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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary Appendix

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Supplementary Table 1. Empirical evidence for a vaccine-mediated reduction in SARS-CoV-2 infection from a comprehensive list of randomized clinical trials. *95th percentile confidence intervals (CI) not published.

	N			Positives in control	Efficacy	Study Design	Key Results
Moderna Randomized Controlled Trial ^{1,2}	N(vaccinated) = 14134 N(placebo) = 14073	7/27/2020 - 10/23/2020 Day 29, prior to second dose	14 (0·1%)	38 (0·3%)		Double blind randomized clinical trial assessing efficacy of the two-dose Moderna mRNA-1273 COVID19 vaccine. Participants are tested only once after vaccination prior to their second dose, so this trial does not test full efficacy of the Moderna mRNA-1273 vaccine on limiting infection.	Moderate efficacy against asymptomatic SARS-CoV-2 infection after one dose of the Moderna vaccine.
Johnson & Johnson Randomized Controlled Trial ³	N(vaccinated = 19301 N(placebo) = 19162	9/21/2020 - 1/22/2021 After day 29	22 (0·1%)		(CI: 32·8 - 76·6%)	Double blind randomized clinical trial assessing efficacy of one-dose Johnson and Johnson vaccine. Participants tested by PCR or serology at day 29 and 71 after vaccination. If the participant has 1) no symptoms on the day before, at or after the PCR positive test and 2) has a SARS-CoV-2 positive RT-PCR/molecular test result or develops a positive serology (non-S protein) test, they are considered a positive result. Other metrics are used to assess efficacy in the citation.	asymptomatic SARS-CoV-2 infection after one dose of the Johnson &
UK Phase I/II AstraZeneca Randomized Controlled Trial (COV002) ⁴	N(vaccinated) = 4244 N(control) = 4290	10/1/2020 - 1/14/2021 >14 days after second dose	173(4·1%)		41·0 - 59·0%)	Double blind randomized control trial held in the UK (COV002) assessing efficacy of two-dose AstraZeneca ChAdOx1 vaccine against a control vaccine. Participants are given a nose and throat swab after being vaccinated weekly for the duration of the study. Results reported are among the participants who received two standard doses.	positive SARS-CoV-2 test after both

Supplementary Table 2. Empirical evidence for a vaccine-mediated reduction in SARS-CoV-2 infection and/or transmission from a comprehensive list of observational studies. *95th percentile confidence intervals (CI) not published.

		Time of assessment	fully	Positives in partially vaccinated		Effectiveness or Relative Risk	Study Design	Key Results
Pfizer-BioNTech Vaccine Effectiveness in Israel ⁵	596,618	12/20/2020 – 2/1/2021 Fully vaccinated = 7 days after second dose Partially vaccinated = 21 – 27 days after first dose	NA	NA	NA	Fully vaccinated vs unvaccinated: 92% (CI: 88-95%) Partially vaccinated vs unvaccinated: 60% (CI: 53-66%)	Retrospective study with matched controls assessing the effectiveness of Pfizer-BioNTech vaccination on preventing spread in Israel. Asymptomatic infection was defined as PCR positivity without patient-reported symptoms during follow-up.	
SIREN Study of UK Healthcare Workers ⁶	N(partially vaccinated) = 87278 person-days	12/7/2020 – 2/5/2021 Fully vaccinated = 1 week after second dose Partially vaccinated = 21 days after first dose	9 (4 per 10,000 person-days)		977 (14 per 10,000 person-days)	Fully vaccinated vs unvaccinated: 85% (CI: 74-96%) Partially vaccinated vs unvaccinated: 70% (CI: 53-87%)	Prospective study among UK healthcare workers assessing Pfizer-BioNTech and AstraZeneca vaccine effectiveness on infection (biweekly PCR tests). Study mostly white and female. Cohort includes a large number of seropositive participants (~1/3 cohort).	High effectiveness against SARS-CoV-2 infection in a cohort of individuals fully vaccinated with either the Pfizer-BioNTech or AstraZeneca vaccine.
Pfizer-BioNTech Vaccine Effectiveness in Qatar (vs B.1.1.7) ⁷	N(unvaccinated) =	2/1/2021– 3/31/2021 Fully vaccinated = 14 days after second dose	50 (9.7%)	NA	16,354 (50-6%)	Fully vaccinated vs unvaccinated: 89·5% (CI: 85·9–92·3%)	infection among vaccinated and matched unvaccinated individuals in Qatar. Prevalence of B.1.1.7 and B.1.351 comprised the majority of infections in Qatar at the time, so effectiveness is determined for each of these variants individually. The mass immunization campaign in Qatar primarily used the Pfizer-BioNTech vaccine,	High effectiveness against SARS-CoV-2 B.1.1.7 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.
Pfizer-BioNTech Vaccine Effectiveness in Qatar (vs B.1.351) ⁷	N(vaccinated) = 877 N(unvaccinated) = 38,273		179 (20·4%)	NA	19,396 (50·7%)	Fully vaccinated vs unvaccinated: 75·0% (CI: 70·5–78·9)	so the effectiveness of this vaccine.	Moderately high effectiveness against SARS-CoV-2 B.1.351 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.

