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RESEARCH ARTICLE

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Postvaccination SARS-CoV-2 infection among healthcare workers: A systematic review and meta-analysis

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Abstract

Healthcare workers (HCWs) remain on the front line of the battle against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19) infection and are among the highest groups at risk of infection during this raging pandemic. We conducted a systematic review and meta-analysis to assess the incidence of postvaccination SARS-CoV-2 infection among vaccinated HCWs. We searched multiple databases from inception through August 2021 to identify studies that reported on the incidence of postvaccination SARS-CoV-2 infection among HCWs. Meta-analysis was performed to determine pooled proportions of COVID-19 infection in partially/fully vaccinated as well as unvaccinated individuals. Eighteen studies with 228 873 HCWs were included in the final analysis. The total number of partially vaccinated, fully vaccinated, and unvaccinated HCWs were 132 922, 155 673, and 17 505, respectively. Overall pooled proportion of COVID-19 infections among partially/fully vaccinated and unvaccinated HCWs was 2.1% (95% confidence interval [CI] 1.2–3.5). Among partially vaccinated, fully vaccinated and unvaccinated HCWs, pooled proportion of COVID-19 infections was 2.3% (CI 1.2–4.4), 1.3% (95% CI 0.6–2.9), and 10.1% (95% CI 4.5–19.5), respectively. Our analysis shows the risk of COVID-19 infection in both partially and fully vaccinated HCWs remains exceedingly low when compared to unvaccinated individuals. There remains an urgent need for all frontline HCWs to be vaccinated against SARS-CoV-2 infection.

KEYWORDS
COVID-19, healthcare workers, vaccine

1 | INTRODUCTION

Healthcare workers (HCWs) remain on the front line of the battle against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19) infection, and through interactions in the workplace related to care and proximity to patients, besides household and community interactions, they are among the highest groups at risk of infection during this raging pandemic.[1] At the peak of the pandemic, a large systematic review of 594 studies noted that 152 888 COVID-19 infections and 1413 deaths occurred among HCWs globally. The overall infection and death trends among HCWs followed that of the general population.[2] More recent estimates suggest that more than 233 million cases of the novel coronavirus have been diagnosed globally, resulting in more than 4 million deaths.

In December 2020, two messenger RNA (mRNA) vaccines, the BNT162b2 vaccine from Pfizer–BioNTech and the mRNA-1273 vaccine from Moderna, were approved by the Food and Drug Administration under Emergency Use Authorization for use among persons 16 years of age or older (for the BNT162b2 vaccine) or among those 18 years or older (for the mRNA-1273 vaccine).

Recent data suggest that these vaccines are highly effective under real-world conditions in preventing symptomatic COVID-19 in HCWs, including those at risk for severe COVID-19.[3–5] Despite the global push for vaccination, studies show that vaccine hesitancy among HCWs is still common with acceptance rates ranging widely from 27.7% to 77.3%. Demographic variables such as men, older age, and physicians were positive predictive factors, whereas concerns for safety, efficacy and effectiveness, and distrust of the government were barriers.[6]

In recent months, there have been further concerns about the emergence of SARS-CoV-2 variants, including variants first reported in the United Kingdom (B.1.1.7), South Africa (B.1.351), Brazil (P.1), California (B.1.427/B.1.429), and India (B.1.617).[7,8] As vaccine effective data emerges, we conducted a systematic review and meta-analysis to assess the incidence of postvaccination SARS-CoV-2 infection among vaccinated HCWs.

2 | METHODS

2.1 | Search strategy

The relevant medical literature was searched by two authors (SC and DR) for studies reporting on the incidence and outcomes of postvaccination COVID-19 infection among HCWs. A systematic and detailed search was run in August 2021 in Ovid EBM Reviews, ClinicalTrials.gov, Ovid Embase (1974 +), Ovid Medline (1946+ including epub ahead of print, in-process and other non-indexed citations), Scopus (1970 +), Web of Science (1975 +), and Google Scholar. A literature search was performed to include studies published in all languages, and in the case of non-English studies, an electronic language translation service was used to convert the text to English. An example search strategy using EMBASE is presented as Appendix-S1. Articles were included if data with regard to incidence of postvaccination COVID-19 infection was presented. Only cohort studies were eligible for inclusion. All other study designs including, case series of less than 10 patients, case reports, review articles, and guidelines were excluded.

As the included studies were observational in design, the MOOSE (Meta-analyses Of Observational Studies in Epidemiology) Checklist was followed[9] and is provided as Appendix-S2. PRISMA Flowchart for study selection[10] is provided as Appendix-S3. Reference lists of evaluated studies were further examined to identify other studies of interest.

