COVID-19 in Health-Care Workers: A Living Systematic Review and Meta-Analysis of Prevalence, Risk Factors, Clinical Characteristics, and Outcomes

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Health-care workers (HCWs) are at the frontline of response to coronavirus disease 2019 (COVID-19), being at a higher risk of acquiring the disease and, subsequently, exposing patients and others. Searches of 8 bibliographic databases were performed to systematically review the evidence on the prevalence, risk factors, clinical characteristics, and prognosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among HCWs. A total of 97 studies (all published in 2020) met the inclusion criteria. The estimated prevalence of SARS-CoV-2 infection from HCWs' samples, using reverse transcription–polymerase chain reaction and the presence of antibodies, was 11% (95% confidence interval (CI): 7, 15) and 7% (95% CI: 4, 11), respectively. The most frequently affected personnel were nurses (48%, 95% CI: 41, 56), whereas most of the COVID-19–positive medical personnel were working in hospital nonemergency wards during screening (43%, 95% CI: 28, 59). Anosmia, fever, and myalgia were the only symptoms associated with HCW SARS-CoV-2 positivity. Among HCWs positive for COVID-19 by reverse transcription–polymerase chain reaction, 40% (95% CI: 17, 65) were asymptomatic at time of diagnosis. Finally, severe clinical complications developed in 5% (95% CI: 3, 8) of the COVID-19–positive HCWs, and 0.5% (95% CI: 0.02, 1.3) died. Health-care workers suffer a significant burden from COVID-19, with those working in hospital nonemergency wards and nurses being the most commonly infected personnel.

2019-nCoV; COVID-19; health-care workers; medical workers; SARS-CoV-2

Abbreviations: COVID-19, coronavirus disease 2019; HCW, health-care worker; PPE, personal protective equipment; RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

The pandemic of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has already caused more than 14 million infections and 600,000 deaths globally (1). Although SARS-CoV-2 infection has a lower mortality rate compared with infections caused by the severe acute respiratory syndrome virus or Middle East respiratory syndrome virus, its long incubation period and lower virulence have resulted in many asymptomatic carriers (2). Several studies have shown that asymptomatic carriers contribute substantially to the spread of the virus, even by merely breathing in a room (3–5). Among asymptomatic carriers and individuals at risk because of asymptomatic coronavirus transmission, health-care workers (HCWs) represent an important, yet understudied, population (6). Health-care workers may experience an increased risk of SARS-CoV-2 infection due to their close contact with highly infectious patients, but also due to exposure to undiagnosed or subclinical infectious cases. This could be even more problematic, considering the poor access to personal protective equipment (PPE) worldwide (7). A recent report of the Centers for Disease Control and Prevention showed that, as of April 9, 2020, 9,282 known coronavirus disease 2019 (COVID-19) cases were in HCWs in the United States with numbers probably underestimated (8).

Currently, there is no clarity regarding the prevalence of SARS-CoV-2 infection among HCWs according to specific clinical settings, limiting the possibility of designing effective preventive measures to limit the transmission of the virus within a hospital, and from hospitals to the community (9, 10). Furthermore, it is unknown whether the clinical characteristics and outcomes of HCWs may be different from those of the general population, considering that the repeated exposure to the virus may lead to higher SARS-CoV-2 viral load and, therefore, to worse clinical outcomes (11, 12). Therefore, characterizing SARS-CoV-2 infection within HCWs is critical for achieving optimal control of the pandemic. With the present systematic review and meta-analysis, we aimed to identify, analyze, and quantify the prevalence, risk factors, clinical characteristics, and outcomes of COVID-19 among HCWs.

METHODS

This systematic review and meta-analysis was conducted following a recently published guideline on how to perform a systematic review and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Web Table 1, available at https://academic.oup.com/aje) (13, 14).

Data sources and strategy

Medline, Embase, Latin American and Caribbean Health Sciences Literature (LILACS), Cochrane, Web of Science, the World Health Organization COVID-19 database, Google Scholar, and Living Evidence on COVID-19, a database developed by the Institute of Social and Preventive Medicine, University of Bern, were searched to identify relevant articles from inception until July 8, 2020, without language restrictions. The following search terms related to the COVID-19 infection in HCWs were used: coronavirus disease 2019, Coronaviridae, SARS-CoV-2, SARS coronavirus, 2019-nCov, prevalence, screening, clinical characteristics, clinical course, severity of illness, and outcomes, among others. We limited our search to human studies, with no language restriction. The complete search strategy is described in the Web Appendix 1.

Study selection and eligibility criteria

All observational studies (eg, cross-sectional, cohort, case-control studies, and case series) except for case reports were included. We included studies that reported the prevalence of COVID-19 in HCWs, using either reverse transcription–polymerase chain reaction (RT-PCR) or a serum antibodies assay. We also included studies evaluating the risk factors for SARS-CoV-2 infection and those analyzing the clinical characteristics and outcomes of laboratory-confirmed COVID-19 among HCWs. We excluded those articles that evaluated HCWs with suspected but not laboratory-confirmed SARS-CoV-2 infection. Two independent reviewers screened the titles and abstracts according to the selection criteria.

Data synthesis and analysis

Methods of data extraction, quality assessment, and living systematic review can be found in Web Appendix 2.

On the basis of the data from each study (extracted by 2 independent investigators), we first estimated the global prevalence of SARS-CoV-2 infection by each test used for screening (RT-PCR vs. antibodies tests). Before pooling, all proportions were transformed using the Freeman-Tukey double arcsine method. For dichotomous risk factors, results were expressed as odds ratios with 95% confidence intervals. Heterogeneity of results was assessed using the I^2 measure of inconsistency; however, regardless of heterogeneity, random-effects models were chosen for all the analyses. Screening criteria, geographic location, HCW professions, the clinical setting, and the mean of daily new cases of SARS-CoV-2 per million inhabitants (15) in the country during the period in which the study was carried out were prespecified as characteristics for assessment of heterogeneity and were evaluated using stratified analyses and univariate random-effects meta-regression. All analyses were conducted using STATA, version 15.1 (StataCorp LP, College Station, Texas). For main analysis, $P < 0.05$ was considered significant. To account for multiple testing, in the stratified analysis, we considered $P = 0.01$ as significant.