Mayo Clinic Pre- procedure Testing of Patients ⁸	N(unvaccinated) = 45327	12/17/2020 – 2/8/2021 Partially vaccinated = any vaccination given before screening test	NA	42 (1·4%)	1,436 (3·2%)	Adjusted relative risk of vaccinated vs unvaccinated: 0.35 (CI: 0.26 – 0.47)	Frequency of PCR+ asymptomatic infections among vaccinated and unvaccinated healthcare workers. Results reflect the effectiveness of the Pfizer-BioNTech vaccine.	Moderate effectiveness against asymptomatic SARS-CoV-2 infection among individuals partially vaccinated with the Pfizer-BioNTech vaccine.
Mayo Clinic and Associated Health System Patients ⁹	N(unvaccinated) = 31,069	12/1/2020 – 2/8/2021 Fully vaccinated = 36 days after first dose (2 doses) Partially vaccinated = days 22-28 after first dose	4 cases/ 8,041 (82,686 person-days) [0·048%]	22 cases/ 19,634 (129,119 person-days) [0·17%]	Overall: 661 /31,069 (825,106 person-days) [2·13%]	Fully vaccinated vs unvaccinated: 88·7% (CI: 68·4-97·1%) Partially vaccinated vs unvaccinated: 74·2% (CI: 58·4-84·7%)	Retrospective study comparing PCR positivity among vaccinated and unvaccinated patients within the Mayo Clinic and associated health system.	High effectiveness against asymptomatic SARS-CoV-2 infection among fully vaccinated individuals.
Healthcare workers in Cambridge University Hospitals NHS Foundation Trust ¹⁰	1,989 tests N(partially vaccinated) = 3,535 tests	1/18/2021 – 1/31/2021 Partially vaccinated <12 days post dose 1 Fully vaccinated >12 days post dose 1 or unvaccinated	>12 days post vaccine: 4 (0·20%)	<12 days post vaccine: 13 (0·37%)	26 (0·80%)	>12 days post vaccine vs unvaccinated: 75%* <12 days post vaccine vs unvaccinated: 54%*	Healthcare workers in Cambridge University Hospitals NHS Foundation Trust system were tested weekly for asymptomatic COVID19. Results reflect the effectiveness of the Pfizer-BioNTech vaccine.	
Healthcare workers in the University of Texas Southwestern Medical Center ¹¹	8,121 N(partially vaccinated) = 6,144 N(unvaccinated) = 8,969	12/15/2020 – 1/28/2021; Fully vaccinated = 7 days after second dose of BNT162b2 or 14 days after second dose of mRNA-1273 Partially vaccinated = first dose to 7 days after	4 (0·05%)	112 (1·82%)	234 (2·61%)	Fully vaccinated vs unvaccinated: 98%*	This study compares the rates of SARS-CoV-2 infection among healthcare workers in the UTSW Medical Center, stratified by vaccination status.	High effectiveness against SARS-CoV-2 infection among fully vaccinated individuals.