2.2 | Data abstraction and quality assessment

Data on study-related outcomes from the individual studies were abstracted independently onto a standardized form by at least two authors (SC and SRK). Authors (DR and OCC) cross-verified the collected data for possible errors and two authors (SC and SRK) performed the quality scoring independently. We used the Newcastle–Ottawa scale, which is a quality score consisting of 8 questions, to assess the quality of cohort studies.[11]

2.3 | Outcomes assessed

1. Overall pooled proportion of positive COVID-19 infections in fully, partially, and unvaccinated HCWs.
2. Pooled proportion of COVID-19 infections in partially vaccinated HCWs.
3. Pooled proportion of COVID-19 infections in fully vaccinated HCWs.
4. Pooled proportion of COVID-19 infections in unvaccinated HCWs.
5. Pooled proportion of vaccinated HCWs hospitalized for COVID-19 infection.
6. Pooled proportion of vaccinated HCWs admitted to ICU for COVID-19 infection.
7. Pooled proportion of vaccinated HCWs died from COVID-19 infection.

2.4 | Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates in each case following the methods suggested by DerSimonian and Laird using the random-effects model and results were expressed in terms of pooled proportion (PP) along with relevant 95% confidence intervals (CIs).[12] When the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis.[13] A p-value of < 0.05 was defined as statistically significant. We assessed heterogeneity between study-specific estimates by using Cochran Q statistical test for heterogeneity, 95% confidence interval (CI), and the I^2 statistics.[13–15] In this, values of <30%, 30%–60%, 61%–75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively. We assessed publication bias, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test.[16] When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie's "Trim and Fill" test were used to ascertain the impact of the bias.[17]

All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 3 (BioStat).

3 | RESULTS

3.1 | Search results and population characteristics

All search results were exported to Endnote where 22 obvious duplicates were removed leaving 92 citations. Eighteen studies with 228 873 HCWs were included in the final analysis. The total number of partially vaccinated, fully vaccinated, and unvaccinated HCWs were 132 922, 155 673, and 17 505, respectively. A schematic diagram demonstrating our study selection is illustrated in Supplementary Figure 1.

3.2 | Characteristics and quality of included studies

Six studies originated from India,[18–23] seven from the USA,[1,24–29] two from Israel,[30,31] and one each from Pakistan,[32] United Kingdom,[33] and Indonesia.[34] Further details of patient characteristics, category of healthcare workers, follow-up time and type of infection, symptomatic, or asymptomatic are presented in Tables 1 and 2.

Ten of the included studies were retrospective in design while four were prospective. Based on the New–Castle Ottawa scoring system, all included studies were considered to be of high quality.

3.3 | Meta-analysis outcomes

1. **Overall pooled proportion of positive COVID-19 infections in fully, partially, and unvaccinated HCWs**: Across 18 studies, the overall pooled proportion of COVID-19 infections was 2.1% (95% CI 1.2–3.5; I^2 99.5%) Figure 1.
2. **Pooled proportion of COVID-19 infections in partially vaccinated HCWs**: Among partially vaccinated HCWs, across 14 studies, the overall pooled proportion of COVID-19 infections was 2.3% (95% CI 1.2–4.4; I^2 99%) Figure 2.
3. **Pooled proportion of COVID-19 infections in fully vaccinated HCWs**: Among fully vaccinated HCWs, across 16 studies, the overall pooled proportion of COVID-19 infections was 1.3% (95% CI 0.6–2.9; I^2 99.3%) Figure 3.
4. **Pooled proportion of COVID-19 infections in unvaccinated HCWs**: Among unvaccinated HCWs, across 8 studies, the overall pooled proportion of COVID-19 infections was 10.1% (95% CI 4.9–19.5; I^2 99.5%) Figure S2.
5. **Pooled proportion of vaccinated HCWs hospitalized for COVID-19 infection**: The overall pooled proportion of both fully and partially vaccinated HCWs hospitalized for COVID-19 infection was 5.7% (95% CI 3.5–9.1; I^2 48.4%) Figure S3.
6. **Pooled proportion of vaccinated HCWs admitted to ICU for COVID-19 infection**: The overall pooled proportion of both fully and partially vaccinated HCWs requiring intensive care unit admission for COVID-19 infection was 2.6% (95% CI 0.4–15.4; I^2 84%) Figure S4.
7. **Pooled proportion of vaccinated HCWs died from COVID-19 infection**: The overall pooled proportion of both fully and partially vaccinated HCWs dying from COVID-19 infection was 1.2% (95% CI 0.3–5.7; I^2 72.6%) Figure S5.

4 | VALIDATION OF META-ANALYSIS RESULTS

4.1 | Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. We found that exclusion of any single study did not significantly affect the primary outcome or influence the heterogeneity.

4.2 | Heterogeneity

We assessed the dispersion of the calculated rates using the I^2 percentage values as reported in the meta-analysis outcomes section. We found considerable heterogeneity in our outcomes. This is likely due to variations in the sample size of each individual study, the type of COVID-19 vaccine administered, and variation in mean follow-up time.

