections seven days after the second dose (incidence density of four per 10000 person-days of follow-up).³⁹ Within 14 days before and after the date of a positive SARS-CoV-2 test, 10 (13%) of the vaccinated cases were asymptomatic, 32 (40%) had typical COVID-19 symptoms, 13 (16%) had other symptoms, and 25 (31%) did not complete the questionnaire. The Alpha variant was dominant at the time of the study.

WALES

- An observational data-linkage study of older care home residents in Wales with SARS-CoV-2 testing from December 2020 to March 2021 reported that 148/14,104 (1.05%) individuals had a positive test following vaccination.²⁸ 40% of individuals had a positive test ≤ 7 days, 60% ≤ 14 days, 85% ≤ 21 days, 90% ≤ 28 days, and over 95% ≤ 35 days. Ninety percent of the residents had received AstraZeneca and 10% had received Pfizer-BioNTech. In the 7-day post-vaccination analysis, there was evidence to suggest an increased risk of infection after vaccination for those receiving the Pfizer-BioNTech vaccine compared to the Oxford-AstraZeneca vaccine, but no statistically significant difference in the 21-day landmark analysis.

ENGLAND

- A single-centre observational study of the Pfizer-BioNTech vaccine among HCWs in England who were routinely screened in January 2021 reported that 4/1358 (0.3%) vaccinated HCWs had a positive SARS-CoV-2 test ≥ 14 days after first dose.²⁹ The Alpha variant was dominant at that time.
- A study in England from November 2020 to February 2021 matched older (aged 80 to 83 years) Pfizer-BioNTech vaccine recipients with younger (aged 76 to 79 years) persons not yet eligible to receive the vaccine.⁴¹ The authors reported that of the SARS-CoV-2 cases that attended the hospital, 5.3 per 100,000 of the vaccinated cohort were hospitalized for COVID-19, compared to 9.4 per 100,000 (hospitalized) amongst unvaccinated controls. They also report that documented infections peaked 14 days after the first dose, and hospitalizations peaked between days 23 and 26. The Alpha variant was dominant at the time of the study. There was an outbreak occurring at the time, which likely influenced the timing of the infections in the vaccinated and unvaccinated groups.
- A longitudinal cohort study of HCWs in Oxfordshire, UK who were screened routinely from March 2020 to February 2021 reported that 38 unvaccinated seronegative HCWs attended hospital within -2 to +28 days of a SARS-CoV-2 positive result (14.2/million person-days); of these, 27 had a COVID-19 primary diagnostic code and 16 were admitted for COVID-19, whereas two previously seronegative vaccinated HCWs required hospital review (6.9 per million person-days), neither were admitted.⁴⁰ No symptomatic infections were observed following two vaccine doses. None of the HCWs that received two doses of a vaccine (including the 32 that become infected over the study period) or were unvaccinated and previously seropositive required hospital review or admission. Over the study period, the Alpha variant became the dominant strain, before decreasing. HCWs were offered the AstraZeneca or Pfizer-BioNTech COVID-19 vaccines.

Italy

- A mandatory health surveillance study of HCWs in Italy found that during the study period, January 25 to April 13, 2021, there were 92 SARS-CoV-2 infections among HCWs, and 40 of these cases (43%) were among fully vaccinated HCWs (≥ 7 days after second dose).¹³ HCWs were vaccinated with the Pfizer-BioNTech vaccine. Of the fully vaccinated workers, 15 (37%) were symptomatic and 25 (63%) were asymptomatic, compared to workers who were not fully vaccinated, of whom 32 (62%) were symptomatic and 20 (38%) were asymptomatic (OR 0.39, 95% CI 0.17 – 0.91, $p < 0.05$). During the study period, the dominant SARS-CoV-2 variant was Alpha.

