Public Health Ontario | Santé publique Ontario

SYNTHESIS

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COVID-19 Real-World Vaccine Effectiveness – What We Know So Far

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 are intended to provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

The development of these documents includes a systematic search of the published literature as well as scientific grey literature (e.g., ProMED, CIDRAP, Johns Hopkins Situation Reports) and media reports, where appropriate. Relevant results are reviewed and data extracted for synthesis. All "What We Know So Far" documents are reviewed by PHO subject-matter experts before posting.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in these documents is only current as of the date of posting.

Key Findings

- Most of the real-world vaccine effectiveness (VE) data is from Israel, the United Kingdom (UK), the United States (US) and Canada for the mRNA vaccines (Pfizer-BioNTech COVID-19 vaccine [BNT162b2] and Moderna COVID-19 vaccine [mRNA-1273]). There is limited VE data for the viral vector vaccines currently approved for use in Canada. While there is some VE data from the UK for the Oxford/AstraZeneca (AZD1222/ChAdOx1-S) vaccine, no VE data was identified for the Johnson & Johnson (Janssen Vaccine) JNJ-78436735/Ad26.COV2.S vaccine.

- In general, VE is about 60-80% for preventing COVID-19 infection 3-4 weeks after receiving a single dose of Pfizer, Moderna or AstraZeneca vaccine, although this varies by population (i.e. general population, older adults, long-term care residents and health care workers). VE increases to greater than 85% after a second dose.

- VE for preventing severe disease and COVID-19-related hospitalization ranges from 70 to 90% for the Pfizer, Moderna and AstraZeneca vaccines. VE estimates for mortality, largely from those receiving the Pfizer vaccines, is generally greater than 70% and as high as 96% in terms of reducing deaths attributable to COVID-19.

- Emerging data evaluating the impact of COVID-19 vaccines at the population level demonstrates that vaccination is associated with reduced spread in populations, regions, or facilities with higher rates of vaccination or those that were vaccinated earlier than others.

Background

Vaccine efficacy and vaccine effectiveness measure the proportionate reduction in cases among vaccinated persons compared to those not vaccinated. Vaccine efficacy refers to the reduction in disease incidence when a study is carried out under ideal conditions (e.g., clinical trial), whereas vaccine effectiveness refers to a vaccine's ability to prevent illness in people vaccinated in the real world setting. Both vaccine efficacy and effectiveness are determined by calculating the risk of disease among vaccinated and unvaccinated persons, and determining the percentage reduction in risk of disease among vaccinated persons relative to unvaccinated persons. For example, a VE of 80% translates to an 80% reduction in disease occurrence among the vaccinated group, or a 80% reduction in the number of cases you would have expected if the group had not been vaccinated.[1]

This WWKSF document is a synthesis of available real-world VE data for vaccines approved by Health Canada as of March 12, 2021. Health Canada has authorized four COVID-19 vaccines for use in Canada: Pfizer-BioNTech COVID-19 vaccine (BNT162b2), Moderna COVID-19 vaccine (mRNA-1273) and more recently Oxford University/AstraZeneca (AZD1222/ChAdOx1-S) and Janssen/Johnson & Johnson COVID-19 vaccine (JNJ-78436735/Ad26.COV2.S). In Canada, the brand names of the Oxford University/AstraZeneca (AZD1222/ChAdOx1-S) vaccine are AstraZeneca COVID-19 vaccine and COVISHIELD as there are 2 different manufacturers.[2] See COVID-19- What We Know So Far About…Herd Immunity for information on vaccine efficacy for Pfizer-BioNTech and Moderna vaccines.

Methods

To identify relevant evidence on this topic, systematic searches in MEDLINE and Embase were conducted on March 9, 2021 by PHO Library Services. A grey literature search including pre-prints was also conducted on March 11, 2021 by PHO Library Services. It is recognized that there may be additional information not captured in this document. Relevant results were reviewed and data extracted for synthesis. All data reported for VE refers to vaccine effectiveness, unless otherwise stated.

