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COVID-19 and healthcare workers: A systematic review and meta-analysis



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ABSTRACT

Background: The COVID-19 pandemic has focused attention on the challenges and risks faced by frontline healthcare workers (HCW). This study aimed to describe the clinical outcomes and risk factors for SARS-CoV-2 infection in HCW.

Methods: Three databases were surveyed and 328 articles were identified. Of these, 225 articles did not meet inclusion criteria; therefore, 97 full-text articles were reviewed. Finally, after further revision, 30 articles were included in the systematic review and 28 were used for meta-analysis.

Results: Twenty-eight studies were identified involving 119,883 patients. The mean age of the patients was 38.37 years (95% CI 36.72–40.03) and males comprised 21.4% (95% CI 12.4–34.2) of the population of HCW. The percentage of HCW who tested positive for COVID-19 was 51.7% (95% CI 34.7–68.2). The total prevalence of comorbidities in seven studies was 18.4% (95% CI 15.5–21.7). The most prevalent symptoms were fever 27.5% (95% CI 17.6–40.3) and cough 26.1% (95% CI 18.1–36). The prevalence of hospitalisation was 15.1% (95% CI 5.6–35) in 13 studies and of death was 1.5% (95% CI 0.5–3.9) in 12 studies. Comparisons of HCW with and without infection showed an increased relative risk for COVID-19 related to personal protective equipment, workplace setting, profession, exposure, contacts, and testing.

Conclusion: 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 hospitalisation of 15.1% and mortality of 1.5%. Further data are needed to track the continued risks in HCW as the pandemic evolves and health systems adapt.

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Introduction

On 21 December 2019, a pneumonia-like outbreak of an unknown cause or origin was found to be emerging in Wuhan, Hubei Province, China. Due to the rapidly increasing cases and unclear protocol regarding medical care, bronchoalveolar lavage samples of patients were isolated and analysed by 03 January 2020. The reports showcased a new strain of coronavirus, initially termed 2019-nCoV by the Chinese Center for Disease Control and Prevention (CDC) (Zhang, 2020) and then later named SARS-CoV-2 by the International Committee on Taxonomy of Viruses. On 11 March 2020, the World Health Organization

declared the COVID-19 outbreak a pandemic, sending millions into a state of panic and emergency, with many federal governments developing strategies to protect their citizens (World Health Organization).

With limited understanding of this novel coronavirus strain and being at the frontline, healthcare workers (HCW) were soon deemed as one of the groups with the highest risk of exposure to COVID-19 infection. By late January 2020, CDC China reported transmission of COVID-19 to 16 healthcare workers, as a result of being in contact with patients from the outbreak (Li, 2020c). It was speculated that HCW infection could potentially contribute to exacerbating the chain of transmission in hospitals and outside health facilities, and therefore proper protection of HCW against COVID-19 through mandating protective protocols had to be prioritised (Black et al., 2020).

Along with focusing on the impact of COVID-19 on the general population, numerous studies have since been published in different parts of the world outlining the implication of this virus

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on healthcare systems, pertaining to the challenges and risks faced by the frontline and high-risk HCW. The focus of these research studies has ranged from describing clinical characteristics of HCW with COVID-19, investigating the risk factors involved in acquiring the infection, transmission dynamics among HCW, to stating the observed complications and outcomes of the infection.

This study aimed to combine a systematic review of the published data, with a meta-analysis to determine the risk and clinical outcomes of infection in HCWs at the frontline of diagnosing and caring for COVID-19 infected patients. Furthermore, as part of the qualitative discussion, it aimed to explore the risk factors that may have been involved in the transmission of COVID-19 to HCW.

Methods

Study protocol

The protocol for this study was generated according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) recommendations. The PRISMA checklist was used to guide the reporting (Shamseer et al., 2015).

Information sources and search strategy

PubMed, Scopus and Google Scholar were the three databases that were searched, from 01 May to 09 July 2020, by five independent researchers. All five researchers independently evaluated the search results after finishing the database search process. The search keywords were broadly grouped into four categories: “healthcare”, “risk”, “COVID-19” and “miscellaneous” (Supplementary Table 1).

Eligibility criteria

Full-text, peer reviewed articles from 01 January to 09 July 2020 discussing SARS-CoV-2 only amongst HCW populations were included. Articles that were not in English or an English translation was not available, and articles without comprehensive data, comments or viewpoints related to HCW were excluded from the analysis.

Study selection

Full texts of the selected articles were compared with the pre-determined inclusion and exclusion criteria after the initial search results were screened by title and abstract.