RESULTS

The initial search yielded 4,107 studies, of which 97 studies met the inclusion criteria (Figure 1). A total of 230,398 participants were evaluated in the included studies, mostly women (69.98%) and with a mean age of 40 (standard deviation, 11) years (8, 16–59). Of the 97 studies, 70 reported data regarding the prevalence of SARS-CoV-2 infection in HCWs (total screened HCWs, $N = 96{,}813$) (16–19, 23, 25–27, 29, 31, 34–40, 42–44, 50–99), 38 studies analyzed the clinical characteristics of infected medical workers ($n = 32{,}144$) (8, 20–22, 24, 28, 30–33, 35, 45–47, 51, 53, 58, 60, 65, 66, 69, 72, 75, 78–81, 94, 100–108), and 13 studies evaluated risk factors for COVID-19 positivity among HCWs (25, 35, 45, 49, 58, 64, 66, 68, 71, 90, 94, 109, 110).

SARS-CoV-2 infection prevalence in HCWs using RT-PCR

In 46 studies, researchers evaluated the prevalence of SARS-CoV-2 infection among HCWs using RT-PCR. Of those, 31 studies were based in clinical facilities in Europe, 9 in the United States, and 6 in Asia (16, 17, 19, 23, 25, 27, 29, 31, 35–40, 42, 44, 45, 51–55, 58–60, 63, 65–69, 71, 72, 75, 76, 79–85, 87, 88, 93–96) (Figure 2). The prevalence of SARS-CoV-2 infection ranged from 0.4% in the study of Olalla et al. (59) among 498 Spanish HCWs, to 57.06% in the study of Breazzano et al. (19), carried out in New York City. Among 75,859 HCWs screened for COVID-19 using RT-PCR, the estimated pooled prevalence of SARS-CoV-2 infection was 11% (95% confidence interval (CI): 7,

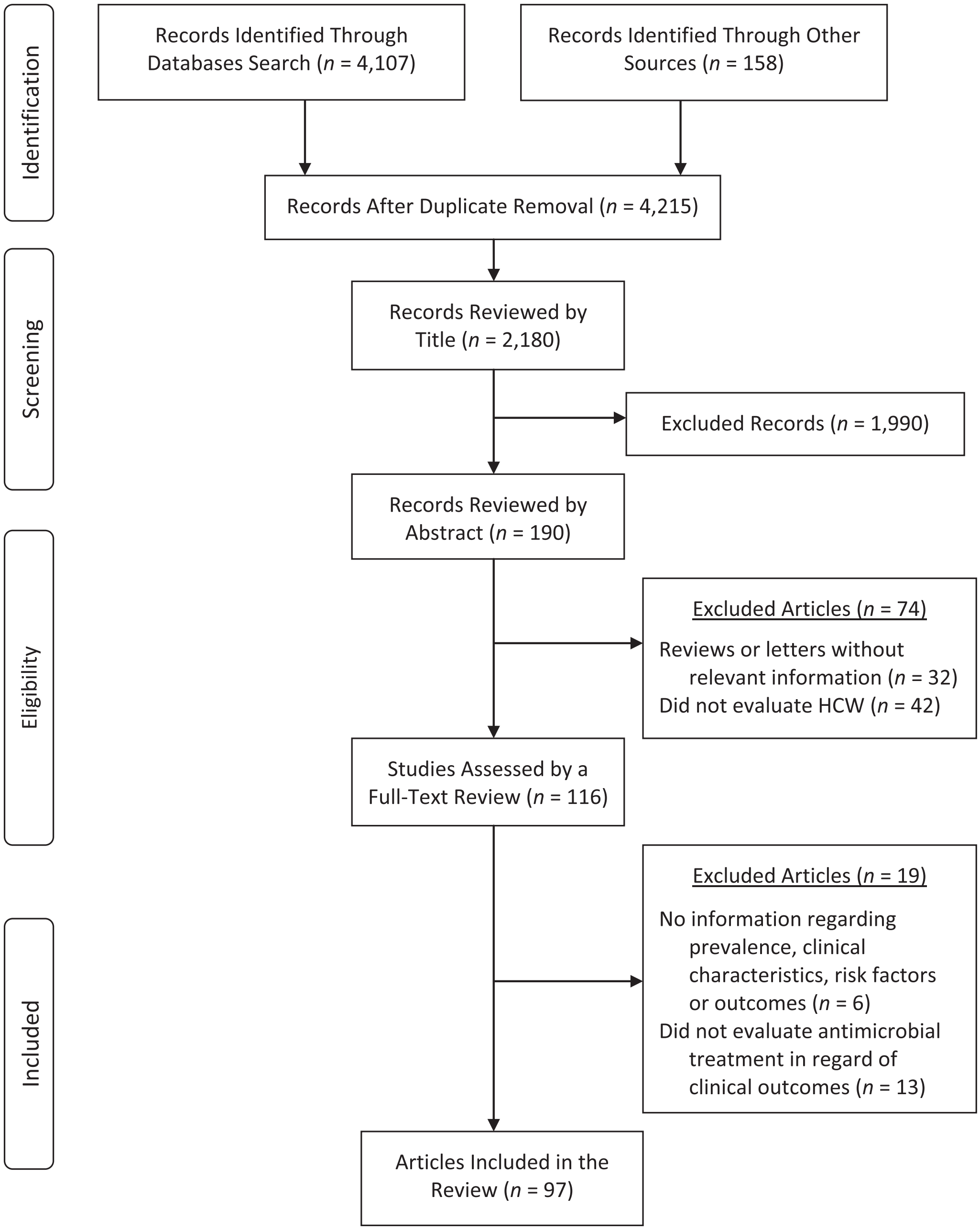

Figure 1. Preferred reporting items for systematic reviews and meta-analyses flowchart summarizing the study search and selection process.

15; P for heterogeneity < 0.001, $I^2 = 98\%$) (Figure 3, Web Figure 1). Furthermore, the prevalence among symptomatic HCWs was the highest (19%, 95% CI: 12, 28; P for heterogeneity < 0.001, $I^2 = 99\%$), followed by that observed in studies including symptomatic and asymptomatic individuals (8%, 95% CI: 3, 16; P for heterogeneity < 0.001, $I^2 = 99\%$). Finally, asymptomatic HCWs had the lowest prevalence of SARS-CoV-2 infection (5%, 95% CI: 1, 13; P for heterogeneity < 0.001, $I^2 = 98\%$) (Figure 3, Web Figure 1, Table 1).