Results

The majority of VE studies are from Israel (n= 7), the UK (n= 5) and the US (n= 5), with additional data from Canada (n=3) and Denmark (n=1). Most of the currently available VE data is for the Pfizer-BioNTech COVID-19 vaccine (herein referred to as Pfizer) (Israel, UK, US, Canada, Denmark) and Moderna COVID-19 vaccine (herein referred to as Moderna) (US, Canada). There was limited VE data for the Oxford/AstraZeneca COVID-19 vaccine (herein referred to as AstraZeneca). No VE data for the Janssen/Johnson & Johnson vaccine was identified in the studies reviewed.

SARS-CoV-2 Infection, Symptomatic Disease and Asymptomatic Infection

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, confirmed by positive SARS-CoV-2 polymerase chain reaction (PCR) test may include asymptomatic and/or symptomatic disease depending on the jurisdictional testing strategy and population under consideration. For example, in some jurisdictions, the general population may only be eligible for testing if individuals are symptomatic or have exposure to a confirmed case, whereas in other jurisdictions, workers and/or patients/residents in healthcare settings may take part in asymptomatic testing often as part of screening efforts. Therefore, in this document, SARS-CoV-2 infection refers to both asymptomatic and symptomatic

COVID-19 disease unless otherwise specified. The administration schedule for Pfizer, Moderna and AstraZeneca vaccines are intended to be 2 doses, 3-12 weeks apart.[3] As it takes time to develop immunity, vaccines are not expected to offer protection in the first 2 weeks following administration of the first vaccine dose.[4]

GENERAL POPULATION

Between 2-3 weeks after a single dose of Pfizer vaccine, Israeli studies have reported a VE of approximately 50% for SARS-CoV-2 infection overall,[4,5] 57% for symptomatic disease and 29% for asymptomatic infection.[4] Although estimates vary, VE appears to increase 3 weeks after the first dose of Pfizer vaccine. Dagan et al. reported a VE of 60% for SARS-CoV-2 infection, 66% for symptomatic disease and 52% for asymptomatic infection between days 20-27, whereas Hunter et al. estimated a VE of 90% for SARS-CoV-2 infection 21 days after a first dose.[4,6]

One to 2 weeks after the second dose of either Pfizer or Moderna vaccine, Israeli and American studies have reported VE for symptomatic and asymptomatic SARS-CoV-2 infection to be 89%-94%.[4,7]

OLDER ADULTS

In an Israeli study of older adults over 60 years of age, VE for SARS-CoV-2 infection was 44% 13-24 days after one dose of the Pfizer vaccine.[5] In another study of individuals over 70 years of age, VE was estimated to be 50% for SARS-CoV-2 infection and 64% for symptomatic disease 21-27 days after the first dose.[4] A study of this same age group in the UK found a VE of 60-75% for prevention of symptomatic disease after 28 days of receiving a first dose of either Pfizer or AstraZeneca vaccine.[8]

Israeli and UK studies reported high VE following the second dose of vaccine in older adults. Bernal Lopez et al. reported a VE of 85-90% for prevention of symptomatic disease in those over 70 years of age 14 days after the second dose of either the Pfizer or AstraZeneca vaccine.[8] Israeli studies of adults over 60 years of age demonstrated a VE of 95-96% for prevention of SARS-CoV-2 infection and 96-98% for prevention of symptomatic disease 1-2 weeks after a second dose of the Pfizer vaccine.[4,9] The vast majority of data pertaining to older adults refers to individuals living in the community; however, some studies included those residing in long-term care (LTC) homes or did not specify whether residents of LTC were included.