4.3 | Publication bias

Based on visual inspection of the funnel plot for our study outcomes, we found no evidence of publication bias. Quantitative assessment demonstrated Egger's 2-tailed *p*-value of 0.4 Supplementary Figure 6A–C.

5 | DISCUSSION

Our analysis shows the risk of COVID-19 infection in both partially and fully vaccinated HCWs remains exceedingly low when compared to unvaccinated individuals. We found that while the pooled proportion of unvaccinated HCWs contracting COVID-19 was as high as 47%, this decreased to 2.3% for partially vaccinated and 1.3% for fully vaccinated HCWs. At the time of writing, the COVID-19 pandemic continues to rage across the world and HCWs account for a large number of infected people.[35] These individuals are both not only victims of the disease, but also potential spreaders.[36] Therefore, protecting HCWs from SARS-CoV-2 infection would not only be beneficial for themselves, but also for their household contacts and patients. Vaccine acceptance among HCWs and hesitancy remains a concern with studies showing that nurses and assistant nurses were less prone to accept vaccination against COVID-19 than physicians.[37] Our study is crucial in that it is the first in the literature to systematically review and analyze the incidence of COVID-19 infections among partially/fully vaccinated or unvaccinated HCWs.

In December 2020, two messenger RNA (mRNA) vaccines, the BNT162b2 vaccine from Pfizer–BioNTech and the mRNA-1273 vaccine from Moderna, were approved by the Food and Drug Administration under Emergency Use Authorization for use among persons 16 years of age or older (for the BNT162b2 vaccine) or among those 18 years or older (for the mRNA-1273 vaccine).[38,39] The US Advisory Committee on Immunization Practices recommended the prioritization of health care personnel during the early phase distribution of these vaccines to ensure that the spread of infection in health care settings was reduced. Vaccination of health care personnel in the United States was initiated in December 2020, and by early March 2021, more than half the frontline health care personnel in the United States had been vaccinated with Covid-19

TABLE 1 Study characteristics and patient details

Author	Design	Vaccine type	Total patients enrolled	Healthcare worker type		Total COVID-19 positive patients	Age, years [*SD*] (range)	Sex (male/female)
				Physician	Nonphysician			
Amit, 2021	Retrospective, NR, Single-Center, December 2020–January 2021, Israel	Pfizer-BioNTech COVID-19 vaccine (BNT162B2)	4081	NR	NR	22	45.3 (9.85) [31–61]	8/14 (positives)
Azamgarhi, 2021	Retrospective, NR, Single-Center, UK	Pfizer-BioNTech COVID-19 vaccine (BNT162B2)	2235	231/2235 (Surgeons/medics) [PV 183, FV 48]	Administrative and clerical 629, Nursing 494, Allied health professionals 240, Clinical support staff 234, Portering and catering 225, Professional scientific and technical staff 182	49	584 (16–34), 1234 (35–54), 417 (>55)	722/1513 (total)
Bouton, 2021	Prospective, NR, Single-Center, December 9, 2020 and February 23, 2021, USA	Pfizer-BioNTech COVID-19 Vaccine (BNT162B2) and Moderna Covid Vaccine (mRNA-1273)	10 590	NR	NR	425	40 (13)	18/78 (positives)
Tang, 2021	Prospective, NR, Single-Center, December 17, 2020–March 20, 2021, USA	Pfizer-BioNTech COVID-19 vaccine (BNT162B2)	5217	NR	NR	236	–	1038/2014 (vaccinated)
Cucunawangsiha, 2021	Retrospective, NR, Single, Center, Indonesia	2021, CoronaVac (Sinovac Biotech)	1040	NR	NR	13	32.5 (5.9)	5/8/2021 (positives)
Hall, 2021	Prospective, NR, Multi-center, December 8, 2020–February 5, 2021, USA	Pfizer-BioNTech COVID-19 vaccine (BNT162B2) and Oxford-AstraZeneca COVID-19 Vaccine (ChAdOx1 nCoV-19 adenoviral [AZD1222])	23 324	2451 (Vaccinated 2332, Unvaccinated 189)	Administrative or executive 3600, Nursing or health-care assistant 9826, Midwife 566, Specialist staff 1418, Estates, porters, or security 222, Pharmacist 351, Health-care scientist 820, Others 4000	80	46.1 (36–54.1)	3632/19 692 (total)
Issac, 2021	Prospective, NR, Single-Center, January 27, 2021–July 15, 2021, India	ChAdOx1 nCoV-19	324	18/324 (Vaccinated 18, Unvaccinated 0)	Nurses 165, Pharmacist 17, Physiotherapist 4, Dietician 1, Administration 8, Accounts & Finance 24, Medical records 4, Lab & Diagnostics 50, Housekeeping 23, Biomedical Engineering 1, Maintenance 4, Quality department 4, Ambulance driver 1	41	34.09 (9.43)	52/272 (vaccinated)

(Continues)

TABLE 1 (Continued)