Among HCWs with positive results, 48% were nurses (95% CI: 41, 56; P for heterogeneity < 0.001, $I^2 = 98\%$), followed by physicians (25%, 95% CI: 16, 35; P for heterogeneity < 0.001, $I^2 = 99\%$) and other HCWs (23%, 95% CI: 12, 36; P for heterogeneity < 0.001, $I^2 = 99\%$). Most of the personnel positive for SARS-CoV-2 were working in hospital nonemergency wards during the screenings (43%, 95% CI: 28, 59; P for heterogeneity < 0.001, $I^2 = 91\%$), followed by the operating rooms and surgery services (24%, 95% CI: 17, 31; P for heterogeneity: 0.05, $I^2 = 60\%$) (16,

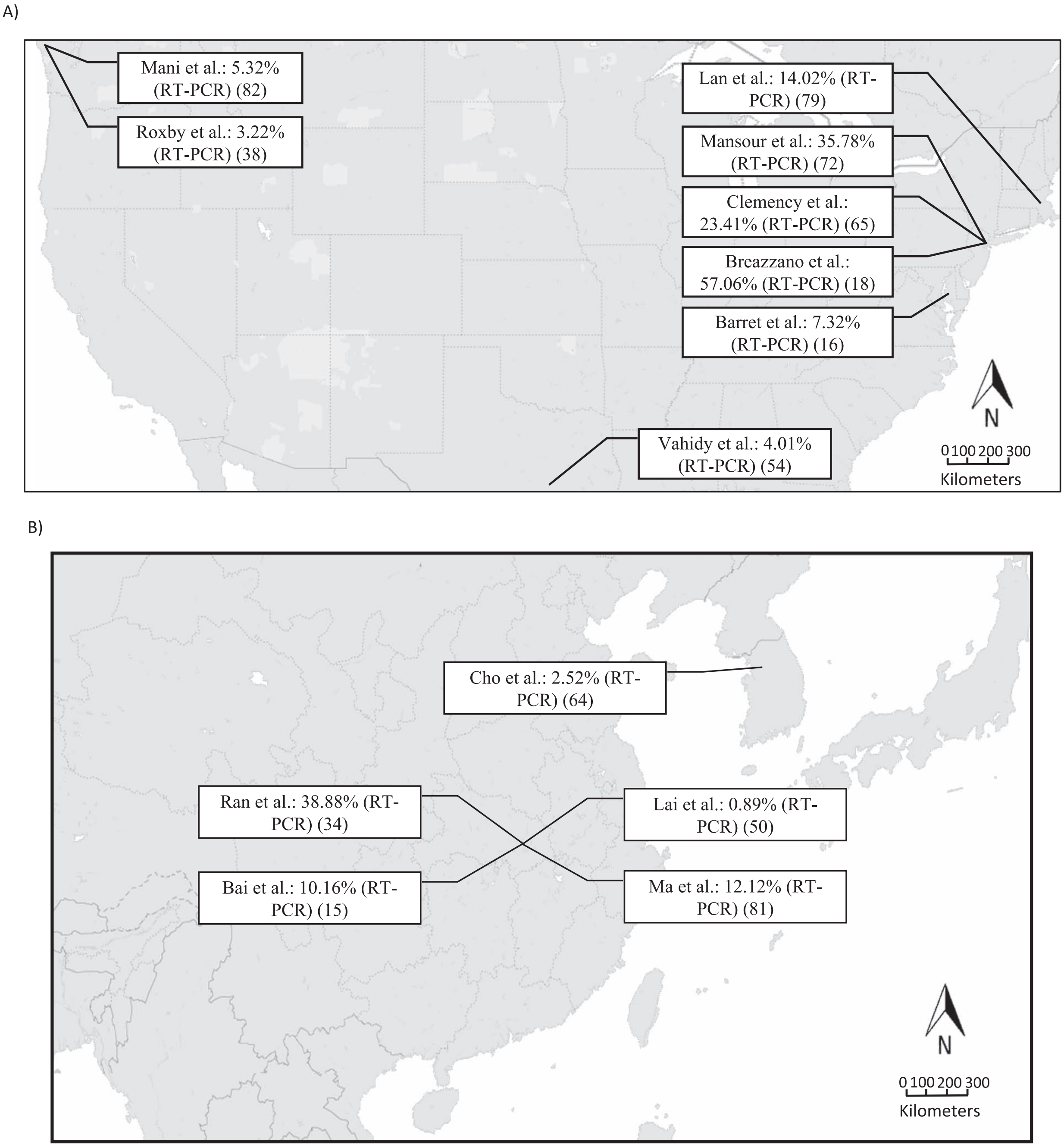

Figure 2 Continues

17, 21, 23, 25–28, 39, 40, 42–45, 46, 50, 51, 53–55, 60–64, 67, 68, 74, 75, 81, 83–85, 95, 104, 106, 107) (Web Figure 2 and Table 2).

Stratification analysis, supported by meta-regression analysis, showed that the symptoms criteria ($P = 0.002$) for performing SARS-CoV-2 RT-PCR screenings were significantly associated with SARS-CoV-2 infection prevalence among HCWs (Web Figure 3); no role of other factors was observed (Web Figure 4, Web Table 2).