		second dose of BNT162b2 or 14 days after second dose of mRNA-1273						
Healthcare workers in UCSD and UCLA ¹²	4,167 N(partially vaccinated) = 5,794	12/16/2020 – 2/9/2021; Fully vaccinated = 15 days after second dose Partially vaccinated = 1-7 days after first dose	7 (0·17%)	145 (2·50%)	NA	partially	This study compares the rates of SARS-CoV-2 infection among healthcare workers in the UCSD and UCLA, stratified by vaccination status.	High effectiveness against SARS-CoV-2 infection among fully vaccinated individuals.
Healthcare workers at Hadassah Hebrew University Medical Center ¹³	4,079 N(partially	12/20/2020 – 1/31/2021; Fully vaccinated = 6-7 weeks after first dose Partially vaccinated = between first dose and 1 week since first dose	5 (0·12%)	50 (0.94%)	NA	partially	This study compares the rates of SARS-CoV-2 infection among healthcare workers in the Hadassah Hebrew University Medical Center, stratified by vaccination status. Results reflect the effectiveness of the Pfizer-BioNTech vaccine.	High effectiveness against SARS-CoV-2 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.
Pfizer-BioNTech Vaccine Effectiveness in U.K. Household Transmission ¹⁴	N(visits by partially vaccinated individuals) =	12/1/2020 – 5/8/2021 Fully vaccinated: Visits post-second dose ≥21d following first dose Partially vaccinated: 0 to 21+ days after first dose, no second dose	72 (0·08%)	718 (0·33%)	11,469 (0-93%)	unvaccinated: 80% (CI: 73-85%)	through a large-scale community-based survey across the United Kingdom. Results reflect the	High effectiveness against SARS-CoV-2 infection among individuals fully vaccinated with Pfizer- BioNTech vaccine.

ChAdOx1 Vaccine Effectiveness in U.K. Household Transmission ¹⁴	N(visits by fully vaccinated individuals) = 47,413 N(visits by partially vaccinated individuals) = 350,523 N(visits by unvaccinated individuals) = 1,235,803		21 (0.04%)	534 (0·15%)	11,469 (0.93%)	Fully vaccinated vs unvaccinated: 79% (CI: 65-88%) Partially vaccinated vs unvaccinated: 61% (CI: 54-68%)		Moderately high effectiveness against SARS-CoV-2 infection among individuals fully vaccinated with AstraZeneca vaccine.
Nursing Home Residents in the US ¹⁵	N(partially vaccinated) = 5,194 N(unvaccinated) = 3,990	Until 3/31/2021 Fully vaccinated: >14 days following second dose Partially vaccinated: 15- 28 days after first dose Unvaccinated: 0-14 days after first dose	29 (0·2%)	179 (1.0%)	115 (2.9%)	Fully vaccinated vs unvaccinated: 93%* Partially vaccinated vs unvaccinated: 66%*	Residents of nursing homes were tested for infection every 3-7 days during outbreaks within the nursing home or upon development of symptoms or exposure. Asymptomatic infection was defined as no documented symptoms 5 days before the positive test to 14 days afterwards. Results reflect the effectiveness of Pfizer-BioNTech and Moderna vaccines.	against asymptomatic SARS-CoV-2 infection among individuals fully
Healthcare Workers at the Tel Aviv Sourasky Medical Center ¹⁶	57,274 person-days N(unvaccinated) = 25,359 person-days	12/20/2020 - 2/25/2021 Fully vaccinated: >7 days following second dose Unvaccinated: 0-14 days after first dose	4 (0·0070%)	NA	17 (0·067%)	Fully vaccinated vs unvaccinated: 90%* (Adjusted)	workers on a weekly or monthly basis for	High effectiveness against asymptomatic SARS-CoV-2 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.