LONG-TERM CARE RESIDENTS

Canadian data from Ontario, British Columbia and Quebec demonstrate a VE of 80% for preventing SARS-CoV-2 infections in LTC residents 2-3 weeks following a single dose of either Pfizer or Moderna vaccine.[10–12] In Ontario, VE was 89% for LTC residents 8 weeks after the start of vaccination at which point 92% had received a first dose of Pfizer or Moderna vaccine, and 67% had received a second dose.[12] This is in contrast to data from Denmark which reported no significant VE between 14 days after the first dose of the Pfizer vaccine to before the second dose, given 24 days after first dose (interquartile range [IQR]: 20-52), and a VE of 52% less than 7 days after the first dose which increased to 64% more than 7 days after the second dose of vaccine. However, measuring VE less than 14 days after a vaccine dose likely underestimates its effectiveness, which could account for lower estimates in the Denmark data.

HEALTHCARE WORKERS

The VE for healthcare workers (HCW) in Israel, England, US and Canada 2-3 weeks after receiving a single dose of Pfizer or Moderna vaccine is 72-80% for COVID-19 infection and symptomatic disease.[10,11,13–17] This is in contrast to results from Denmark where a VE of 17% was observed >14 days

after the first dose (before the second dose) of Pfizer vaccine; however, due to a relatively short timeframe between doses (median 25 days [IQR: 20-51]), it is difficult to determine the impact of a single dose from this study. The VE less than 7 days after the second dose was 46%, this increased to 90% after 7 days following the second dose.[18] In Ontario, the VE for HCW in LTC facilities 8 weeks after the start of vaccination was 79%, at which point 55% had received at least 1 dose of Pfizer or Moderna vaccine and 45% had received 2 doses.[12]

(See Table 1 for study details.)

COVID-19 Transmission

There is some VE data at the population-level, estimating the impact of the Pfizer and Moderna vaccines on COVID-19 transmission in the community[19–21] and LTC[13] settings in the US and Israel.[16] An analysis of early statewide vaccination efforts in the US found that vaccination was effective in reducing daily COVID-19 case growth rates by 0.124, 0.347, 0.345, 0.464, 0.490, and 0.756 percentage point declines, respectively, in the 1-5, 6-10, 11-15, 16-20, 21-25, and 26 or more days after the start of vaccination (i.e. administration date of first COVID-19 vaccine dose).[19] A separate analysis of vaccination rates and COVID-19 incidence found that the cumulative county-level vaccination rate was significantly associated with a corresponding decline in COVID-19 incidence; that is, higher vaccination rates translated to a decreased county-level COVID-19 incidence.[20] In Israel, where COVID-19 cases and hospitalizations started to decline after implementation of a national vaccine campaign that prioritized vaccination of older individuals, an analysis between early-vaccinated cities and late-vaccinated cities found a larger and earlier decrease in the number of COVID-19 cases and hospitalizations of older individuals (> 60 years) in earlier compared to later-vaccinated cities. While a concurrent lockdown could have influenced results, the study authors note that these same downward trends in older individuals were not observed during previous lockdowns in which clinical measures had similar dynamics across age groups.[21]

A US study of over 2000 nursing homes in one county found that spread of SARS-CoV-2 infection decreased at a faster rate in homes that held a vaccine clinic administering the first dose of Pfizer vaccine compared with homes that did not (although vaccination rates were not reported). While a decreasing trend in new infections was observed prior to the start of the vaccine clinics, three weeks after the vaccine clinic, there was a 48% decline in new resident cases in vaccinated homes compared with a 21% decline in non-vaccinated homes, and a 33% decline in new staff cases in vaccinated homes compared with an 18% decline in non-vaccinated homes. [13]

Given the challenge in preventing and detecting asymptomatic spread of COVID-19, the impact of vaccines on asymptomatic disease transmission is particularly important. Data from individuals in Israel receiving the Pfizer vaccine indicate that VE for preventing asymptomatic infection 14 to 20 days after the first dose, 21 to 27 days after the first dose, and more than 7 days after the second dose is 29%, 52% and 90%, respectively.[4] This suggests vaccines will play a key role in prevention of COVID-19 transmission, as noted in the above population-based studies.