Israel

- A CDC report from April 2021 reported that 22 (0.54%) of the 4,081 vaccinated HCWs in Israel tested positive for COVID-19 one to ten days after the first dose of the Pfizer-BioNTech vaccine (median 3.5 days).³²
- In a study of HCWs in a medical centre in Israel, 7,214 staff had received their first dose of the Pfizer-BioNTech vaccine and 6,818 had received their second dose by January, 2021.³³ Between December 19, 2020 and January 24, 2021, 170 HCWs were infected with COVID-19; 89 (52%) were unvaccinated, 78 (46%) tested positive after the first dose, and three (2%) tested positive after the second dose.³³ The SARS-CoV-2 infection rate was 7.4 per 10,000 person days in unvaccinated workers, compared to 5.5 per 10,000 person days one to 14 days after the first dose of the vaccine, and 3.0 per 10,000 person days between 15 to 28 days after the first dose of the vaccine.³³
- A retrospective cohort study examined the effectiveness of the Pfizer-BioNTech vaccine in Israel. The study examined individuals 16 years of age and older who were vaccinated with Pfizer-BioNTech vaccine between December 19, 2020 and January 15, 2021.³⁴ They found that the cumulative incidence of SARS-CoV-2 infection was 0.57% ($n=2,484$) during days one to 12 following first dose of the vaccine and 0.27% ($n=614$) in days 13 to 24.³⁴
- In a study at a medical centre in Israel, of 725 individuals who received at ≥ 1 dose of the Pfizer-BioNTech vaccine, 32 tested positive for COVID-19 after the first dose, and three tested positive after the second dose.³⁰
- Between December 20, 2020 and February 9th, 2021 in Israel, 3,623,573 individuals received a first dose of the Pfizer-BioNTech vaccine, and 2,263,178 had received their second dose.⁴⁵ Of those that were vaccinated, 43,889 individuals tested positive for SARS-CoV2, 2,778 were hospitalized due to COVID-19 and 1,911 were hospitalized with severe or critical conditions or died. A sub-analysis of those over 60 years of age, found that a greater number of cases were identified between one and 13 days after receiving the first dose ($n= 7,438$) compared to 14 to 20 days after receiving the first dose ($n=5,262$), zero to six days after receiving the second dose ($n=1,199$), 7 to 13 days after receiving the second dose ($n=1, 202$) or more than 14 days after receiving the second dose ($n= 295$).⁴⁵
- A retrospective cohort study was conducted between December 20, 2020 and February 25, 2021 in Israel with 6,710 HCWs who underwent periodic testing for symptomatic and asymptomatic SARS-CoV-2 infection as per workplace screening protocols.³¹ 5,953 (88.7%) received at ≥ 1 dose of the Pfizer-BioNTech vaccine, 5,517 (82.2%) received two doses, and 757 (11.3%) were not

vaccinated. Symptomatic SARS-CoV-2 infection occurred in eight fully vaccinated HCWs (> 7 days after second dose) versus 38 unvaccinated HCWs (4.7 vs 149.8 per 100,000 person-days). Asymptomatic SARS-CoV-2 infection occurred in 19 fully vaccinated versus 17 unvaccinated HCWs (11.3 vs 67.0 per 100,000 person-days).

- Using national surveillance system data in Israel between January 24 and April 3, 2021, the SARS-CoV-2 incidence rate was 91.5 per 100,000 person-days in unvaccinated compared to 3.1 per 100,000 person-days in fully vaccinated individuals (defined as those for whom 7 days had passed since receiving the second dose of vaccine).⁴² For asymptomatic SARS-CoV-2 infection, the incidence rate was 40.9 versus 1.8 per 100,000 person-days for unvaccinated and fully vaccinated individuals, respectively. For symptomatic infection, the incidence rate was 4.6 versus 0.3 per 100,000 person-days, for unvaccinated and fully vaccinated individuals, respectively. For COVID-19-related hospitalization, the incidence rates was 2.7 versus 0.2 per 100,000 person-days, for unvaccinated and fully vaccinated individuals, respectively; and, 0.6 versus 0.1 per 100,000 person-days against COVID-19-related death for unvaccinated and fully vaccinated individuals, respectively.

France

- A case series in a geriatric rehabilitation ward during an outbreak reported that out of 16 SARS-CoV-2 positive patients, five had been fully vaccinated (not defined), and only one of those five was symptomatic and they were immunocompromised. Of those five, the time from their second dose to a positive SARS-CoV-2 test ranged from eight to 29 days. In contrast, seven of the 11 unvaccinated cases were symptomatic.¹⁴ The vaccinated participants were given the Pfizer-BioNTech COVID-19 vaccine. During the study period, there was a cluster of Alpha cases at the facility.

India

- According to an April 14, 2021 media report, the Indian Council of Medical Research (ICMR) reported two to four infections after COVID-19 vaccination per 10,000 people.⁴⁹ The ICMR reported that about 11 million individuals had received the Covaxin vaccine and of these, 4,208 (0.04%) tested positive for SARS-CoV-2 after the first dose, while only 695 (0.006%) tested positive after the second dose.³⁵ Of the 116 million individuals who received the COVISHIELD vaccine, 17,145 (0.014%) tested positive after receiving the first dose, while 5,014 (0.004%) tested positive after getting the second dose.³⁵
 - Covaxin is a COVID-19 vaccine developed by Bharat Biotech in collaboration with the ICMR - National Institute of Virology (NIV).⁵⁰ It is an inactivated vaccine and uses Whole-Virion Inactivated Vero Cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to cause pathological effects. Additionally, because they contain dead virus, it is incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection.
 - COVISHIELD (manufactured by Serum Institute of India) is the same vaccine as AstraZeneca COVID-19 Vaccine (manufactured by AstraZeneca) and both are ChAdOx1-S recombinant vaccines developed by AstraZeneca and Oxford University.⁵¹

Citation

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