Nationwide Public Health Surveillance in Israel ¹⁷		Fully vaccinated: >7 days following second	3,632 (0·0018%)		49,138 (0·041%)	Fully vaccinated vs unvaccinated: 91·5% (Adjusted CI: 90·7- 92·2%)	This study used nationwide surveillance data to retrospectively assess the effect of the Pfizer-BioNTech vaccine on asymptomatic infection. Asymptomatic infection was defined as lack of characteristic COVID-19 symptoms at the time of interview.	High effectiveness against asymptomatic SARS-CoV-2 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.
Pfizer-BioNTech Vaccine among Essential Workers in the US within the HEROES- RECOVER Network (CDC) ¹⁸	120,653 person-days N(partly vaccinated) = 49,516 person-days N(unvaccinated) = 127,971 person-days	Partially vaccinated:	3 (0.0025%)	8 (0-016%)	156 (0·12%)	Fully vaccinated vs unvaccinated: 93% (Adjusted CI: 78-98%) Partially vaccinated vs unvaccinated: 80% (Adjusted CI: 60–90%)	Prospective nationwide study assessing SARS-CoV- 2 positivity among vaccinated and unvaccinated first responders with weekly nasal samples, regardless of symptomatic status. Results reflect the effectiveness of the Pfizer-BioNTech and the Moderna vaccines.	efficacy against
Moderna Vaccine among Essential Workers in the US within the HEROES- RECOVER Network (CDC) ¹⁹	N(fully vaccinated) = 40,394 person-days N(partly vaccinated) = 31,231 person-days N(unvaccinated) = 127,971 person-days	Unvaccinated: unvaccinated or <14 days after first dose	2 (0.0049%)	3 (0-0096%)	156 (0·12%)	Fully vaccinated vs unvaccinated: 82% (Adjusted CI: 20-96%) Partially vaccinated vs unvaccinated: 83% (Adjusted CI: 40–95%)	Prospective nationwide study assessing SARS-CoV-2 positivity among vaccinated and unvaccinated first responders with weekly nasal samples, regardless of symptomatic status. Results reflect the effectiveness of the Pfizer-BioNTech and the Moderna vaccines.	against asymptomatic
Effect of ChAdOx1 Vaccine on Household Transmission of SARS-CoV-2 in England ¹⁹		1/4/2021 - 2/28/2021 Vaccinated index case: ≥21 days following first dose	NA	196 (5·72%)	96,898 (10·1%)	Vaccinated vs unvaccinated adjusted odds ratio: 0.52 (CI: 0.43–0.62)	The household contacts of vaccinated or matched unvaccinated individuals who test positive for SARS-CoV-2 were monitored for whether they themselves test positive 2-14 days after the index case. Note: most vaccinated individuals in this study had received only one dose of a two-dose course. The results reflect the ability of the Pfizer-BioNTech or ChAdOx1 vaccines to directly prevent	Moderate effectiveness of the Pfizer-BioNTech or ChAdOx1 vaccines at preventing transmission of SARS-CoV-2 after one dose.
Effect of Pfizer- BioNTech Vaccine on	N(contacts of vaccinated) = 5,939		NA	371 (6·25%)		Vaccinated vs unvaccinated adjusted	transmission.	

Household Transmission of SARS-CoV-2 in England ¹⁹	N(contacts of unvaccinated) = 960,765					odds ratio: 0·54 (CI: 0·47–0·62)		
Effect of Moderna vaccine among Mayo Clinic and Associated Health Personnel ²⁰	N (partially vaccinated) = 1,166	1/1/2021 - 3/31/2021 Fully vaccinated: >14 days after second dose Partially vaccinated >14 days from first dose and ≤14 days from second dose	NA	NA	997 (4·2%)	unvaccinated: 91·2% (CI: 80·6–96·1%)	positivity among vaccinated and unvaccinated healthcare personnel undergoing routine testing. The results reflect the ability of the mRNA vaccines to prevent infection.	High effectiveness against SARS-CoV-2 infection in a cohort of individuals fully vaccinated with either the Moderna or Pfizer- BioNTech vaccine.
Effect of Pfizer- BioNTech vaccine among Mayo Clinic and Associated Health Personnel ²⁰	N (fully vaccinated) = 40,887 N (partially vaccinated) = 2,038 N (unvaccinated) = 23,931		NA	NA		Fully vaccinated vs unvaccinated: 78·1% (CI: 71·1–82·0%) Partially vaccinated vs unvaccinated: 96·8% (CI: 95·3–97·8%)		