PRISMA 2009 Flow Diagram

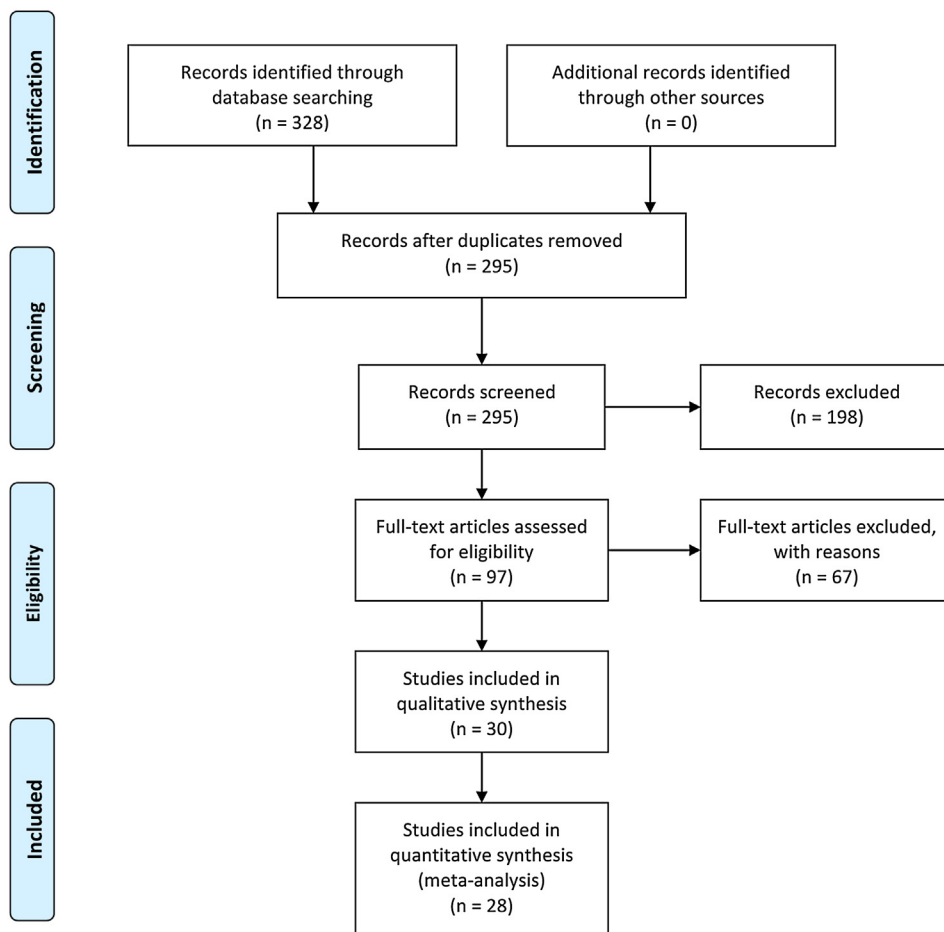


Figure 1. PRISMA flowchart of study selection process.

Data collection

The following variables were obtained for all the selected papers: name of authors, year and date of publication, study design, publishing country, and total number of HCW in the study. Regarding the quantitative part of the study, information from the selected articles was extracted by the five independent researchers and then pooled together. Data pertaining to demographics (age and gender), comorbidities (diabetes mellitus, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), and hypertension), clinical manifestations (fever, cough, fatigue,

sputum, headache, haemoptysis, sore throat, diarrhoea, nausea and vomiting), blood investigations (anaemia, white blood cells, high lactate dehydrogenase (LDH), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and high creatinine), complications (unilateral pneumonia, bilateral pneumonia, reactive airway disease, RNA anaemia, shock, hospitalisation, discharge and death) were extracted to Microsoft Excel. Data were screened by a single researcher for duplicates. For the qualitative analysis of the study, 30 articles were thoroughly reviewed by six independent researchers to identify risk factors contributing to COVID-19 infection of HCW.

Table 1
Summary of characteristics of articles included in the study.

No.	Author	Journal	Date (MM/YY)	Country	Study type	N (total population)	N HCW with COVID-19	Quality score	Reference
1	Zhan et al.	N Engl J Med	02/20	China	Cross-sectional	23	23	8	Zhan (2020)
2	Chu et al.	J Med Virol	03/20	China	Retrospective cohort	54	38	10	Chu (2020)
3	Xing et al.	Euro Surveill	03/20	China	Case series	2	2	8	Xing et al. (2020)
4	Marjolein et al.	JAMA Netw Open	03/20	Netherlands	Cross-sectional	1353	86	8	Marjolein (2020)
5	Zheng et al.	Clin Infect Dis	03/20	China	Cross-sectional	2457	2457	8	Zheng et al. (2020)
6	Li YK et al.	Curr Med Sci	03/20	China	Retrospective cohort	148	12	10	Li et al. (2020)
7	Reusken et al.	Euro Surveill	03/20	Netherlands	Cross-sectional	1097	45	10	Reusken et al. (2020)
8	Ran et al.	Clin Infect Dis	03/20	China	Retrospective cohort	72	28	11	Ran et al. (2020)
9	McMichael et al.	N Engl J Med	03/20	United States of America	Retrospective cohort	50	50	9	McMichael (2020)
10	Sun et al.	J Infect	03/20	China	Cross-sectional	32	32	7	Sun et al. (2020)
11	Burrer et al.	MMWR Morb Mortal Wkly Rep	04/20	United States of America	Cross-sectional	8945	8495	10	Burrer (2020)
12	Wei et al.	J Microbiol Immunol Infect	04/20	China	Prospective cohort	14	12	10	Wei et al. (2020)
13	Kimball et al.	MMWR Morb Mortal Wkly Rep	04/20	United States of America	Cross-sectional	–	1	9	Kimball et al. (2020)
14	Wang et al.	J Hosp Infect	04/20	China	Cross-sectional	80	80	8	Wang et al. (2020)
15	Schwierzeck et al.	Dtsch Arztebl Int	04/20	Germany	Cross-sectional	957	52	9	Schwierzeck et al. (2020)
16	Canova et al.	Swiss Med Wkly	04/20	Switzerland	Cross-sectional	21	0	8	Canova et al. (2020)
17	Tostmann et al.	Euro Surveill	04/20	Netherlands	Cross-sectional	803	90	9	Tostmann et al. (2020)
18	Heinzerling et al.	MMWR Morb Mortal Wkly Rep	04/20	United States of America	Cross-sectional	43	43	8	Heinzerling et al. (2020)
19	Breazzano et al.	J Clin Invest	04/20	United States of America	Cross-sectional	264	101	9	Breazzano et al. (2020)
20	Nguyen et al.	Lancet Public Health	05/20	United States of America	Prospective cohort	99,795	1922	11	Nguyen et al. (2020b)
21	Lai et al.	JAMA Netw Open	05/20	China	Case-series	110	110	9	Lai et al. (2020)
22	Chow et al.	JAMA Netw Open	05/20	United States of America	Cross-sectional	48	48	8	Chow et al. (2020)
23	Korth et al.	J Clin Virol	05/20	Germany	Cross-sectional	316	5	9	Korth et al. (2020)
24	Felice et al.	J Community Health Res	05/20	Italy	Cross-sectional	388	18	9	Felice et al. (2020)
25	Jin et al.	Mil Med Res	05/20	China	Cross-sectional	103	84	8	Jin et al. (2020)
26	Cabas et al.	Res Social Adm Pharm	05/20	Italy	Cross-sectional	1632	15	9	Cabas et al. (2021)
27	Chen et al.	J Infect	05/20	China	Prospective cohort	105	18	11	Chen et al. (2020)
28	Garzaro et al.	Med Lav	05/20	Italy	Cross-sectional	830	80	9	Garzaro et al. (2020)
29	Guo et al.	J Bone Joint Surg Am	05/20	China	Cross-sectional	24	24	10	Guo et al. (2020)
30	Rivera-Izquierdo et al.	Int J Environ Res Public Health	06/20	Spain	Prospective cohort	76	76	11	Rivera-Izquierdo et al. (2020)

Statistical approach

The distribution of the categorical dichotomous variables was described by calculating percentages. The mean and 95% confidence intervals (CI) were calculated for continuous data. For studies reporting the mean with 95% CI or the range of the data, the formula (upper limit-lower limit)/4 was used to extract the standard deviation. Meta-analysis using the random-effect model was performed to estimate the pooled prevalence and 95% CI. The pooled percentage, prevalence and corresponding 95% CI were calculated in order to indicate the weighted effect size for all binary variables. The measure of heterogeneity was reported by including Cochran's Q statistics and I² index, with the level of heterogeneity defined as poor <25, moderate >50, and high >75, and the Tau square (T²) test. Publication bias was assessed with a funnel plot and Egger's test.