Severe Disease, COVID-19-related Hospitalization and Death

GENERAL POPULATION

In studies of the general population, VE for prevention of severe disease, hospitalization and death is roughly between 80-90% 3-4 weeks after the first dose of vaccine. A Scottish study of their national vaccine program reported a VE of 85% (Pfizer vaccine) and 94% (AstraZeneca vaccine) for preventing COVID-19-related hospitalization 28-34 days after a single dose of vaccine in the general population.[22]

However, as this study had several important methodological limitations, this data was not used to inform recommendations by the National Advisory Committee on Immunization (NACI) pertaining to the AstraZeneca vaccine for individuals 65 years of age and older in Canada. For example, an unexpectedly high VE for hospitalization 7-13 days after vaccination was biologically implausible since it takes at least 2 weeks for immunity to develop. There was potentially incomplete adjustment of confounders in the statistical analyses, and inclusion of only a small number of individuals vaccinated with AstraZeneca in the period 28 days and more from vaccination.[3] In Israel, VE was 62% for prevention of severe disease and 75% for prevention of hospitalization, 14-20 days after first dose of Pfizer vaccine; this increased to 80% and 78% respectively 21-27 days after the first dose.[4] In the same study, VE for prevention of death was 84% 3 weeks after the first dose.[4]

One to 2 weeks after a second dose of Pfizer vaccine, Israeli studies indicate a VE of 92- 94% and 87-93% for preventing severe disease and hospitalization, respectively.[4,9]

OLDER ADULTS

Most studies of older adults report a VE of 70-80% for hospitalization 2-4 weeks after the first dose of vaccine. A test negative case-control study of individuals over 80 years of age hospitalized for COVID-19 or other acute respiratory disease in the UK found VE to be 71% for Pfizer and 80.4% for AstraZeneca at least 14 days after the first dose.[23] A test negative case-control study of those over 70 years of age in the UK found VE to be 80% for prevention of hospitalization and 85% for prevention of death 28 days after receiving a first dose of either Pfizer or AstraZeneca vaccine.[8]

For adults over 60 years of age in Israel, VE for prevention of severe disease and hospitalization less than 14 days after the second dose was about 79-83%; this increased to 97-98% after 14 or more days following vaccination.[9] In addition, approximately 2 months after initiation of a national immunization campaign in Israel where 85% of individuals older than 60 years of age were vaccinated with 2 doses, there was a 68% decrease in hospitalization and 67% decrease in severe hospitalization compared to the peak period when there was no vaccination campaign.[21]

LTC RESIDENTS

Data from one LTC home in Quebec demonstrated a VE of 40% for the prevention of serious SARS-CoV-2 infection (not defined) and 50% for prevention of death 2 weeks following the first dose of Pfizer vaccine.[11] In Ontario, 8 weeks after starting vaccination of LTC residents with Pfizer or Moderna vaccine, the estimated VE for preventing mortality was 96%.[12]

(See Table 2 for study details)

Vaccine Effectiveness and Variants of Concern (VOC)

Several studies discussed VE with respect to VOC 202012/01 (also known as the UK variant, lineage B.1.1.7). One Israeli study concluded that the reported VE reflects an average effectiveness over multiple VOC, including B.1.1.7, which became increasingly prevalent (up to 80%) over the study period.[4] Two studies from the UK concluded that VE was demonstrated against B.1.1.7, as it was the dominant lineage circulating at the time of these studies.[8,14] There was no mention of VE against other VOC in the studies reviewed.