Healthcare workers of St. Jude Children's Research Hospital ²¹	149,718 person-days N(partially vaccinated) = 32,481 person-days	12/17/2020 - 3/20/2021 Fully vaccinated: ≥7 days after second dose Partially vaccinated ≥12 days from first dose and before second dose	6 (0-031%)	10 (0.0051%)	29 (0·019%)	Fully vaccinated vs unvaccinated incident rate ratio: 0·10 (CI: 0·04–0·22) Partially vaccinated vs unvaccinated incident rate ratio: 0·58 (CI: 0·30–1·13)	This study utilized routine SARS-CoV-2 testing to determine the effectiveness of the Pfizer-BioNTech vaccine on asymptomatic infection among healthcare workers.	High effectiveness against SARS-CoV-2 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.
Effectiveness of Vaccination an Outbreak of the R.1 Variant within a Skilled Nursing Home in Kentucky ²²		3/1/2021 - 3/30/2021 Fully vaccinated: ≥14 days after second dose	18 (25·4%)	NA	6 (75·0%)	Fully vaccinated vs unvaccinated: 66-2% (CI: 40-5–80-8%)	A positive test in an asymptomatic healthcare worker on 3/1/2021 led to daily, rapid, point-of-care testing of all residents. Positive tests were confirmed by same-day PCR testing. Results reflect the effectiveness of the Pfizer-BioNTech vaccine to prevent infection.	Moderate effectiveness against SARS-CoV-2 infection among nursing home residents fully vaccinated with the Pfizer-BioNTech vaccine.
Effectiveness of the Pfizer- BioNTech Vaccine in a Nationwide Historical Cohort Study ²³		1/1/2021 - 2/11/2021 Fully vaccinated: ≥7 days after second dose Partially vaccinated: ≥14 days after first dose and <7 days after second dose	6 per 10,000 person-days		53 per 10,000 person-days	Fully vaccinated vs unvaccinated: 89% (CI: 82–94%) Partially vaccinated vs unvaccinated: 69% (CI: 49–79%)	A subset of individuals within a health management organization who repeatedly received SARS-CoV-2 tests were identified and stratified by vaccination status. Results reflect the effectiveness of the Pfizer-BioNTech vaccine to prevent infection.	

Healthcare Workers in Treviso, Italy ²⁴	216,098 person-days	12/27/2020 - 3/24/2021 Fully vaccinated: ≥7 days after second dose	4 (0·018%)		15 (0.019%)	unvaccinated: 95·1% (CI: 62·4–99·4%)	were tested every 8 days or upon report of characteristic COVID-19 symptoms. Results reflect the effectiveness of the Pfizer-BioNTech vaccine to prevent infection.	High effectiveness against SARS-CoV-2 infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine.
Effect of Pfizer- BioNTech vaccine on Household Transmission in Israel ²⁵	N(fully vaccinated) =		NA	NA	NA	unvaccinated: Susceptibility of infection: 80·5% (CI: 78.9–82·1%)	within households was obtained from Maccabi Healthcare Services in Israel. Vaccine effectiveness against infection, against infectiousness given infection, and overall transmission prevention were calculated using the study's household transmission model. The results reflect the ability of the Pfizer-	The Pfizer-BioNTech vaccine has high overall effectiveness against transmission by significantly reducing primary infection and mildly reducing infectiousness of vaccinated individuals.

Supplementary Table 3. Empirical evidence for a vaccine-mediated reduction in SARS-CoV-2 infection from a selection of observational studies with the Delta variant.