Results

Search results

Three databases—PubMed, Scopus and Google Scholar—were searched from 01 May 2020 to 09 July 2020 using predefined keywords and a search strategy (Supplementary Table 1). The

literature retrieval flowchart is represented in Figure 1. During the initial phase of the search, 328 articles were identified; 33 duplicates were removed. After screening the abstracts, 198 articles were further excluded due to failure to meet the inclusion criteria. Ninety-seven full-text articles were downloaded and reviewed. Of these, 67 were excluded due to lack of sufficient data, comment or viewpoint, as well as three articles that were in languages other than English and where an English translation of the article was not available. The final count of articles for systematic review was 30, and 28 of those articles, published from February 2020 to June 2020, were used for meta-analysis (Figure 1 and Table 1).

Table 1 provides a summary of characteristics of the included articles. A great variety of articles from different countries were noted: 13 were from China, seven from USA, three each from Netherlands and Italy, two from Germany, and one from Spain. The most common study type amongst the articles was cross-sectional (n = 19) and the remaining were a mix of retrospective and prospective cohort studies, with the exception of one case-series article (Table 1).

Twenty-nine variables were included in the meta-analysis (Tables 2–6). Most of the studies showed considerable heterogeneity (I² > 75%) (Table 2). Fewer studies had evidence of bias, as demonstrated by Egger's test (p > 0.05) (Table 2).

Table 2
Meta-analysis of healthcare workers.

Item	No. of studies	Prevalence%	95% CI	n	Q	I ²	T ²	p-value	Egger's test
Demographical characteristics									
Age (years, mean)	24	38.73	37.83–39.63	23	2,326.49	99.01	3.104	<0.001	0.0572
Male	27	21.4	12.4–34.2	26	7,356.1	99.6	2.796	<0.001	0.8925
Comorbidity	7	18.4	15.5–21.7	6	25.30	76.29	0.0037	<0.001	0.5678
DM	9	1.5	0.3–8.2	8	763.46	98.95	6.311	<0.001	0.2436
Hypertension	7	2.5	0.2–27.9	6	584.15	98.90	12.69	<0.001	0.2374
CVD	5	2.4	0.7–7.5	4	8.01	50.06	0.878	0.091	0.0743
COPD	5	2.4	0.9–6.4	4	6.83	41.43	0.519	0.145	0.1083
Clinical manifestations									
Tested positive	28	51.7	34.7–68.2	27	2,611.19	98.97	2.908	<0.001	0.0001
Fever	20	24.6	12.2–43.4	19	11,287.11	99.83	3.61	<0.001	0.2096
Cough	21	23.3	13.6–37	20	9,652.89	99.79	2.15	<0.001	0.1306
Fatigue	16	22.1	14.9–31.6	15	3,139.76	99.52	0.805	<0.001	0.2816
Sputum	5	17.6	10.1–28.8	4	10.33	61.27	0.28	0.035	0.8148
Headache	16	15.1	9.0–22.6	15	3,241.08	99.54	0.82	<0.001	0.2982
Sore throat	15	13.7	9.4–19.5	14	1,507.93	99.07	0.49	<0.001	0.1912
Diarrhoea	16	9.8	5.3–17.2	15	3,142.05	99.52	1.53	<0.001	0.1981
Nausea and vomiting	10	11.8	5.8–22.6	9	143.86	93.74	1.19	<0.001	0.9016
Laboratory findings									
Leucocytosis	7	49.4	10.3–89.2	6	122.59	95.11	7.53	<0.001	0.9856
Leukopenia	4	13	5.5–27.8	3	20.92	85.66	0.75	<0.001	0.1634
Lymphopenia	4	29.1	12–55.1	3	40.52	92.60	1.112	<0.001	0.4001
High creatinine	2	22.6	7.2–52.5	1	18.44	94.58	0.869	<0.001	NA
High LDH	2	12.2	0.4–84.3	1	35.59	97.19	6.753	<0.001	NA
High CRP	3	17.3	5.1–45	2	25.33	92.11	1.321	<0.001	0.6070
Complications									
Unilateral Pneumonia	2	26.8	19.4–35.8	1	0.505	0	0	0.4736	NA
Bilateral Pneumonia	5	78.7	43.9–94.6	4	43.26	90.75	90.75	<0.001	0.2858
Ground glass Opacity	5	67.5	41.4–86	4	28.46	85.95	1.092	<0.001	0.3812
ARDS	2	12.2	0–97.8	1	15.74	93.65	16.344	<0.001	NA
Outcomes									
Hospitalisation	13	15.1	5.6–35	14	176.195	93.19	3.167	<0.001	0.4417
Discharge	7	47.5	10.9–87	6	96.035	93.74	6.289	<0.001	0.7948
Death	12	1.5	0.5–3.9	11	80.56	86.35	2.066	<0.001	0.1700

Abbreviations: No., number; CI, confidence interval; LDH, lactate dehydrogenase; ARDS, acute respiratory distress syndrome; n, degree of freedom; CRP, C-reactive protein; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; ARDS, acute respiratory distress syndrome.
Q, Cochran's Q statistic for heterogeneity.
T², Tau-squared measure of heterogeneity.
I², Index for the degree of heterogeneity.

Meta-analysis results

Demographic characteristics

The total number of patients analysed across the 28 studies was 119,883. The mean age of the patients was 38.37 years (95% CI 36.72–40.03) and males comprised 21.4% (95% CI 12.4–34.2) of the population of HCW (Table 2).

Comorbidities

The total prevalence of comorbidities in the seven included studies was 18.4% (95% CI 15.5–21.7), the most prevalent being

hypertension 2.5% (95% CI 0.2–27.2), CVD 2.4% (95% CI 0.7–7.5), COPD 2.4 (95% CI 0.9–6.4), and diabetes 1.4% (95% CI 0.1–12.9) (Table 2).