Author	Design	Vaccine type	Total patients enrolled	Healthcare worker type		Total COVID-19 positive patients	Age, years [*SD*] (range)	Sex (male/female)
				Physician	Nonphysician			
Jacobson, 2021	Retrospective, December 18, 2020–April 02, 2021, USA	Pfizer-BioNTech COVID-19 Vaccine (BNT162B2) and Moderna Covid Vaccine (mRNA-1273)	30 000	NR	NR	189	40.8 [11.2] [Mean], 38 (32–48) [Median]	64/125 (positive)
Maroof, 2021	Prospective, Feburay 2021–June 2021, Multicenter, Pakistan	Sino-pharm Vaccine	39 512	NR	NR	124	38.8 [11]	86/38 (positives)
Mathema, 2021	Retrospective, December 2020–April 2021, Multicenter, USA	Pfizer-BioNTech COVID-19 Vaccine (BNT162B2) and Moderna Covid Vaccine (mRNA-1273)	37 500	NR	NR	138	45 (19–77) [Median] [*N* = 121] (positives)	31/90 [N = 121] (positives)
North, 2021	Prospective, cohort, December 30, 2020–April 2, 2021, Multicenter, USA	Pfizer-BioNTech COVID-19 Vaccine (BNT162B2) and Moderna Covid Vaccine (mRNA-1273)	2247	873/2247 (Physician/Nurse practitioner/ Physician assistant)	Administration 104, Environmental/Food services 10, Nursing 558, Patient Care Services (PT, OT, SLP, etc.) 217, Research-related activities 357, Others 125	19	37 (30–50)	476/1760 (total)
Pandurangaiah, 2021	Retrospective, Feburary 2021–May 07, 2021, Single-center, India	Covishield/Covaxin	182	32/182 (Doctors)	71/182 (Nurses), 37/182 (Para-medical staff), 42/182 (Other)	6	–	47/135 (total)
Sabnis, 2021	Prospective, First dose of COVID-19 vaccine till June 10, 2021, Single-center, India	Covishield (SII-ChAdOx1 nCoV-19)	461	51/461 (Doctors)	410/461 (Others)	86	34.18 (22–77)	NR
Vaishya, 2021	Retrospective, observational, cohort, January 16, 2021–June 15 2021, Multicenter, India	AstraZeneca Covid Vaccine (ChAdOx1-S/nCoV-19 [recombinant]) (Covishield 26,375, Covaxin 1,967)	28 342	2256/28,342 (Clinical)	7760/28 342 (Nursing), 5172/ 28 342 (Administration), 3000/ 28 342 (Para-medical staff)	1,438	33.04 (18–80)	14 980/ 13 362 (total)
Keehner, 2021	Retrospective, December 16, 2020–February 9, 2021, Multicenter, USA	Pfizer-BioNTech COVID-19 Vaccine (BNT162B2) and Moderna Covid Vaccine (mRNA-1273)	36 659	NR	NR	379	–	–

TABLE 1 (Continued)

Author	Design	Vaccine type	Total patients enrolled	Healthcare worker type		Total COVID-19 positive patients	Age, years [*SD*] (range)	Sex (male/female)
				Physician	Nonphysician			
Tyagi, 2021	Retrospective, January 16, 2021–till date, Single-center, India	85 (Covishield), 28 (Covaxin) 113 (vaccinated)	123	NR	NR	19	42 (22–70)	75/48 (total)
Sharma, 2021	Cross-sectional study (May 31, 2021–June 6, 2021), January 2021–March 2021 (Subjects Data), Single-center, India	158 (Covishield), 168 (Covaxin)	326	259/326 (Medical doctors and Interns)	52/326 (Frontline health workers), 12/326 (Lab technicians), 3/326 (Nurses)	65	29.1 (85.9)	212/114
Angel, 2021	Single-center, retrospective cohort study, December 20, 2020, and February 25, 2021, Israel	Pfizer-BioNTech BNT162b2	6710	1231/5953 (Vaccinated), 44/757 (Unvaccinated)	2421/5953 (Vaccinated), 324/757 (Unvaccinated) [Administration], 1438/5953 (Vaccinated), 263/757 (Unvaccinated) [Nursing], 721/5953 (Vaccinated), 98/757 (Unvaccinated) [Other health professions], 142/5953 (Vaccinated), 28/757 (Unvaccinated) [Missing data]	270	44.3 [12.5]	2245/4465