Prevalence of antibodies against SARS-CoV-2 in HCWs

The prevalence of antibodies against SARS-COV-2 in HCWs using serum antibody tests was evaluated in 28 studies. The data regarding the sensitivity and specificity of the antibody detection kits used in each study are provided in Web Table 3; sensitivity ranged from 75% to 100% and specificity was 80% or higher. Among 27,445 HCWs screened for the presence of antibodies, a pooled

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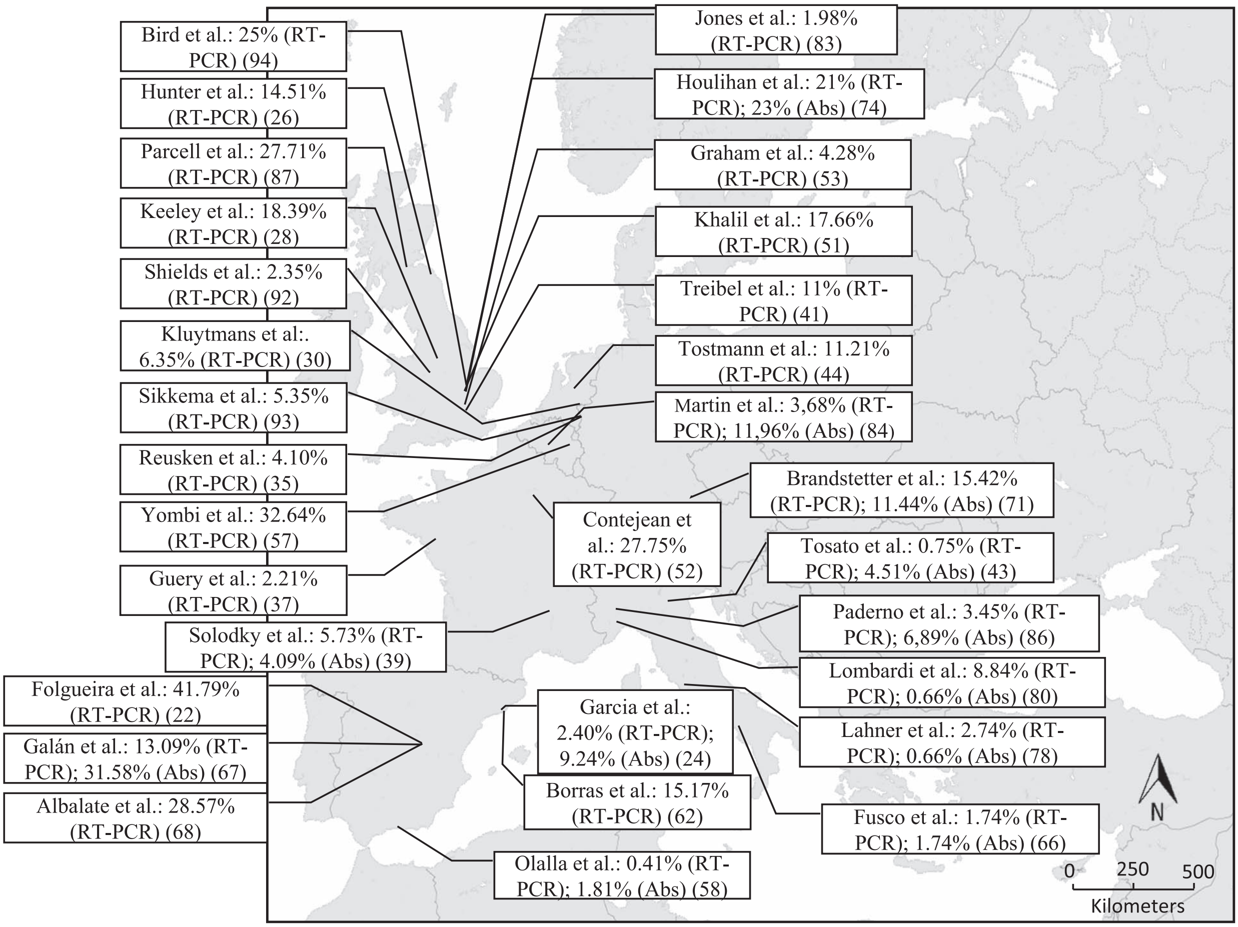

Figure 2. Geographic distribution of studies that reported data on severe acute respiratory syndrome coronavirus 2 prevalence in health-care workers, 2020.

infection prevalence of 7% (95% CI: 4, 11; P for heterogeneity < 0.001, $I^2 = 99\%$) was estimated. The prevalence of COVID-19 infection was similar after comparing the screening criteria of studies ($P = 0.543$) and comparing the mean number of new daily cases of SARS-CoV-2 infection per 1 million inhabitants in the country during the previous 2 weeks to the study initiation ($P = 0.787$) (Web Figure 5).

Prevalence of COVID-19 in HCWs after exposure to undiagnosed infected patients

Eight studies analyzed the scenario of direct exposure of HCWs to an individual or a group of SARS-CoV-2–infected patients without knowing their infection status. The studies comprised a total of 1,126 HCWs screened after in-hospital exposure, highlighting the lack of PPE use in 57.37% ($n = 646$) of the exposed workers. From the studies including HCWs without proper PPE use, 4.7% ($n = 28$) of the exposed individuals had a positive RT-PCR or antibody test result during the contact tracings. On the other hand, no single case of COVID-19 was attributed to the exposure to the index case in the studies that included HCWs with proper PPE use. In line with this trend, Chen et al (63) reported that adequate PPE use was associated with a reduced risk of seroconversion in HCWs exposed to patients with COVID-19 (OR, 0.127, 95% CI: 0.017, 0.968) (43, 50, 61, 64, 70, 72, 76, 92).

Clinical characteristics and outcomes of HCWs positive for COVID-19

The clinical characteristics or outcomes of HCWs infected by the SARS-CoV-2 were evaluated in 37 studies, based on 31,866 HCWs positive for COVID-19 (69% women; mean age: 40.1 (standard deviation, 12.33) years) (8, 20–22, 24, 28, 30–33, 35, 45–47, 51, 53, 58, 60, 65, 66, 69, 72, 75, 78–81, 94, 100–108). Among the 11,772 HCWs positive for COVID-19 with data regarding comorbidities, the pooled prevalence of hypertension, cardiovascular disease, type 2 diabetes, and chronic obstructive pulmonary