Clinical manifestations

Across 28 studies, 51.7% (95% CI 34.7–68.2) of HCW tested positive for COVID-19. Regarding the symptoms of COVID-19 amongst HCW, the most prevalent finding was fever 27.5% (95% CI 17.6–40.3), followed by cough 26.1% (95% CI 18.1–36), fatigue 23.4% (95% CI 12.7–39), sputum 17.6% (95% CI 10.1–28.8), headache 15.1% (95% CI 9.0–24.1), sore throat 13.3% (95% CI 8.2–20.9), nausea and

Table 3
Demographical characteristics and comorbidities.

Author	Date	N	Mean age	Age range	Male	N (%)	Comorbidities	Diabetes	Hypertension	Cardiovascular disease	COPD/lung disease
Burrer et al.	04/2020	8945	42	16–>65	2464 (27.5%)	1779 (19.9%)	N/A	N/A	N/A	N/A	N/A
Chu et al.	03/2020	54	39	26–73	36 (66.7%)	N/A	N/A	N/A	N/A	N/A	N/A
Wei et al.	04/2020	14	36	27–51	4 (28.6%)	1 (7.7%)	0	0	0	0	0
Xing et al.	03/2020	2	30	20–40	1 (50%)	N/A	N/A	N/A	N/A	N/A	N/A
Zhan et al.	02/2020	23	55	29–72	17 (73.9%)	5 (21.7%)	N/A	N/A	N/A	N/A	N/A
Marjolein et al.	03/2020	1353	49	22–66	15 (1.1%)	N/A	N/A	N/A	N/A	N/A	N/A
Wang et al.	04/2020	80	39	N/A	31 (38.7%)	N/A	1 (1.2%)	10 (12.5%)	2 (2.5%)	1 (1.2%)	
Nguyen et al.	05/2020	99,795	42	N/A	16,965 (17%)	N/A	2495 (2.5%)	N/A	1597 (1.6%)	13,073 (13.1%)	
Zheng et al.	03/2020	2457	N/A	N/A	681 (27.7%)	N/A	N/A	N/A	N/A	N/A	
Schwierzeck et al.	04/2020	957	35	N/A	370 (38.7%)	N/A	N/A	N/A	N/A	N/A	
Canova et al.	04/2020	21	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Ran et al.	03/2020	72	31	21–66	22 (30.6%)	N/A	N/A	N/A	N/A	N/A	
Lai et al.	05/2020	110	36.5	N/A	31 (28.2%)	14 (12.7%)	1 (0.9%)	12 (10.9%)	0 (0%)	2 (1.8%)	
Chow et al.	05/2020	48	43	22–79	11 (22.9%)	N/A	N/A	N/A	N/A	N/A	
Tostmann et al.	04/2020	803	N/A	N/A	19 (2.4%)	N/A	N/A	N/A	N/A	N/A	
Reusken et al.	03/2020	1097	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Heinzerling et al.	04/2020	43	39	27–60	7 (16.3%)	N/A	N/A	N/A	N/A	N/A	
Breazzano et al.	04/2020	264	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Korth et al.	05/2020	316	N/A	N/A	112 (35.4%)	N/A	N/A	N/A	N/A	N/A	
Felice et al.	05/2020	388	N/A	N/A	N/A	63 (16.2%)	N/A	N/A	N/A	N/A	
McMichael et al.	03/2020	50	43.5	21–79	12 (24%)	18 (36%)	5 (10%)	4 (8%)	4 (8%)	N/A	
Jin et al.	05/2020	103	35	N/A	39 (37.9%)	N/A	N/A	N/A	N/A	N/A	
Cabasa et al.	05/2020	1632	40.7	30–60	336 (20.6%)	269 (16.5%)	N/A	N/A	N/A	N/A	
Sun et al.	03/2020	32	33.8	22–56	4 (12.5%)	N/A	N/A	N/A	N/A	N/A	
Chen et al.	05/2020	105	30	26–39.5	2 (1.9%)	N/A	N/A	N/A	N/A	N/A	
Rivera-Izquierdo et al.	06/2020	76	45.8	N/A	23 (30.3%)	N/A	5 (6.6%)	8 (10.5%)	N/A	5 (6.6%)	
Garzaro et al.	05/2020	830	46	N/A	276 (33.2%)	N/A	N/A	N/A	N/A	N/A	
Guo et al.	05/2020	24	36.1	25–48	23 (95.8%)	N/A	1 (4.2%)	N/A	N/A	N/A	

Abbreviations: COPD, chronic obstructive pulmonary disease; N/A, not available; N, number.

Table 4
Clinical manifestations.