	N		Positives in fully vaccinated		Positives in unvaccinated		Study Design	Key Results
Effectiveness of Pfizer-BioNTech Vaccine against symptomatic Delta infection in England ²⁶ Effectiveness of ChAdOx1	N(fully vaccinated) = 15,749 N(partially vaccinated) = 8,641 N(unvaccinated) = 96,371 N(fully vaccinated) =	≥14 days after second dose Partially vaccinated: ≥21 days after first dose up to the day before second dose was received.	122 (0·10%) 218 (0·15%)	137 (0·11%) 1,356 (0·92%)	4,043 (2·74%)	(CI: 85·3–90·1%) Partially vaccinated vs unvaccinated: 35·6% (CI: 22·7–46·4%) Fully vaccinated vs	study comparing vaccine effectiveness against symptomatic infections caused by the Alpha and Delta variants in England, during the period of circulating Delta variant.	High effectiveness against symptomatic infection among individuals fully vaccinated with the Pfizer-BioNTech vaccine, and moderate effectiveness among individuals vaccinated with the ChAdOx1 vaccine against symptomatic infection caused by the Delta variant.
Vaccine against symptomatic Delta infection in England ²⁶	8,244 N(partially vaccinated) = 42,829 N(unvaccinated) = 96,371					unvaccinated: 67.0% (CI: 61·3–71·8%) Partially vaccinated vs unvaccinated: 30·0% (CI: 24·3–35·3%)		
Effectiveness of Pfizer- BioNTech Vaccine against Delta infection in Qatar ²⁷	N(fully vaccinated) = 877,354 N(partially vaccinated) = 906,078	3/23/21 (when Delta variant was detected in community) - 7/21/21 Fully vaccinated: ≥14 days after second dose	209	19	vaccinated 1602 against partially	unvaccinated: 59·6% (CI: 50·7–66·9%)	control study examining effectiveness of Pfizer-BioNTech and Moderna vaccines against SARS-CoV-2 infections caused	Moderate effectiveness among individuals vaccinated with the Pfizer-BioNTech vaccine, and high effectiveness among individuals vaccinated with the Moderna

Effectiveness of Moderna Vaccine against Delta infection in Qatar ²⁷	N(fully vaccinated) = 409,041 N(partially vaccinated) = 490,828	Partially vaccinated: ≥14 days after first dose, no second dose	22		fully vaccinated 1,629 against partially vaccinated	Fully vaccinated vs unvaccinated: 86·1% (CI: 78·0–91·3%) Partially vaccinated vs unvaccinated: 79·7% (CI: 60·8–89·5%)		vaccine against infection by the Delta variant.
Effectiveness of Pfizer- BioNTech Vaccine against SARS-CoV-2 infection in Nursing Home Residents During Widespread Circulation of the Delta Variant ²⁸	N(visits by fully vaccinated individuals) = 3,248,732 N(visits by unvaccinated individuals) = 953,861	6/21/21-8/1/21, period when ≥ 50% of SARS-CoV-2 viruses sequenced were the Delta variant Fully vaccinated: ≥14	1,939	NA	ŕ		undergoing regular SARS-CoV-2 testing were identified and stratified by vaccination status. Results reflect the effectiveness of the Pfizer-BioNTech or Moderna vaccines to prevent infection during circulation of the Delta	Mild effectiveness against infection of SARS-CoV-2 during widespread circulation of Delta variant among individuals fully vaccinated with the Pfizer-BioNTech or Moderna vaccine.
Effectiveness of Moderna Vaccine against SARS-CoV-2 infection in Nursing Home Residents During Widespread Circulation of the Delta Variant ²⁸	N(visits by fully vaccinated individuals) = 1,763,014 N(visits by unvaccinated individuals) = 953,861	days after second dose	1,060	NA		Fully vaccinated vs unvaccinated: 50·6% (CI: 45·0–55·7%)		

REACT-1 Round 13 Final report: Effectiveness of Pfizer-BioNTech and ChAdOx1 Vaccines against infection during widespread Delta circulation ²⁹	59,662	Fully vaccinated:	197	102		odds ratio: 0.25 (CI: 0.20–0.30) Partially vaccinated vs unvaccinated adjusted odds ratio: 0.56 (CI: 0.44–0.73)	representative surveillance program in England based on swab results from individuals tested for SARS-CoV-2. Results reflect the effectiveness of the Pfizer-BioNTech and ChAdOx1 vaccines to prevent infection	High effectiveness against infection of SARS-CoV-2 during widespread circulation of Delta variant among individuals fully vaccinated with the Pfizer-BioNTech or ChAdOx1 vaccines.
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