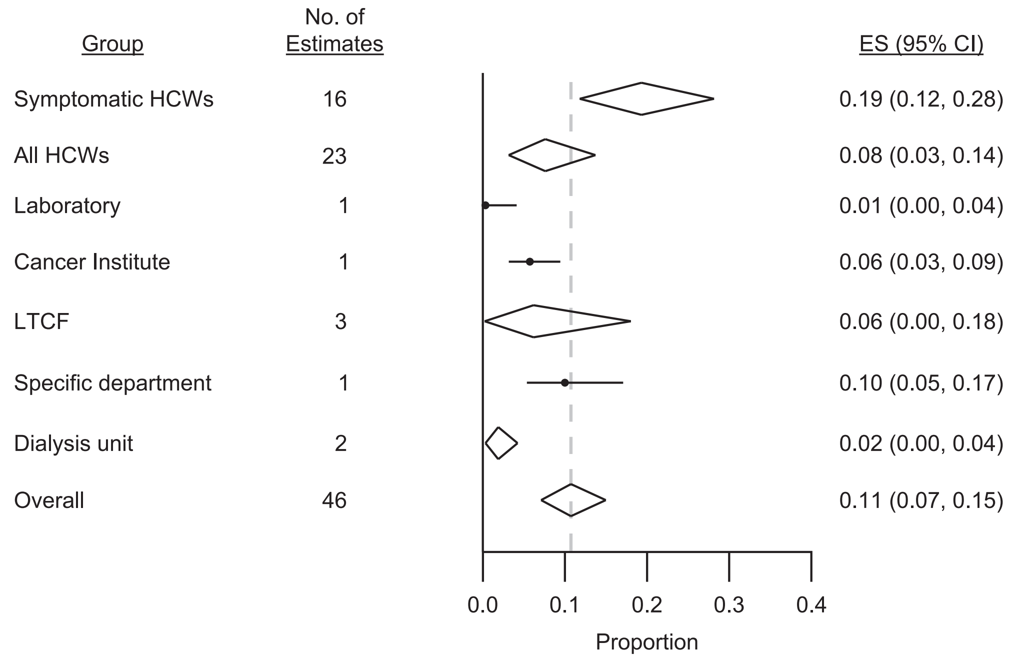

Figure 3. Severe acute respiratory syndrome coronavirus 2 infection prevalence in health-care workers (HCWs) using reverse transcription–polymerase chain reaction, 2020. The results are presented as fractions. The overall summary estimates presented are calculated using random-effects models. ES, effect size; LTCF, long-term care facility.

disease was 7% (95% CI: 4, 10; P for heterogeneity: 0.35, I^2 = 10%), 3% (95% CI: 1, 8; P for heterogeneity: 0.19, I^2 = 39%), 4% (95% CI: 2, 7; P for heterogeneity: 0.01, I^2 = 63%), and 3% (95% CI: 1, 6; P for heterogeneity: 0.01, I^2 = 77%), respectively. Furthermore, based on data from 15 studies, including 12,089 HCWs, the pooled prevalence of individuals with COVID-19 diagnosed by RT-PCR who did not show symptoms at time of diagnosis was 40% (95% CI: 17, 65; P for heterogeneity < 0.001, I^2 = 99%) (17, 25, 38, 39, 51, 52, 60, 63, 72, 75, 81, 82, 83, 103, 111) (Web Figure 6).

Among HCWs symptomatic for COVID-19, the most frequently reported symptoms were fever (57% (n = 29 studies), 95% CI: 50, 64; P for heterogeneity < 0.001, I^2 = 96%) and dry cough (57% (n = 29 studies), 95% CI: 50, 65; P for heterogeneity < 0.001, I^2 = 97%), followed by malaise (43% (n = 1 study), 95% CI: 26, 61; P for heterogeneity < 0.001, I^2 = 96%) and myalgia (48% (n = 10 studies), 95% CI: 35, 62; P for heterogeneity < 0.001, I^2 = 92%) (Table 3). Finally, 8 studies reported the severity of the disease, including intensive care unit admission (8, 21, 24, 28, 30, 33, 46, 51). Among these, a pooled prevalence of 5% (95% CI: 3, 8; P for heterogeneity < 0.001, I^2 = 95%) for severe disease was estimated. Finally, 11 studies provided information regarding death in this population (8, 20, 24, 33, 51). An estimated 0.5% (95% CI: 0.02, 1.3; P for heterogeneity < 0.001, I^2 = 96%) of all the HCWs reported as infected by the SARS-CoV-2 died because of complications of the disease.

Factors associated with SARS-CoV-2 infection in HCWs

The factors potentially associated with SARS-CoV-2 infection in HCWs were analyzed in 15 studies. From these, 4 studies provided sufficient data from infected and noninfected HCWs to perform a meta-analysis for anosmia and 5 provided data for fever. Our analysis of these indicated a significantly higher risk of COVID-19 with the presence of these symptoms (OR = 28.37, 95% CI: 9.45, 85.16, P for heterogeneity = 0.002, I^2 = 79% for anosmia; and OR = 4.86, 95% CI: 2.83, 8.37; P for heterogeneity < 0.001, I^2 = 84% for fever) (Web Table 4). Furthermore, Rudberg et al (90) also found a significantly higher risk of a positive RT-PCR result in HCWs with anosmia (OR = 28.43, $P < 0.001$) or fever (OR = 6.27, $P < 0.001$).

A similar result was observed for myalgia, a symptom that was significantly associated with SARS-CoV-2 infection (n = 3 studies; OR = 3.06, 95% CI: 1.24, 7.56; P for heterogeneity = 0.001, I^2 = 86%). Finally, Clemency et al. (66) evaluated the predictive value of different symptoms for COVID-19 diagnosis, highlighting the loss of taste and smell, with a positive predictive value of 0.5 and a negative predictive value of 0.85; fever, with a positive predictive value of 0.31 and a negative predictive value of 0.83; and myalgia, with a positive predictive value of 0.27 and a negative predictive value of 0.80. On the other hand, no significant associations were found for fatigue (n = 5 studies; OR = 2.41, 95% CI: 0.92, 6.27; P for heterogeneity < 0.001, I^2 = 92%) (25, 45, 58) and sore throat (n = 4 studies;

Table 1. Characterization of Studies Describing Coronavirus Disease 2019 Prevalence in Health-Care Workers Using Reverse Transcription–Polymerase Chain Reaction, 2020