Author	Date	N	N (%) Fever N (%)	Cough N (%)	Sore throat N (%)	Fatigue N (%)	Sputum N (%)	Headache N (%)	Haemoptysis N (%)	Diarrhoea N (%)	Nausea and vomiting N (%)
Burrer et al.	04/2020	8945	3196 (35.7%)	3694 (41.3%)	1790 (20%)	3122 (34.9%)	N/A	3048 (34%)	N/A	1507 (16.8%)	923 (10.3%)
Chu et al.	03/2020	54	36 (66.7%)	17 (31.5%)	1 (1.8%)	9 (16.7%)	3 (5.6%)	N/A	N/A	3 (5.6%)	1 (1.8%)
Wei et al.	04/2020	14	12 (85.7%)	10 (71.4%)	7 (50%)	14 (100%)	5 (35.7%)	8 (57.1%)	N/A	9 (64.3%)	2 (14.3%)
Xing et al.	03/2020	2	1 (50%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Zhan et al.	02/2020	23	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Marjolein et al.	03/2020	1353	46 (3.4%)	66 (4.9%)	34 (2.5%)	65 (4.8%)	N/A	49 (3.6%)	N/A	16 (1.2%)	15 (1.1%)
Wang et al.	04/2020	80	65 (81.2%)	47 (58.7%)	N/A	28 (35%)	19 (23.7%)	8 (10%)	N/A	15 (18.7%)	N/A
Nguyen et al.	05/2020	99,795	2795 (2.8%)	6986 (7.0%)	10,079 (10.1%)	13,772 (13.8%)	N/A	12,275 (12.3%)	N/A	3493 (3.5%)	N/A
Zheng et al.	03/2020	2457	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Schwierzeck et al.	04/2020	957	78 (8.1%)	345 (36%)	309 (32.3%)	11 (1.1%)	N/A	191 (20%)	N/A	35 (3.7%)	N/A
Canova et al.	04/2020	21	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	21
Ran et al.	03/2020	72	24 (33.3%)	17 (23.6%)	2 (2.8)	N/A	N/A	2 (2.8%)	N/A	2 (2.8%)	N/A
Lai et al.	05/2020	110	67 (60.9%)	62 (56.4%)	55 (50%)	66 (60%)	16 (14.5%)	33 (30%)	1 (0.9%)	39 (35.4%)	15 (13.6%)
Chow et al.	05/2020	48	36 (75%)	42 (87.5%)	12 (25%)	14 (29.2%)	N/A	20 (41.7%)	N/A	16 (33.3%)	8 (16.7%)
Tostmann et al.	04/2020	803	51 (6.3%)	53 (6.6%)	36 (4.5%)	57 (7.1%)	N/A	64 (8%)	N/A	N/A	N/A
Reusken et al.	03/2020	1097	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Heinzerling et al.	04/2020	43	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Breazzano et al.	04/2020	264	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Korth et al.	05/2020	316	1 (0.3%)	0 (0%)	0 (0%)	1 (0.3%)	N/A	2 (0.6%)	N/A	1 (0.3%)	N/A
Felice et al.	05/2020	388	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
McMichael et al.	03/2020	50	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Jin et al.	05/2020	103	50 (48.5%)	35 (34%)	N/A	43 (41.7%)	N/A	N/A	N/A	N/A	3 nausea (2.9%) 2 vomiting (1.9%)
Cabasa et al.	05/2020	1632	127 (7.8%)	137 (8.4%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sun et al.	03/2020	32	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chen et al.	05/2020	105	2 (1.9%)	6 (5.7%)	3 (2.9%)	N/A	N/A	2 (1.9%)	N/A	3 (2.9%)	N/A
Rivera-Izquierdo et al.	06/2020	76	34 (44.7%)	47 (61.8%)	34 (44.7%)	64 (84.2%)	N/A	48 (63.2%)	N/A	31 (40.8%)	17 nausea (22.4%) 7 vomiting (9.2%)
Garzaro et al.	05/2020	830	152 (18.3%)	305 (36.7%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Guo et al.	05/2020	24	20 (83.3%)	15 (62.5%)	2 (8.3%)	17 (70.8%)	N/A	8 (33.3%)	N/A	9 (37.5%)	N/A

Abbreviations: N, number; N/A, not available.

vomiting 11.8% (95% CI 5.8–22.6), and diarrhoea 10.6% (95% CI 5.9–18.4) (Table 2).

Blood investigations and imaging

The most prevalent laboratory finding was leucocytosis 49.4% (95% CI 10.3–89.2), followed by lymphopenia 29.1% (95% CI 12–55.1), high creatinine 22.6% (95% CI 7.2–52.5), high CRP 17.3% (95% CI 5.1–45), leukopenia 13% (95% CI 5.5–27.8), and high LDH 12.2% (95% CI 0.4–84.3). Regarding radiological imaging, the most common pneumonia finding was bilateral pneumonia, with a prevalence of 78.7% (95% CI 43.9–94.6). Other findings included

ground-glass opacity with a prevalence of 67.5% (95% CI 41.4–86) and unilateral pneumonia with a prevalence of 26.8% (95% CI 19.4–35.8) (Table 2).

Course of illness, complications and outcomes

Two studies reported ARDS as a complication of COVID-19 infection, with a prevalence of 12.2% (95% CI 0–97.8). Across 13 studies, using the random-effect model to find the pooled prevalence and 95% CI, the prevalence of hospitalisation of HCW was 15.1% (95% CI 5.6–35) and across seven studies, prevalence of discharge from the hospital was 47.5% (95% CI 10.9–87). In 12

Table 5
Laboratory investigations.

Author	Date	N	N (%)					
			Leucocytosis N (%)	Leukopenia N (%)	Lymphopenia N (%)	High creatinine N (%)	High LDH N (%)	High CRP N (%)
Burrer et al.	04/2020	8945	N/A	N/A	N/A	N/A	N/A	N/A
Chu et al.	03/2020	54	N/A	N/A	N/A	N/A	N/A	N/A
Wei et al.	04/2020	14	N/A	N/A	N/A	N/A	N/A	N/A
Xing et al.	03/2020	2	N/A	N/A	N/A	N/A	N/A	N/A
Zhan et al.	02/2020	23	N/A	N/A	N/A	N/A	N/A	N/A
Marjolein et al.	03/2020	1353	N/A	N/A	N/A	N/A	N/A	N/A
Wang et al.	04/2020	80	5 (6.2%)	19 (23.7%)	38 (47.5%)	19 (23.7%)	37 (46.2%)	N/A
Nguyen et al.	05/2020	99,795	N/A	N/A	N/A	N/A	N/A	N/A
Zheng et al.	03/2020	2457	N/A	N/A	N/A	N/A	N/A	N/A
Schwierzeck et al.	04/2020	957	N/A	N/A	N/A	N/A	N/A	N/A
Canova et al.	04/2020	21	N/A	N/A	N/A	N/A	N/A	N/A
Ran et al.	03/2020	72	N/A	N/A	N/A	N/A	N/A	N/A
Lai et al.	05/2020	110	N/A	N/A	N/A	N/A	N/A	N/A
Chow et al.	05/2020	48	N/A	N/A	N/A	N/A	N/A	N/A
Tostmann et al.	04/2020	803	N/A	N/A	N/A	N/A	N/A	N/A
Reusken et al.	03/2020	1097	N/A	N/A	N/A	N/A	N/A	N/A
Heinzerling et al.	04/2020	43	N/A	N/A	N/A	N/A	N/A	N/A
Breazzano et al.	04/2020	264	N/A	N/A	N/A	N/A	N/A	N/A
Korth et al.	05/2020	316	N/A	N/A	N/A	N/A	N/A	N/A
Felice et al.	05/2020	388	N/A	N/A	N/A	N/A	N/A	N/A
McMichael et al.	03/2020	50	N/A	N/A	N/A	N/A	N/A	N/A
Jin et al.	05/2020	103	N/A	24.1%	39.5%	N/A	N/A	31.8%
Cabasa et al.	05/2020	1632	N/A	N/A	N/A	N/A	N/A	N/A
Sun et al.	03/2020	32	N/A	N/A	N/A	N/A	N/A	N/A
Chen et al.	05/2020	105	N/A	N/A	N/A	N/A	N/A	N/A
Rivera-izquierdo et al.	06/2020	76	N/A	N/A	N/A	N/A	N/A	N/A
Garzaro et al.	05/2020	830	N/A	N/A	N/A	N/A	N/A	N/A
Guo et al.	05/2020	24	N/A	3 (12.5%)	14 (58.3%)	N/A	N/A	6 (25%)

Abbreviations: LDH, lactate dehydrogenase; CRP, C-reactive protein; N/A, not available.

studies, prevalence of death was 1.5% (95% CI 0.5–3.9) (Table 2). Funnel plots of hospitalisations and deaths are shown in Figure 2, and these indicate a minimal risk of bias related to death rates, but more potential bias in terms of reporting hospitalisation rates.