TABLE 2 Study details

Author	Patients			COVID-19 positive			COVID + HCW type	
	Partial vaccination	Full vaccination	Unvaccinated	Partial vaccination	Full vaccination	Unvaccinated	Physician	Nonphysician
Amit, 2021	4081	–	–	22/4081	–	–	6/22	Nurse 5/22, Secretary 3/22, Laundry handler 1/22, Food handler 1/22, Technologist 1/22, Psychologist 1/22, Scientist 1/22, Phlebotomist 1/22, Cleaning services 1/22, Logistics 1/22
Azamgarhi, 2021	1409	–	826	23/1409	–	26/826	NR	NR
Bouton, 2021	7109	5913	3481	96/7109	17/5913	329/3481	13/96	Health care support worker 9/96, Nurse 31/96, Nurse Practitioner/ Physician Assistant 5/96, Administrative Staff 3/ 96, Environmental Services 2/96, Medical technician 6/96, OT, PT or speech therapist 1/96, Pharmacy worker 5/96, Respiratory Therapist 2/ 96, Others 17/96
Tang, 2021	3052	2776	2165	41/3052	10/2776	185/2165	NR	NR
Cucunawangsiha, 2021	–	1040	–	–	13/1040	–	NR	Nurse 5/13, Admission clerk 2/13, Housekeeper 1/13, Lab staff 1/13, Finance staff 1/13, Hospital security 1/13, ICU staff 1/13, Medical treatment center staff 1/13
Hall, 2021	20 641	1607	2683	71/20641	9/1607	977/2683	NR	NR
Issac, 2021	–	243	80	–	16/243	35/80	1/41	Nurses 34/41, Pharmacist 2/ 41, Lab & Diagnostics 9/ 41, Housekeeping 2/41, Physiotherapy 1/41, Medical records 1/41, Maintenance 1/41

TABLE 2 (Continued)

Author	Patients			COVID-19 positive			COVID + HCW type	
	Partial vaccination	Full vaccination	Unvaccinated	Partial vaccination	Full vaccination	Unvaccinated	Physician	Nonphysician
Jacobson, 2021	23 090	22 271	6910	150/23090	39/22 271	471/6910	22/189 (Physician/ physician assistant/ nurse practitioner)	Nursing 42/189, Medical Assistant 17/189, Respiratory therapy/ physical therapy/ occupational therapy 5/189, Other 76/189, Housekeeping/food services 22/189
Maroof, 2021	–	39 512	–	–	124/39 512	–	31/124 (Doctors)	28/124 (Nurses), 20/124 (Paramedics), 45/124 (Support Staff)
Mathema, 2021	23 697	22 458	–	105/23697	33/22 458	–	NR	NR
North, 2021	2036	1923	593	10/2036	3/1923	6/593	10/19 (Physician/Nurse practitioner/Physician assistant)	2/19 (Admin), 3/19 (Research), 1/19 (Food services), 2/19 (Nursing), 1/19 (Patient care services)
Pandurangaiah, 2021	18	164	–	1/18	5/164	–	NR	NR
Sabnis, 2021	–	461	–	–	86/461	–	19/86 (Doctors)	27/86 (Nurses/Technicians), 40/86 (Para-medical staff)
Vaishya, 2021	5125	23 217	–	269/5125 (within 2 weeks 46, after 2 weeks 223)	1169/23 217 (within 2 weeks 69, after 2 weeks 1100)	–	153/1438 (Clinical)	448/1438 (Nursing), 264/ 1438 (Administration), 140/1438 (Para-medical)
Keehner, 2021	36 659	28 184	–	342/36 659	37/28 184	–	NR	NR
Tyagi, 2021	6	107	10	1/6	18/107	–	NR	NR
Sharma, 2021	46	280	–	12/46	53/280	–	55/65	10/65
Angel, 2021	5953	5517	757	127/5761	27/5372	116/757	NR	NR

Author	Asymptomatic COVID-19 positive			Symptomatic COVID-19 positive			Time to symptom onset (d: days)	Median F/u time (d: days)	COVID-19 Outcomes		
	Partial vaccination	Full vaccination	Unvaccinated	Partial vaccination	Full vaccination	Unvaccinated			Hospitalized	ICU	Death
Amit, 2021	11/22	–	–	11/22	–	–	3.5 (0–10) [Median]	–	–	–	–
Azamgarhi, 2021	2/23	–	6/26	21/23	–	20/26	3.5 (0–10)	–	–	–	–
Bouton, 2021	20/96	–	–	76/96	–	–	1-14 d (67), 15 + d (29)	–	–	–	–

(Continues)

TABLE 2 (Continued)