First Author, Year (Reference No.)	No. of Participants	Setting	Selection Criteria	City, Country
Kluytmans, 2020 (31)	86	Hospital, all services	HCWs with fever or (mild) respiratory symptoms	Breda, The Netherlands
García-Basteiro, 2020 (25)	583	Hospital, all services	All HCWs who deliver care and services to patients, either directly as physicians or nurses, or indirectly as assistants, technicians, stretcher bearers, or other support staff (e.g., administrative officers, cleaning, kitchen, laundry, maintenance)	Barcelona, Spain
Breazzano, 2020 (19)	2,088	Hospitals at the city level. Data reported by each postgraduate director	Medical residents in universities located in New York City. Screened according to symptoms	New York City, NY, USA
Tosato, 2020 (44)	133	Laboratory department	All workers in the laboratory department.	Padova, Italy
Keeley, 2020 (29)	1,533	Hospital, all services	All HCWs	Sheffield, UK
Tostmann, 2020 (45)	803	Hospital, all services	HCWs with symptoms suggestive of COVID-19	Nijmegen, The Netherlands
Reusken, 2020 (36)	1,097	Hospital, all services	HCWs with any respiratory symptoms, even mild respiratory complaints.	Noord-Brabant Province, The Netherlands
Hunter, 2020 (27)	1,654	Hospital, all services including ambulance service staff	Staff with compatible symptoms (i.e., new continuous cough or fever)	Newcastle upon Tyne, UK
Ran, 2020 (35)	72	Hospital, all services	All HCWs	Wuhan, China
Solodky, 2020 (40)	244	Hospital, Cancer Institute	Voluntary HCWs	Lyon, France
Guery, 2020 (38)	136	Long-term care facility	All HCWs	Nantes, France
Treibel, 2020 (42)	400	Hospitals at a city level	All HCWs	London, UK
Roxby, 2020 (39)	62	Long-term care facility	All HCWs	Seattle, WA, USA
Lai, 2020 (51)	335	Hospital, all services	All HCWs	Wuhan, China
Graham, 2020 (54)	70	Long-term care facility	Asymptomatic HCWs	London, UK
Vahidy, 2020 (55)	2,887	Hospital, all services	Asymptomatic HCWs	Houston, TX, USA
Olalla, 2020 (59)	498	Hospital, all services	Asymptomatic HCWs	Marbella, Spain
Yombi, 2020 (58)	536	Hospital, all services	Symptomatic HCWs	Brussels, Belgium
Khalil, 2020 (52)	266	Hospital, all services	All HCWs	London, UK
Contejean, 2020 (53)	1,344	Hospital, all services	Symptomatic HCWs	Paris, France
Barrett, 2020 (17)	546	Hospital, all services	All HCWs who reported (1) $\geq$20 hours of hospital work weekly; (2) occupations with regular patient exposure (e.g., residents, fellows, attending physicians, dentists, nurse practitioners, physician assistants, registered nurses, technicians, respiratory therapists, physical therapists); and (3) regular direct patient contact ($\geq$3 patients/shift) expected in the next 3 months	Newark, NJ, USA
Bai, 2020 (16)	118	Hospital, Neurosurgery Department	All HCWs	Wuhan, China
Folgueira, 2020 (23)	1,438	Hospital, city-level	All HCWs	Madrid, Spain

Table continues

Table 1. Continued

First Author, Year (Reference No.)	No. of Participants	Setting	Selection Criteria	City, Country
Antonio-Villa, 2020 (60)	34,263	Hospital, all services	All HCWs	Mexico City, Mexico
Borras-Bermejo, 2020 (63)	2,655	Long-term care facility	All HCWs	Catalonia, Spain
Cho, 2020 (65)	278	Hospital, all services	Symptomatic HCWs	South Korea
Clemency, 2020 (66)	961	Hospital, all services	Symptomatic HCWs	New York City, NY, USA
Fusco, 2020 (67)	115	Hospital, all services	Asymptomatic HCWs	Naples, Italy
Galán, 2020 (68)	2,590	Hospital, all services	HCW with positive immunoglobulin G and symptoms in the past 14 days	Madrid, Spain
Albalate, 2020 (69)	14	Hospital, all services	Symptomatic HCWs	Madrid, Spain
Bhattacharya, 2020 (71)	106	Hospital, all services	All HCWs	Kolkata, India
Houlihan, 2020 (75)	200	Hospital, all services	All HCWs	London, UK
Lahner, 2020 (79)	2,115	Hospital, all services	All HCWs	Rome, Italy
Lan, 2020 (80)	592	Hospital, all services	All HCWs	Massachusetts, USA
Lombardi, 2020 (81)	1,573	Hospital, all services	All HCWs	Milan, Italy
Ma, 2020 (82)	33	Hemodialysis unit	All HCWs	Wuhan, China
Mani, 2020 (83)	3,477	Hospital, all services	Symptomatic HCWs	Seattle, WA, USA
Jones, 2020 (84)	4,800	Hospital, all services	Symptomatic HCWs	London, UK
Martin, 2020 (85)	326	Hospital, all services	Symptomatic HCWs	Brussels, Belgium
Paderno, 2020 (87)	58	Otorhinolaryngology clinic	Symptomatic HCWs	Brescia, Italy
Parcell, 2020 (88)	1,173	Hospital, all services	Symptomatic HCWs	Tayside, UK
Shields, 2020 (93)	554	Hospital, all services	All HCWs	Birmingham, UK
Sikkema, 2020 (94)	1796	Hospital, all services	Symptomatic HCWs	Breda and Tilburg, Netherlands
Bird, 2020 (95)	152	Hospital, all services	Symptomatic HCWs	Leicester, UK
Wee, 2020 (96)	1,642	Hospital, all services	Symptomatic HCWs	Singapore
Brandstetter, 2020 (72)	201	Hospital, all services	All HCWs	Regensburg, Germany

Abbreviations: HCW, health-care worker; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

OR = 0.55, 95% CI: 0.30, 1.01; *P* for heterogeneity: 0.02, I^2 = 75%) (Web Table 4) (45, 58).