Risk factors

Thirty articles were thoroughly revised by six independent researchers looking for risk factors contributing to HCW COVID-19 infection. Of 30 articles, seven yielded information regarding the pertinent risk factors. A summary of the main points regarding risk factors in the respective articles can be found in Table 7. The identified risk factors were categorised into the following six entities: personal protective equipment (PPE), workplace setting, profession, exposure, contacts, and testing (Table 7).

Discussion

This systematic review and meta-analysis summarised the available clinical information and characteristics of HCW with COVID-19, as well as the risk factors involved in making them more susceptible to the infection. The PRISMA guidelines were followed and 30 articles were filtered in three online databases (Shamseer et al., 2015). This article analysed 119,883 HCW, with a 51.7% prevalence of testing positive for COVID-19 from the analysable reports. Note that many of these reports included only HCW with COVID-19 infections. The articles were primarily from China, and additional countries included USA, Netherlands, Italy, Germany, and Spain (Table 1).

Of the HCW who were analysed, a wide spectrum of symptoms, comorbidities and complications were observed. As a group, HCW were generally found to be a young working age population (mean age 38.73 years), and the clinical characteristics of this group were likely similar to others in this age distribution. It was found that the predominant symptoms in HCW with COVID-19 included fever, closely followed by cough and fatigue (Guan et al., 2020; Li et al.,

2020b; Sun et al., 2020). Patients with comorbidities have been shown to have a greater risk of symptomatic infection with COVID-19, with a worse prognosis than those without (Sanyaolu et al., 2020). In this study, 18.4% of the infected healthcare workers had pre-existing conditions. While hypertension was deemed to be the most prevalent (2.5%), CVD and COPD closely followed with a prevalence of 2.4%, and diabetes was present in 1.4%. These findings contrast with preliminary data related to comorbidities in the general population of COVID-19 patients found in a meta-analysis of reports from China, where the prevalence of these comorbidities was higher: hypertension in 15.8%, CVD in 11.7%, diabetes in 9.4%, and COPD in 1.4%. The generally lower prevalence rates of comorbidities in HCW compared with the general population is likely explained by ‘The Healthy Worker Effect’ phenomenon, which has been described by some as “the reduction of mortality or morbidity of occupational cohorts when compared with the general population” (Shah, 2009).

Along with comorbidities, this study additionally explored the main laboratory findings in COVID-19 infection: leucocytosis, lymphopenia and an elevated CRP. In line with the laboratory results in this study, other studies have reported a decrease in CD4+ and CD8+ cells, attributed to lymphocyte consumption during the infection process, and an increased cytokine release, which is correlated with disease severity and mortality (Huang et al., 2020; Li et al., 2020a; Qin et al., 2020; Ruan et al., 2020). Bilateral pneumonia was the most observed imaging finding within the current analysis for HCW, followed by ground-glass opacity. Ground-glass opacity was found to be the most common finding amongst patients in the general population, whereas consolidations were more frequently seen amongst those who were deemed to be severely ill (Li et al., 2020b). No results for the presence of shock, anaemia or elevated ESR were described in the analysed papers.

The outcomes of COVID-19 in HCW remained markedly better compared with those reported from most studies from the general

Table 6
Course of disease and complications.

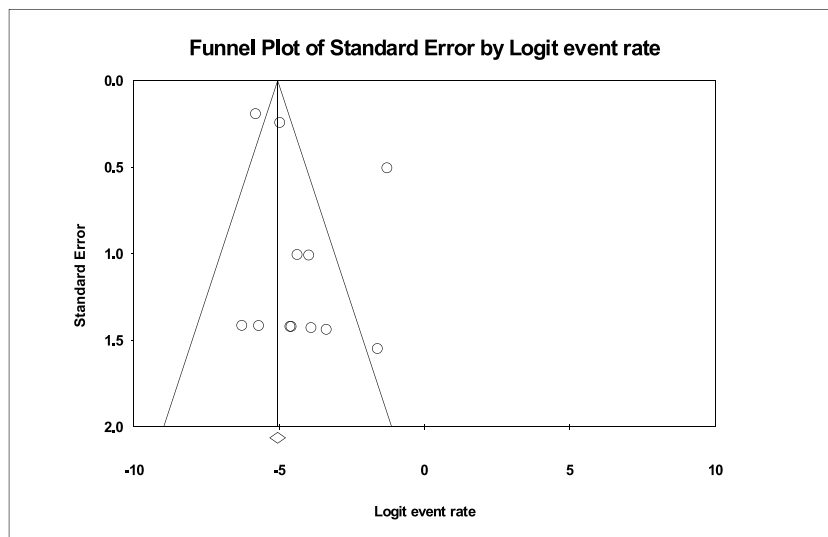
Author	Date	N	N (%) Unilateral pneumonia N (%)	Bilateral pneumonia N (%)	Ground-glass opacity N (%)	ARDS N (%)	Hospitalisation N (%)	Discharge N (%)	Death N (%)
Burrer et al.	04/ 2020	8945	N/A	N/A	N/A	N/A	723 (8.1%)	N/A	27 (0.3%)
Chu et al.	03/ 2020	54	N/A	46 (85.2%)	39 (72.2%)	N/A	54 (100%)	15 (27.8%)	1 (1.8%)
Wei et al.	04/ 2020	14	N/A	12 (85.7%)	12 (85.7%)	N/A	14 (100%)	14 (100%)	0 (0%)
Xing et al.	03/ 2020	2	1 (50%)	0 (0%)	0 (0%)	N/A	2 (100%)	2 (100%)	0 (0%)
Zhan et al.	02/ 2020	23	N/A	N/A	N/A	16 (69.6%)	23 (100%)	0 (0%)	23 (100%)
Marjolein et al.	03/ 2020	1353	N/A	N/A	N/A	N/A	27 (2%)	N/A	N/A
Wang et al.	04/ 2020	80	N/A	79 (98.7%)	N/A	3 (4%)	80 (100%)	78 (97.5%)	1 (1.25%)
Nguyen et al.	05/ 2020	99,795	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Zheng et al.	03/ 2020	2457	N/A	N/A	N/A	N/A	N/A	N/A	17 (0.7%)
Schwierzeck et al.	04/ 2020	957	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Canova et al.	04/ 2020	21	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ran et al.	03/ 2020	72	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lai et al.	05/ 2020	110	29 (26.4%)	49 (44.5%)	45 (40.9%)	N/A	N/A	N/A	N/A
Chow et al.	05/ 2020	48	N/A	N/A	N/A	N/A	3 (6.2%)	N/A	0 (0%)
Tostmann et al.	04/ 2020	803	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Reusken et al.	03/ 2020	1097	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Heinzerling et al.	04/ 2020	43	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Breazzano et al.	04/ 2020	264	N/A	N/A	N/A	N/A	2 (0.8%)	2 (0.8%)	0 (0%)
Korth et al.	05/ 2020	316	N/A	N/A	N/A	N/A	0 (0%)	N/A	N/A
Felice et al.	05/ 2020	388	N/A	N/A	N/A	N/A	1 (0.3%)	N/A	N/A
McMichael et al.	03/ 2020	50	N/A	N/A	N/A	N/A	3 (6%)	N/A	0 (0%)
Jin et al.	05/ 2020	103	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cabasa et al.	05/ 2020	1632	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sun et al.	03/ 2020	32	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chen et al.	05/ 2020	105	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Rivera-Izquierdo et al.	06/ 2020	76	N/A	N/A	N/A	N/A	11 (14.5%)	N/A	N/A
Garzaro et al.	05/ 2020	830	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Guo et al.	05/ 2020	24	N/A	N/A	21 (87.5%)	N/A	15 (62.5%)	16 (66.7%)	0 (0%)