Appendix

Table 1: Vaccine Effectiveness (VE) for Prevention SARS-CoV-2 Infection, Symptomatic Disease and Asymptomatic infection

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
General Population (<60 y) (N=2,992,441)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	0-13 days after 2nd dose	77-81%
General Population (<60 y) (N=2,992,441)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	≥14 days after 2nd dose	94%
General Population (>16 y, no upper age limit, N=503,875) Mean age = 59.7 y (SD = 14.7)	Chodick (Israel) 12/19/2020-01/17/2021	Pfizer	SARS-CoV-2 infection (PCR confirmed)	13-24 days after 1st dose	51%
General Population (>16 y, no upper age limit, N=596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	Estimated vaccine effectiveness for SARS-CoV-2 infection (PCR confirmed), symptomatic disease and asymptomatic illness	14-20 days after 1st dose	46% (95% CI: 40-51) Symptomatic: 57% (95% CI: 50-63) Asymptomatic: 29% (95% CI: 17-39)
General Population (>16 y, no upper age limit, N=596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	Estimated vaccine effectiveness for SARS-CoV-2 infection (PCR confirmed), symptomatic disease and asymptomatic illness	21-27 days after 1st dose	60% (95% CI: 53-66) Symptomatic: 66% (95% CI: 57–73) Asymptomatic: 52% (95% CI: 41-60)
General Population (>16 y, no upper age limit, N=596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	Estimated vaccine effectiveness for SARS-CoV-2 infection (PCR confirmed), symptomatic disease and asymptomatic illness	>7 days after 2nd dose	92% (95% CI: 88–95) Symptomatic: 94% (95% CI: 87–98) Asymptomatic: 90% (95% CI: 83-94)
General Population (>16 y, no upper age limit, N=503,875) Mean age = 59.7 y (SD = 14.7)	Hunter (Israel) 12/19/2020-01/17/2021	Pfizer	SARS-CoV-2 infection (PCR confirmed)	>21 days after 1st dose	90%

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
General Population (>18 y, no upper age limit, N =31,069) All received at least 1st dose; 26% received 2 doses	Pawlowski (US) 12/01/2020-02/08/2021	Pfizer, Moderna	SARS-CoV-2 infection (PCR positive)	≥15 days after 1st dose	75% (95% CI: 67-81)
General Population (>18 y, no upper age limit, N =31,069) All received at least 1st dose; 26% received 2 doses	Pawlowski (US) 12/01/2020-02/08/2021	Pfizer, Moderna	SARS-CoV-2 infection (PCR positive)	1-2 weeks after 2nd dose	89% (95% CI: 68-97)
Older Adults (>60 y) (N=1,303,244)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	0-13 days after 2nd dose	73%
Older Adults (>60 y) (N=1,303,244)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	≥14 days after 2nd dose	96%
Older Adults (>60 y)	Chodick (Israel) 12/19/2020-01/17/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	13-24 days after 1st dose	44%
Older Adults (≥70 y) LTC residents were excluded	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	SARS-CoV-2 infection (PCR positive) and symptomatic disease	14-20 days after 1st dose	22% (95% CI:–9to-44) Symptomatic: 44% (95% CI: 19-64)
Older Adults (≥70 y) LTC residents were excluded	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	SARS-CoV-2 infection (PCR positive) and symptomatic disease	21-27 days after 1st dose	50% (95% CI: 19-72) Symptomatic: 64% (95% CI: 37-83)
Older Adults (≥70 y) LTC residents were excluded	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	SARS-CoV-2 infection (PCR positive) and symptomatic disease	>7 days after 2nd dose	95% (95% CI: 87-100) Symptomatic: 98% (95% CI: 90-100)
Older Adults (≥70 y, N= 7.5 million) LTC residents were included	Lopez Bernal (England) 12/08/2020-02/19/2021	Pfizer	Symptomatic disease (PCR positive)	28-35 days after 1st dose	Symptomatic: 61-70%