Author	Asymptomatic COVID-19 positive			Symptomatic COVID-19 positive			Time to symptom onset (d: days)	Median F/u time (d: days)	COVID-19 Outcomes		
	Partial vaccination	Full vaccination	Unvaccinated	Partial vaccination	Full vaccination	Unvaccinated			Hospitalized	ICU	Death
Tang, 2021	29/51		79/185	22/51		106/185	NR	Median F/U time – 81 d (unvaccinated); 72 d (vaccinated)	–	–	–
Cucunawangsiha, 2021	–	2/13	–	–	11/13	–	5 (2 – 11)	–	–	–	–
Hall, 2021	15/80		676/977	65/80		543/977		Median F/U time – 59 days post-first dose (median 21, 13–31), 39 days post-second dose (23, 17–28)	–	–	–
Issac, 2021	–	–	–	–	16/243	–	65 (20 – 91)	–	0/16 (FV)	0/16 (FV)	0/16 (FV)
Jacobson, 2021	–	8/39	–	–	31/39	–	8 (3–18)	–	2/189 (FV + PV)	–	0/189 (FV + PV)
Maroof, 2021	–	117/124 [Asymptomatic/Mild]	–	–	7/124	–	36.5 (26-62) [FV]	–	–	–	0/124 (FV)
Mathema, 2021	21/138		–	117/138	–	–	105/138 (1-113 d) [PV], 33/138 (4-104 d) [FV]	–	5/138 (FV + PV)	–	–
North, 2021	4/10	2/3	1/6	–	–	–	FV – 17 days [12, 22], PV – 26 days [15, 36]	–	0/13 (FV + PV)	–	–

TABLE 2 (Continued)

Author	Asymptomatic COVID-19 positive			Symptomatic COVID-19 positive			Time to symptom onset (d: days)	Median F/u time (d: days)	COVID-19 Outcomes		
	Partial vaccination	Full vaccination	Unvaccinated	Partial vaccination	Full vaccination	Unvaccinated			Hospitalized	ICU	Death
Pandurangaiah, 2021	2/182			–	–	–	NR	–	1/6 (FV + PV)	0/6 (FV + PV)	0/6 (FV + PV)
Sabnis, 2021	–	–	–	–	86/461	–	38.42 ± 12.2 days (range 17-70 days)	–	10/86 (FV)	2/86 (FV)	1/86 (FV)
Vaishya, 2021	–	–	–	–	–	–	< or >2 weeks	–	83/1438 (FV + PV)	3/1438 (FV + PV)	0/1438 (FV + PV)
Keehner, 2021	–	–	–	–	–	–	Dose 1 – 1-7d (145), 8-14d (125), 15-21d (47), d22 (15); Dose 2 – 1-7d (22), 8-14d (8), 15d or later (7)	–	–	–	–
Tyagi, 2021	–	–	–	1/19	18/19	–	34.8 d (2-51 d) [FV]	–	1/19 (FV + PV)	–	–
Sharma, 2021	–	–	–	59 (Mild), 6 (Moderate)		–	46 (28.2, 54.7) d [FV]	–	–	–	–
Angel, 2021	63/5761	19/5372	31/757	64/5761	8/5372	85/757	NR	Unvaccinated – 66.0 (66.0-66.0), Vaccinated – 63.0 (52.0-65.0)	–	–	–

PV: Partial vaccination, FV: Full vaccination, HCW: Healthcare workers, NR: Not reported

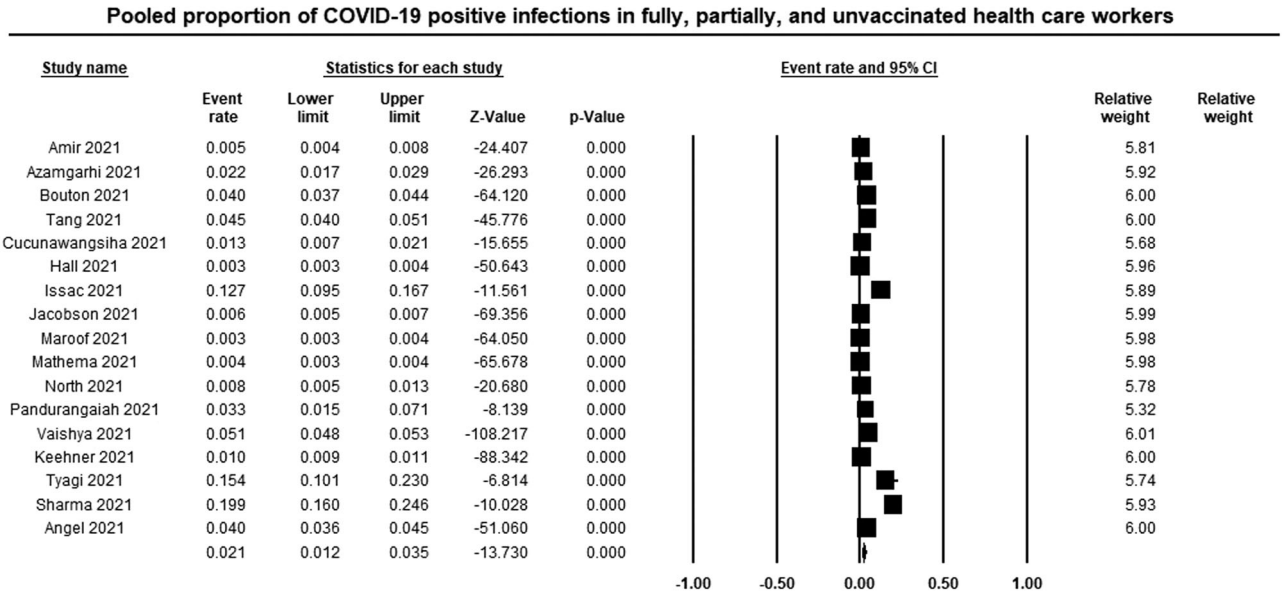

FIGURE 1 Forest plot, pooled proportion of coronavirus disease 2019 infections in fully, partially, and unvaccinated healthcare workers