population. Overall, 15% required hospitalisation, approximately 50% were discharged and death was reported in 1% of HCW with COVID-19. Factors in favour of undesirable outcomes amongst COVID-19 patients included presence of previous comorbidities, especially CVD, secondary infection, and elevated inflammatory markers on laboratory analysis (Ruan et al., 2020). This is in contrast with prior reports of SARS-CoV-1 and MERS amongst HCW. Between 2012 and 2018, 415 MERS-CoV-positive HCW were reported to the WHO, amongst which 24 (5.8%) died as a direct result of the infection (Elkholy et al., 2020). At that time, HCW with renal impairment were noted to be at highest risk of death (Shalhoub et al., 2018). Due to the limited available data on SARS

until 2003, with a relatively low total number of cases reported by the WHO (8096 cases and 774 deaths), comparison with the current pandemic trend is difficult (WHO| Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003, 2015). Evidence of a definitive mortality rate for HCW infected with Sars-CoV-1 was not found. Xiao et al. estimated that deaths in HCW due to SARS-CoV-1 could be up to 164 of the total 774 deaths (21%), although they stated that this number might have been exaggerated due to factors of younger age and good immunity of the frontline HCW (Xiao et al., 2020).

The largest reported series came from a study reaching HCW using a novel smartphone “Covid Symptom Study” application that

A.



B.

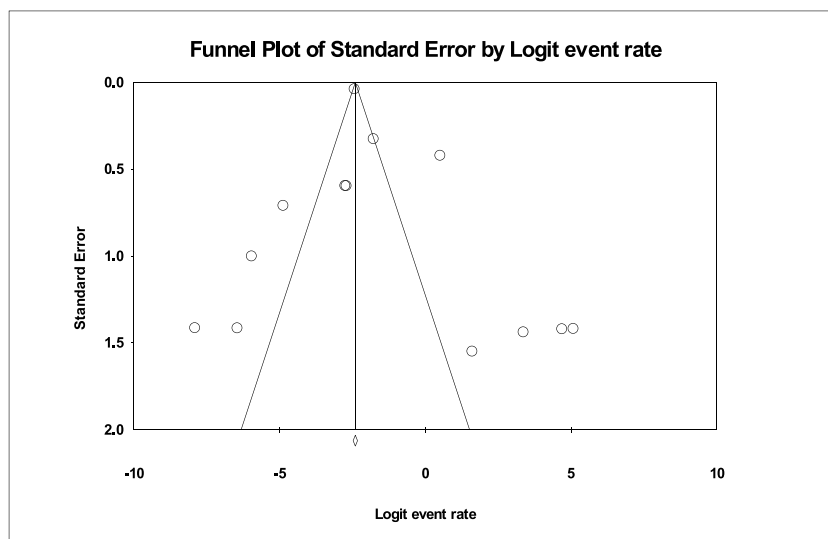


Figure 2. (A) Funnel plot showing death among healthcare workers. The standard errors are well distributed showing minimal bias. (B) Funnel plot showing hospitalisation among HCW with COVID-19. The standard errors are widely distributed and demonstrates more potential bias.

was used by 2,035,395 individuals in the United Kingdom and the United States (Nguyen et al., 2020a). Among these were 99,795 individuals who identified themselves as HCW and reported information related to symptoms and use of PPE. Of the identified HCW there were 1922 (1.9%) that reported testing positive for Covid-19 compared with 3623 (0.18%) general population subjects testing positive for Covid-19. Reported rates of comorbidities in HCW were higher in this series, especially for the presence of lung disease. The methods for obtaining these novel self-reported data will need further verification, and data related to hospitalisation and death were not reported.

This review of risk factors amongst HCW who tested positive for SARS-CoV-2 infection found measurements of risk for the following factors: PPE, workplace setting, profession, exposure, contacts, and testing (Table 7). Face masks were shown to be protective, and having worn one at all times decreased the risk of infection (Chen et al., 2020; Guo et al., 2020). PPE training has been reported to be a protective factor, while lack of N95 masks, reused

PPE and suboptimal hand hygiene practices were risk factors for infection with COVID-19 (Guo et al., 2020; Nguyen et al., 2020b; Ran et al., 2020). The highest risk was reported to be among physicians exposed to COVID-19-positive patients when compared with nurses and general service employees. Physicians at highest risk were those involved in interventional or surgical procedures that generated respiratory aerosols, including within respiratory departments, infection control departments, ICU and surgical departments (Ran et al., 2020). There was no association between risk of infection and length of exposure or distance with positive patients (Garzaro et al., 2020). An overall increased risk of infection was noted in frontline HCW in all healthcare settings as compared with the general community, with a higher risk in HCW working in inpatient settings and nursing homes (Nguyen et al., 2020b). Most of the extracted risk factor data have been reported from China, followed by Italy, US, UK, and Germany. Data reported around December–February by Guo et al. reflected PPE training as the concerned risk factor as opposed to papers published later on from

Table 7
Risk factors of COVID-19 infection in healthcare worker populations.