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
Older Adults (≥70 y, N= 7.5 million) LTC residents were included	Lopez Bernal (England) 12/08/2020-02/19/2021	Pfizer	Symptomatic disease (PCR positive)	14 days after 2nd dose	Symptomatic: 89%
Older Adults (≥70 y, N= 7.5 million) LTC residents were included	Lopez Bernal (England) 12/08/2020-02/19/2021	AstraZeneca	Symptomatic disease (PCR positive)	28-35 days after 1st dose	Symptomatic: 60-73%
LTC Residents (>65 y)	BCCDC (Canada) 12/2020-02/2021	mRNA vaccine (not specified)	SARS-CoV-2 infection	≥14 days after 1st dose	> 80%
CHSLD Residents (N=33,331) 78% vaccinated with single dose	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	10-13 days after first dose	15%
CHSLD Residents (N=33,331) 78% vaccinated with single dose	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	14-20 days after 1st dose	49%
CHSLD Residents (N=33,331) 78% vaccinated with single dose	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	21-27 days after 1st dose	80%
LTC Residents (N=69,799) 92% received 1st dose, 67% received 2 doses	Brown (Canada) 12/14/2020-02/23/2021	Pfizer, Moderna	SARS-CoV-2 infection	8 weeks after start of vaccination program	89% (95% CI: 85-93)
LTC Residents	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	>14 days after first dose to before 2nd dose	No significant VE

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
LTC Residents	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	0-7 days after 2nd dose	52% (95% CI: 27-69)
LTC Residents	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	>7 days after 2nd dose	64% (95% CI: 14-84)
HCW (hospital, N=9109) 79% received 1st dose, 66% received 2 doses (21-22 days after 1st dose)	Amit (Israel) 12/19/2020-01/25/2021	Pfizer	SARS-CoV-2 infection (exposed and symptomatic, PCR positive) and symptomatic disease adjusted for community exposure	1-14 days after 1st dose	30% (95% CI:2-50) Symptomatic: 47% (95% CI: 12-64)
HCW (hospital, N=9109) 79% received 1st dose, 66% received 2 doses (21-22 days after 1st dose)	Amit (Israel) 12/19/2020-01/25/2021	Pfizer	SARS-CoV-2 infection (exposed and symptomatic, PCR positive) and symptomatic disease adjusted for community exposure	15-28 days after 1st dose	75% (95% CI: 72-84) Symptomatic: 85% (95% CI: 71-92)
HCW	BCCDC (Canada) 12/2020-02/2021	Pfizer, Moderna	SARS-CoV-2 infection	≥14 days after 1st dose	> 80%
HCW (N=325,000) (53% vaccinated with single dose)	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	About 8 weeks after start of vaccination program	80%
HCW (N=325,000) (53% vaccinated with single dose)	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	10-13 days after 1st dose	38%
HCW (N=325,000) (53% vaccinated with single dose)	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	14 to 27 days after 1st dose	74-79%

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
HCW (N=325,000) (53% vaccinated with single dose)	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer (75%), Moderna	SARS-CoV-2 infection	≥28 days after 1st dose	80%
HCW (LTC, N = 100,000) 55% received 1st dose, 45% received 2 doses	Brown (Canada) 12/14/2020-02/23/2021	Pfizer, Moderna	SARS-CoV-2 infection	8 weeks after start of vaccination program	79% (95% CI: 71-85)
HCW (hospital)	Dunbar (US) 11/14/2020-01/19/2021	Pfizer, Moderna	SARS-CoV-2 infection (symptomatic, PCR positive)	14-28 days after 1st dose	Symptomatic: 74.6%
HCW (hospital)	Dunbar (US) 11/14/2020-01/19/2021	Pfizer, Moderna	SARS-CoV-2 infection (symptomatic, PCR positive)	>28 days after 1st dose	Symptomatic: ~100%
HCW (hospital, N= 23,324) 89% received 1st dose; 8% received 2 doses	Hall (England) 12/07/2020-02/05/2021	Pfizer	SARS-CoV-2 infection (PCR positive) in antibody-negative cohort	21 days after 1st dose	72% (95% CI: 58-86)
HCW (hospital, N= 23,324) 89% received 1st dose; 8% received 2 doses	Hall (England) 12/07/2020-02/05/2021	Pfizer	SARS-CoV-2 infection (PCR positive) in antibody-negative cohort	7 days after 2nd dose	86% (95% CI: 76-97)
HCW (hospital, N = 2257)	Azamgarhi (England) 01/05/2021-02/16/2021	Pfizer	SARS-CoV-2 Infection (PCR positive)	≥14 days after 1st dose	80% (95% CI: 21-95)
HCW	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	>14 days after first dose, before 2nd dose	17% (95% CI: 4-28)