Ran et al. (35) found that, among 72 HCWs in Wuhan, China, unqualified hand-washing (OR = 2.64, 95% CI: 1.04, 6.71), suboptimal hand hygiene before patient contact (OR = 3.10, 95% CI: 1.43, 6.73,), and inadequate PPE (OR = 2.82, 95% CI: 1.11, 7.18) were risk factors for SARS-CoV-2 infection. Similarly, Wang et al. (49) reported that

Table 2. Areas in Which Coronavirus Disease 2019 Positive Health-Care Workers Were Laboring During Reverse Transcription–Polymerase Chain Reaction Screenings, 2020

Area/Setting	No. of Studies	Proportion, %	95% CI	I^2, %
Clinics/wards	5	43	28, 59	91
Operating room	4	24	17, 31	60
Others	4	29	13, 48	91
Emergency room	5	16	6, 29	91
Intensive care unit	5	9	4, 15	68

Table 3. Prevalence of Symptoms in Coronavirus Disease 2019–Positive Health-Care Workers

Symptom	No. of Studies	Pooled Prevalence, %	95% CI	I^2, %
Fever	29	57	50, 64	96
Cough	26	57	50, 65	96
Malaise	10	48	35, 62	89
Myalgia	22	44	36, 52	96
Headache	22	36	27, 46	97
Sore throat	15	32	23, 42	97
Shortness of breath	21	22	17, 28	95
Diarrhea	21	18	14, 22	87%
Nausea	7	9	6, 14	73%
Chest pain	6	8	1, 18	86%

in a sample of 493 HCWs in Wuhan, China, the risk of COVID-19 in HCWs using medical masks was significantly higher when compared with those using N95 respirators (OR = 464.82, 95% CI: 97.73, infinite), even though this last group had a significantly higher exposure to infected patients. Chatterjee et al. (108) reported similar results, highlighting a higher risk of SARS-CoV-2 infection in HCWs who never used PPE compared with those with usual protection use (OR = 3.72, 95% CI: 2.12, 6.52).

Moreover, the risk of aerosol-generating procedures for HCWs was analyzed by El-Boghdadly et al. (110), who, in their prospective multi-center study, evaluated 1,718 HCWs participating in tracheal intubation of patients with suspected or confirmed COVID-19. The overall incidence of the composite outcome (new laboratory-confirmed COVID-19 or new COVID-19 symptoms requiring self-isolation or hospitalization) was 10.7% over a median follow-up of 32 (range, 18–48) days. Furthermore, 10% of the HCWs involved in tracheal intubation procedures in these cohorts subsequently had the composite outcome (110).

The potential source of infection was studied by García-Basteiro et al. (25), observing that HCWs with a larger household size tended to have more frequently detectable, albeit nonsignificant (P = 0.093) levels of antibodies (immunoglobulin M or immunoglobulin A) against SARS-CoV-2 (25). Kluytmans et al. (31) reported that among 84 HCWs positive for SARS-CoV-2 in 2 hospitals in The Netherlands, only 3% reported having been exposed to an patient with confirmed COVID-19 before symptom onset. Finally, Sikkema et al. (94), by investigating the genome sequences from infected HCWs and patients, reported that the obtained patterns were consistent with multiple introductions into the hospitals through community-acquired infections and local amplification of the viral disease in the community context.

Interestingly, 2 studies evaluated the benefit of pharmacological prophylaxis with hydroxychloroquine to prevent SARS-CoV-2 infection among high-risk HCWs. Both studies showed that the history of having taken maintenance doses of hydroxychloroquine was associated with a significantly lower risk of COVID-19 (71, 109).

Study quality

The majority of studies were of moderate (n = 61, 62.9%) quality, with 29.9% (n = 29) being of high quality and the rest of low quality (n = 7, 7.2%). Web Tables 5–7 present a summary of the studies' quality evaluation.

DISCUSSION

The current evidence shows that approximately a tenth of the HCWs in the screened hospitals had a diagnosis of acute SARS-CoV-2 infection; half of these were nurses. To date, only 7% of the HCWs tested positive for the presence of antibodies indicating SARS-CoV-2 infection. Furthermore, most of the personnel positive for SARS-CoV-2 were working in hospital nonemergency wards during the laboratory screenings. Fever, anosmia, and myalgia were the main associated factors for SARS-CoV-2 infection in the meta-analysis. From the 15 studies in which HCWs were screened irrespective of their symptoms and in which the clinical features of SARS-CoV-2–positive individuals were reported, 40% did not report any symptom compatible with COVID-19 during the screenings. Furthermore, we observed a pooled prevalence of severe COVID-19 of 5% among HCWs, and 0.5% of the infected HCWs died of complications of the disease.

Our findings show a higher prevalence of SARS-CoV-2 infection among HCWs when compared with the data from the general population reported in the literature (112). This difference may be attributable to workplace exposures of the HCWs; nevertheless, only a few studies analyzed the potential source of infection in this population, limiting the possibility of evaluating the impact of nosocomial versus community-acquired infection. Folgueira et al. reported there were no significant differences in the infection rates between the groups of HCWs working in high-, intermediate-, and low-exposure risk settings (23). Furthermore, Hunter et al. found no differences in the proportion of infected HCWs when comparing the ones with patient-facing roles with those without this exposure (25). In addition, the results of the studies of García-Basteiro et al. (25), Kluytmans et al. (31), and Sikkema et al. (94) provided evidence suggesting a relevant role of community transmission of the disease in HCW infections. These results may suggest that household contacts may play a significant role in SARS-CoV-2 infection in HCWs, mainly due to the rapid circulation of the virus in the community. Another reason could be the infection from asymptomatic carriers, considering that approximately half of HCWs infected with SARS-CoV-2 were asymptomatic during the screenings. However, the importance of nosocomial transmission needs to be analyzed in light of the use of PPE and other measures designed to reduce the exposure of HCWs in the work settings but that are not usually applied by the health personnel in low-risk settings or the community context (113).