Reference	Risk factor category	Data
Felice et al. (2020) Nguyen et al. (2020a, Nguyen et al., 2020)	Personal protective equipment (PPE) PPE	<p>PPEs were more readily available in high-risk specialty sectors OR 1.96 (95% CI 0.98–3.94) vs. less likely for HCW with recent onset of symptoms OR 0.48 (95% CI 0.28–0.83) Compared with HCW with adequate PPE supply:</p> <ul style="list-style-type: none"> • Re-use of PPE had an increased risk of a positive COVID-19 test (adjusted HR 1.46, 95% CI 1.21–1.76) vs. those with inadequate PPE (adjusted HR 1.31, 95% CI 1.10–1.56) • Inadequate PPE and caring for patients with documented COVID-19 (adjusted HR 5.91, 95% CI 4.53–7.71) vs. with adequate PPE not caring for patients with suspected or documented COVID-19 • Reusing PPE and exposed to patients with documented COVID-19: (adjusted HR 5.06, 95% CI 3.90–6.57) • Adequate PPE and caring for patients with suspected COVID-19 (adjusted HR 2.39, 95% CI 1.90–3.00) and for those caring for patients with documented COVID-19 (4.83, 3.99–5.85) compared with healthcare workers who did not care for either group
Ran et al. (2020)	PPE	<p>Compared to HCW without infection:</p> <ul style="list-style-type: none"> • Unqualified handwashing: RR 2.64 (95% CI 1.04–6.71, $p < 0.05$) • Suboptimal hand hygiene before contact with patients: RR 3.10 (95% CI 1.43–6.73, $p < 0.01$) • Suboptimal hand hygiene after contact with patients: RR 2.43 (95% CI 1.34–4.39, $p < 0.01$) • Improper PPE: RR 2.82 (95% CI 1.11–7.18)
Chen et al. (2020) Guo et al. (2020)	PPE PPE	<p>Face mask use reduced risk of infection OR 0.127 (95% CI 0.017–0.968)</p> <ul style="list-style-type: none"> • Participating in infection control training was associated with a decreased risk of infection OR 0.12 (95% CI 0.03–0.57) • Non-compliance to wearing N95 masks increased risk OR 5.20 (95% CI 1.09–25.00) • Wearing masks or respirators all the time decreased risk OR 0.15 (95% CI 0.04–0.55) • Suspect patient not wearing mask OR 6.05 (95% CI 1.70–21.51) • Adherence to recommended hand-hygiene practice associated with a decreased risk of infection OR = 0.15 (95% CI 0.04–0.55)
Felice et al. (2020)	Exposure	Those reporting typical symptoms during the last two weeks were more likely, but not statistically significant, to come from high-prevalence regions OR 1.48 (95% CI 0.93–2.37)
Korth et al. (2020)	Exposure	Seroprevalence: Higher in the intermediate-risk (with daily non-COVID-19 patient contact) vs. high-risk group (daily contact to COVID-19 patients on the designated wards and on the intensive care units) OR 0.22 (confidence interval (95% CI 0.04–1.35)
Nguyen et al. (2020a)	Workplace setting	Compared with risk for the general community, risk for front-line healthcare workers was increased in all healthcare settings, but was highest for those working in inpatient settings (adjusted HR 24.30, 95% CI 21.83–27.06) and nursing homes (16.24, 13.39–19.70)
Ran et al. (2020)	Workplace setting	High-risk department (with interventional medical or surgical procedures that generate respiratory aerosols, including the respiratory department, infection department, ICU and the surgical department) vs. general department group (crude RR 2.13, 95% CI 1.45–3.95, $p < 0.05$).
Garzaro et al. (2020)	Workplace setting	Sharing work environment was associated with increased risk OR 2.63 (95% CI 1.34–5.32)
Chen et al. (2020)	Profession	Risk of infection highest in physicians exposed to positive COVID-19 patients OR 346.83 (95% CI 8.924–13479.434) compared with nurses OR 19.523 (95% CI 0.667–571.463) or general service employees OR 13.294 (95% CI 0.265–666.605)
Garzaro et al. (2020)	Profession	<ul style="list-style-type: none"> • Physicians at increased risk OR 2.03 (95% CI 1.18–3.49) • HCWs working in the maternity hospital had more risk of infection OR 2.94 (95% CI 1.72–4.95)
Ran et al. (2020)	Contacts	<ul style="list-style-type: none"> • Diagnosed family member: RR 2.76 (95% CI 2.02–3.77, $p < 0.01$) • Diagnosed patient: RR 0.36 (95% CI 0.22–0.59, $p < 0.01$)
Felice et al. (2020)	Testing	<p>Suspected patient: RR 0.49 (95% CI 0.27–0.89, $p < 0.05$)</p> <ul style="list-style-type: none"> • Testing of symptomatic HCW COVID-19 adjusted OR 3.61 (95% CI 2.15–6.06) vs. asymptomatic, less than a half (45%) of symptomatic HCW was actually screened for COVID-19

March to May, which reported inadequate PPE availability, work environments and contact exposure as the primary risk factors for HCW (Guo et al., 2020).

With the rapid global spread of this novel coronavirus strain, it soon became evident that much research is needed to understand and contain this infection, particularly for frontline HCW. The data encompassed by this review reflect the first 6 months after the official declaration of COVID-19 as a pandemic and the early experience of the disease in HCW with a previously unknown virus. The overall global magnitude of COVID-19 in HCWs was recently documented by a survey of members of the ID-IRI (Infectious Diseases International Research Initiative) from 37 countries through 15 August 2020 (Erdem and Lucey, 2021). They documented 2736 HCW deaths with a mortality rate of 0–0.90/100,000 in the reporting countries. Further data will be needed to continue to understand the evolving implication of this pandemic on the health and well-being of healthcare workers internationally.

Conflict of interest

None declare.

Funding source

None declare.

Ethical approval

Approval was not required for this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ijid.2021.01.013>.

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