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of SARS-CoV-2 infection
HCW	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	0-7 days after 2nd dose	46% (95% CI: 28-59)
HCW	Moustsen-Helms (Denmark) 12/27/2020-02/18/2021	Pfizer	SARS-CoV-2 infection (PCR positive)	>7 days after 2nd dose	90% (95% CI: 82-95)

HCW: healthcare workers, CHSLDs (centres d'hébergement de soins et de longue durée -residential and long-term care centres in Quebec), LTC: long-term care, Pfizer: Pfizer/ BioNTech BNT162b2, Moderna: Moderna mRNA-1273, AstraZeneca: Oxford/ AstraZeneca AZD1222/ChAdOx1-S, PCR: polymerase chain reaction; CI: confidence interval, SARS-CoV-2 infection refers to both asymptomatic and symptomatic disease unless otherwise specified; PCR positive shown only if specifically indicated in study criteria

Table 2: Vaccine Effectiveness (VE) for Prevention of Severe Disease, Hospitalization and Death due to COVID-19

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of Severe Disease, Hospitalization & Death
General Population (< 60 y) (N=2,992,441)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	Severe disease and COVID-19 hospitalization (as per Israeli Ministry of Health)	≥14 days after 2nd dose	Severe disease: 94% Hospitalization: 93%
General Population (> 16 y, no upper age limit, N= 596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	COVID-19–related hospitalization, severe illness (as per National Institutes of Health criteria), death	14-20 days after 1st dose	Severe disease: 62% (95% CI:39–80) Hospitalization: 74% (95% CI: 56–86) Death: 72% (95% CI: 19–100)
General Population (> 16 y, no upper age limit, N= 596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	COVID-19–related hospitalization, severe illness (as per National Institutes of Health criteria), death	21-27 days after 1st dose	Severe disease: 80% (95% CI: 59–94) Hospitalization: 78% (95% CI: 61–91) Death: 84% (95% CI: 44–100)
General Population (> 16 y, no upper age limit, N= 596,618) Median age = 45 (IQR: 35-62)	Dagan (Israel) 12/20/2020-02/01/2021	Pfizer	COVID-19–related hospitalization, severe illness (as per National Institutes of Health criteria), death	>7 days after 2nd dose	Severe disease: 92% (95% CI: 75-100) Hospitalization: 87% (95% CI: 55-100)
General Population (N=5.4 million) 35% received first dose of vaccine.	Vasileiou (Scotland) 12/08/2020-02/15/2021	Pfizer	Hospitalization (COVID-19 as the main cause of admission, or within 28 days of a positive PCR)	28-34 days after 1st dose	Hospitalization: 85% (95% CI: 76-91)
General Population (N=5.4 million)	Vasileiou (Scotland) 12/08/2020-02/15/2021	AstraZeneca	Hospitalization (COVID-19 as the main cause of admission, or within 28 days of a positive PCR)	28-34 days after 1st dose	Hospitalization: 94% (95% CI: 73-99)