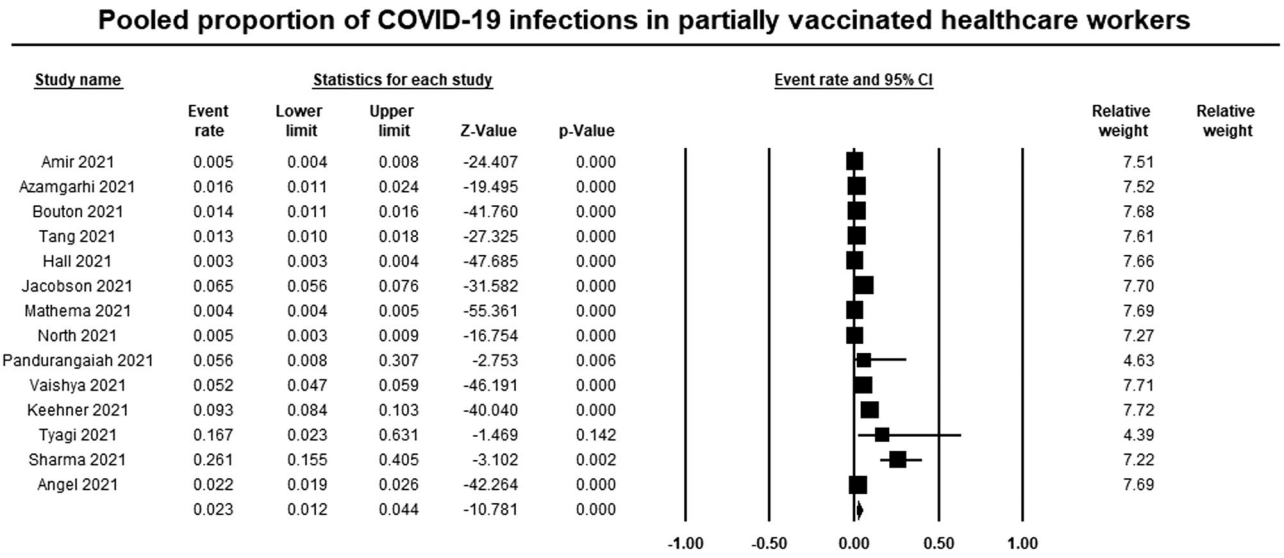

FIGURE 2 Forest plot, pooled proportion of coronavirus disease 2019 infections in partially vaccinated healthcare workers

vaccines.[40] Despite this, vaccine hesitancy in the general population and among HCWs remains a concern.[41,42] A recent review by Biswas et al.[43] reported that the prevalence of COVID-19 vaccination hesitancy worldwide in healthcare workers ranged from 4.3 to as high as 72%, with an average of 22.51% across all studies with 76 471 participants. The authors reported concerns about vaccine safety, efficacy, and potential side effects as top reasons for COVID-19 vaccination hesitancy in HCWs. Given the high prevalence of COVID-19 vaccine hesitancy in healthcare workers, communication and education strategies along with mandates for clinical workers should be considered to increase COVID-19 vaccination uptake in these high-risk individuals.[43] Studies have also shown that vaccination amongst health care workers is associated with a substantial reduction in COVID-19 cases in household contacts consistent with an effect of vaccination on transmission.[44]

At the peak of the pandemic, assessing published data between May 1 and July 9, 2020, researchers found that a significant number of HCW were reported to be infected with COVID-19 during the first 6 months of the COVID-19 pandemic, with a prevalence of hospitalization of 15.1% and mortality of 1.5%.[45] With that in mind, we analyzed the pooled prevalence of COVID-19 infections among HCWs who declined vaccinations and those who either received one or both the vaccines. Our analysis shows that only 5.7% of vaccinated HCWs required hospitalization for COVID-19 infection,