As new strategies have been designed and implemented for the re-opening of economic activities in different countries, the understanding of the role of asymptomatic transmission of SARS-CoV-2 is essential, especially in a clinical setting. According to the World Health Organization, at least 50% of patients who died of COVID-19 were residents in hospitals or nursing homes, which highlights the need to control the spread of infection in a health-care setting. Our findings suggest that almost half of SARS-CoV-2–infected HCWs are asymptomatic during the screenings. However, the contribution of asymptomatic carriers in the transmission of SARS-CoV-2 infection is still not clear. A recent study showed similar viral loads in symptomatic patients compared with asymptomatic individuals, highlighting the transmission potential of SARS-CoV-2 carriers despite their clinical status (114). On the other hand, the findings of Gao et al. (74) suggested potentially low infectivity of asymptomatic SARS-CoV-2 carriers, because none of the 455 contacts who were exposed to an asymptomatic COVID-19 virus carrier had a positive test. These results were in line with the studies performed by Ng et al. (50) and Canova et al. (43), in which none of the exposed HCWs had a subsequent positive SARS-CoV-2 test. Nevertheless, the lack of infection among HCWs in these studies could also be due to adequate use of PPE, hand hygiene, and other standard procedures. Indeed, all asymptomatic patients investigated in the study by Gao et al. (74) wore a mask, reducing further the spread of the infection. Nonetheless, even if this low infectivity is confirmed by other studies, the potential of silent transmission still is an enormous issue that needs to be addressed efficiently, especially in low- and middle-income countries lacking medical resources (e.g., PPE, diagnostic capacity). Considering the results of this study, in which almost half of the HCWs positive for COVID-19, according to RT-PCR results, were asymptomatic, there is an urgent need to promote a process of continuous, systematic screening of all HCWs in high-risk settings, as well as the use of adequate PPE and other standard procedures. Moreover, a low threshold for suspicion of infection in low-risk settings is also needed to promote early isolation to avoid cross-infection (58).

To improve the screening performance and early detection of SARS-CoV-2 infection among HCWs, the analysis of risk factors for COVID-19 positivity is important. In this review, 15 studies analyzed the symptoms and signs associated with SARS-CoV-2 infection among HCWs. Fever (OR = 4.86, 95% CI: 2.38, 8.37; I^2 = 84%), anosmia (OR = 28.37, 95% CI: 9.45, 85.16; I^2 = 79%), and myalgia (OR = 3.06; 95% CI: 1.24, 7.56; I^2 = 86%) proved to be associated with higher odds of COVID-19 in symptomatic HCWs; however, relying on these specific but not sensitive symptoms to define screening criteria may lead to an important proportion of missed COVID-19–positive cases. This was the conclusion of Yombi et al. (58), who assessed the impact of using fever as a predictor for the positivity of SARS-CoV-2 RT-PCR. Their results showed that fever might have a positive impact on the yield of RT-PCR for SARS-CoV-2; nonetheless, when this symptom was required as a criterion for testing, an important number of positive cases were missed. Similar results were reported by Chow et al. (22) in a cohort of HCWs in King County, Washington. In their study, screening only for fever, cough, shortness of breath, or sore throat might have missed 17% of symptomatic HCWs at the time of illness onset. The authors also mentioned that expanding criteria for symptoms screening to include chills and myalgia may still have missed 10% of cases. According to the results of the present systematic review and meta-analysis, malaise (48%) and headache (36%) are additional common symptoms with a high prevalence among HCWs positive for COVID-19 (Table 3). Therefore, the inclusion of these symptoms in the screening criteria for testing may improve the identification of SARS-CoV-2–positive individuals and prevent further transmission (22, 58). Specifically, screening for these symptoms could be useful in low- and middle-income countries with limited testing capacity. However, screening HCWs by symptoms may still miss a significant proportion of COVID-19 cases; therefore, universal screening for all exposed HCWs regardless of symptoms should be the standard strategy to reduce transmission of SARS-CoV-2 in a hospital setting.

The high number of nurses who were positive for SARS-CoV-2 in our study could be explained by the longer time staff nurses usually spend with direct patient care, involving tasks performed at the bedside, drug administration, and being the first line of response in case of any patient complications. That more infected HCWs were observed in hospital nonemergency wards in this study may suggest a difference in PPE use across the settings; the compliance with this measures perhaps is higher in the emergency departments and intensive care units (where the subjective risk perception is higher) compared with non–COVID-19 wards (115–118). However, most of the studies did not report the total number of screened HCWs per area per professional category, limiting the representativeness of the studies and precluding the analysis of the prevalence of SARS-CoV-2 infection by unit or per profession. For instance, nurses comprising the highest number of employees in the health-care setting could explain the high rate of SARS-CoV-2 positivity among nurses compared with other positive HCWs. If future studies confirm nurses as being the most affected personnel and hospital nonemergency wards are associated with higher risk of SARS-CoV-2 infection, then the findings would have important implications for policy makers and hospital administrators in better planning of resources to reduce SARS-CoV-2 transmission in hospitals.

Finally, our findings highlight the risk of clinical complications and death among HCWs. We found that COVID-19 among HCWs is associated with approximately a 0.5% proportion of fatal cases. Although the mortality rate among HCWs is lower compared with that in the general population reported in the literature, better overall health and care among HCWs, different age demography, and other factors could explain these differences. Yet, because of exposure to numerous infected individuals, HCWs, if infected, could be characterized by higher viral load, which is associated with worse clinical outcomes (12).

Strengths and limitations

To our knowledge, this is the first systematic review quantifying the burden of COVID-19 among HCWs. However, limitations in this study merit careful consideration. First, in our analysis, we included evidence mainly deriving from preprint publications, which are not peer-reviewed. Nevertheless, we assessed their quality, highlighting the potential limitations of each study. Second, the heterogeneity of the included studies represented a challenge when pooling the results; thus, we aimed to overcome this limitation by performing different subgroup analyses when estimating the prevalence. Third, an important limitation of the study was the lack of reporting of the test quality (sensitivity and specificity) in most of the included articles; therefore, the prevalence reported from each study could be under- or overestimated depending on the applied test. Fourth, clinical settings and HCW professional categories were determined mainly on the basis of employment, which may not necessarily represent specific exposure levels to COVID-19–positive patients. Fifth, the potential source of SARS-CoV-2 infection in positive HCWs was poorly studied in the included articles; therefore the possibility of analyzing the impact of nosocomial versus community transmission was limited. Last, most of the studies did not report the level of adherence to preventive measures and PPE use, which is an essential factor affecting the transmission of the virus.

To conclude, HCWs represent a population with a significant burden from COVID-19. Health-care workers have a high prevalence of SARS-CoV-2 infection, with a significant proportion of the infected HCWs being asymptomatic carriers, a condition that favors silent transmission in the clinical and community contexts if preventive measures and other standard procedures are not implemented.

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