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of Severe Disease, Hospitalization & Death
35% received first dose of vaccine.					
General Population (> 18 y, no upper age limit, N =31,069) All received first dose; 26% received two doses	Pawlowski (US) 12/01/2020-02/08/2021	Pfizer, Moderna	Hospital admission within 14 days of a positive PCR	Entire study period	Hospitalization: 60% No difference in 14 day ICU admission rate
Older Adults (> 60 y) (N=1,303,244)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	Severe disease and COVID-19 hospitalization (as per Israeli Ministry of Health)	0-13 days after 2nd dose	Severe disease: 81-83% Hospitalization: 79-81%
Older Adults (> 60 y) (N=1,303,244)	Aran (Israel) 12/20/2020-01/23/2021	Pfizer	Severe disease and COVID-19 hospitalization (as per Israeli Ministry of Health)	≥14 days after 2nd dose	Severe disease: 98% Hospitalization: 97%
Older Adults (> 60 y)	Rossman (Israel) 03/20/2020-02/24/2021	Pfizer	Time dependent changes in COVID-19 hospitalization (includes mild, moderate, severe or ventilated/critical illness) and severe hospitalization (includes severe and ventilated/critical illness) as per Israeli Ministry of Health	2 months after start of vaccination campaign (85% of individuals > 60 vaccinated with 2 doses)	Hospitalization: 68% decrease compared to peak period. Severe hospitalization: 67% decrease compared to peak period
Older Adults (≥ 70 y, N= 7.5 million)	Lopez Bernal (England) 12/08/2020-02/19/2021	Pfizer	Hospitalization within 14 days of positive PCR, death within 21 days of positive PCR	Test date >14 days after 1st dose	Hospitalization: 80% Death: 85%
Older Adults (≥ 70 y, N= 7.5 million)	Lopez Bernal (England) 12/08/2020-02/19/2021	AstraZeneca	Hospitalization within 14 days of positive PCR	Test date > 14 days after 1st dose	Hospitalization: 80%
Older Adults (> 80 y) LTC residents were included.	Vasileiou (Scotland) 12/08/2020-02/15/2021	Pfizer, AstraZeneca	Hospitalization (COVID-19 as the main cause of admission, or within 28 days of a positive PCR)	28-34 days after 1st dose	Hospitalization: 81% (95% CI: 65-90)

Population	Study (Country) Study Period	Vaccine	Study Outcomes	Timeframe	VE for Prevention of Severe Disease, Hospitalization & Death
Older Adults (≥ 80 y, hospitalized, N= 168)	Hyams (England) 12/18/2020-02/26/2021	Pfizer (n=108)	Hospitalization (symptomatic respiratory disease, positive PCR on admission)	≥ 14 days after 1st dose	Hospitalization: 71% (95% CI: 43-86)
Older Adults (≥ 80 y, hospitalized, N= 168)	Hyams (England) 12/18/2020-02/26/2021	AstraZeneca (n=60)	Hospitalization (symptomatic respiratory disease, PCR positive on admission)	≥ 14 days after 1st dose	Hospitalization: 80% (95% CI 36-94)
CHSLD Residents at one site (age range not reported) (N=221) 82% vaccinated with single dose	INSPQ (Canada) 12/14/2020-02/10/2021	Pfizer	Serious infection (not defined), death	≥ 14 days after 1st dose	Serious infection: 40% Death: 50%
LTC Residents (N=69,799) Mean = 85 y 92% received first dose, 67% received two doses	Brown (Canada) 12/14/2020-02/23/2021	Pfizer, Moderna	Death	8 weeks after start of vaccination program	Death: 96% (95% CI 92-98)

HCW: healthcare workers, CHSLDs (centres d'hébergement de soins et de longue durée -residential and long-term care centres in Quebec), LTC: long-term care, Pfizer: Pfizer/ BioNTech BNT162b2, Moderna: Moderna mRNA-1273, AstraZeneca: Oxford/ AstraZeneca AZD1222/ChAdOx1-S, PCR: polymerase chain reaction; CI: confidence interval; ICU: intensive care unit

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