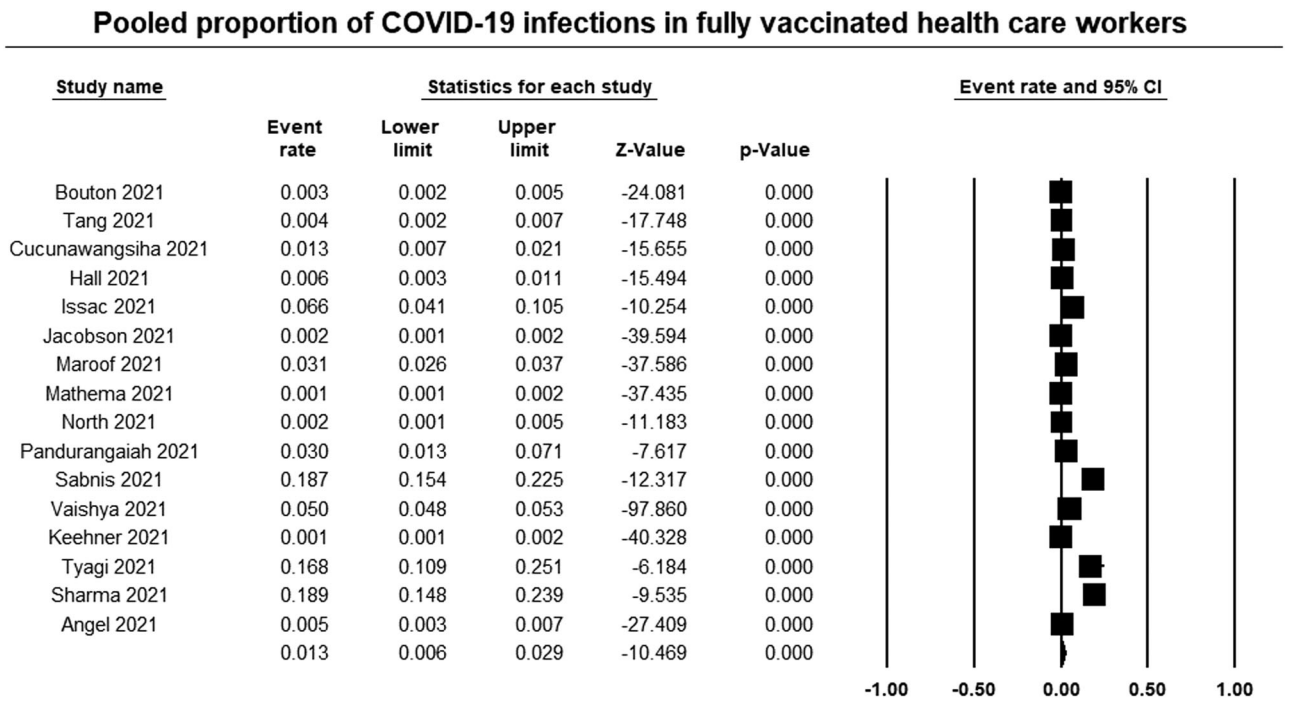

FIGURE 3 Forest plot, pooled proportion of coronavirus disease 2019 infections in fully vaccinated healthcare workers

with 2.6% needing ICU level-of-care. Mortality associated with COVID-19 infection in partially and/or fully vaccinated HCWs remained low at 1.2%.

There are several strengths to our analysis. First, we conducted a systematic literature search with well-defined inclusion criteria, careful exclusion of redundant studies, inclusion of good-quality studies with detailed extraction of data, and rigorous evaluation of study quality. All the included studies in our analysis were of high quality. Second, our analysis included outcomes separately for partially and fully vaccinated HCWs. We calculated the pooled proportion of HCWs requiring hospitalization, ICU admissions and also assessed the mortality associated with COVID-19 infection in vaccinated HCWs. Finally, our analysis included studies from different geographical locations, making our results more generalizable and clinically relevant. However, there are also several limitations to this study, most of which are inherent to any meta-analysis. Firstly, at the time of writing and based on our literature search, a total of 18 studies were included in our analysis. As active research continues to be conducted on the COVID-19 pandemic, it is possible that we may not have captured all the literature, especially studies not indexed in major databases and/or studies that are published ahead of print. Secondly, we were unable to sub-group our outcomes based on which particular vaccine was administered to the cohort of HCWs. Third, we were unable to determine the mean time to infection occurrence post-vaccination, as this information was not consistently reported in all the studies. There was considerable heterogeneity in our study outcomes likely due to variation in the type of vaccination used and median time to infection occurrence. Lastly, ten of the eighteen studies included in our analysis were retrospective in design which may have resulted in selection bias.

Nevertheless, our study is the first in the literature to assess the pooled incidence of postvaccination SARS-CoV-2 infection among health care workers around the world. Our results show a decreased incidence of COVID-19 infection as well as decreased incidence of hospitalization, ICU admission, and deaths, amongst vaccinated HCWs. Our findings support the urgent need for HCWs to consider getting vaccinated against COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Saurabh Chandan and Ojasvini C. Chandan: Conception and design, drafting of the article. Saurabh Chandan and Shahab R. Khan: Study search, review, and selection. Saurabh Chandan, Shahab R. Khan, and Daryl Ramai: Data collection and synthesis. Smit Deliwala and Babu P. Mohan: Statistical analysis of data and interpretation of results. Saurabh Chandan and Antonio Facciorusso: Critical revisions of the manuscript. All authors: critical revision of the article for important intellectual content and final approval of the article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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