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

Sergio Alejandro Gómez-Ochoa, Oscar H. Franco, Lyda Z. Rojas, Peter Francis Raguindin, Zayne Milena Roa-Díaz, Beatrice Minder Wyssmann, Sandra Lucrecia Romero Guevara, Luis Eduardo Echeverría, Marija Glisic*, and Taulant Muka*

Correspondence to Dr. Taulant Muka, MD, MPH, PhD; Institute of Social and Preventive Medicine (ISPM), University of Bern, Mittelstrasse 43, 3012, Bern, Switzerland (e-mail: taulant.muka@ispm.unibe.ch)

Author affiliations:

Research Division, Cardiovascular Foundation of Colombia, Floridablanca, Colombia (Sergio Alejandro Gómez-Ochoa and Lyda Z. Rojas); Public Health and Epidemiological Studies Group, Cardiovascular Foundation of Colombia, Floridablanca, Colombia (Sergio Alejandro Gómez-Ochoa); Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland (Oscar H. Franco, Peter Francis Raguindin, Zayne Milena Roa-Díaz, Marija Glisic and Taulant Muka); Institute of Child Health and Human Development (ICHHD), National Institutes of Health, University of the Philippines Manila, Manila, Philippines (Peter Francis Raguindin); Research Group and Development of Nursing Knowledge (GIDCEN-FCV), Research Institute, Cardiovascular Foundation of Colombia, Floriadablanca, Santander, Colombia (Lyda Z. Rojas and Zayne Milena Roa-Díaz); Public Health & Primary Care Library, University Library of Bern, University of Bern, Bern, Switzerland (Beatrice Minder Wyssmann); Nursing School, Universidad Industrial de Santander, Bucaramanga, Colombia (Sandra Lucrecia Romero Guevara); Chief, Heart Failure Clinic, Cardiovascular Foundation of Colombia, Floridablanca, Colombia (Luis Eduardo Echeverría); Swiss Paraplegic Research, Nottwil, Switzerland (Marija Glisic).

*denotes equal contribution

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ABSTRACT

Health care workers (HCW) are at the frontline response to the new coronavirus disease 2019 (COVID-19), being at a higher risk of acquiring the disease, and subsequently, exposing patients and colleagues. Searches in eight 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 HCW. Ninety-seven studies (All published in 2020), including 230,398 HCW, met the inclusion criteria. From the screened HCW using RT-PCR and the presence of antibodies, the estimated prevalence of SARS-CoV-2 infection was 11% (95%CI; 7%-15%) and 7% (95% CI; 4%-11%), respectively. The most frequently affected personnel were the nurses (48%. 95%CI; 41%-56%), while most of the COVID-19 positive medical personnel were working in hospitalization/non-emergency wards during the screening (43%, 95%CI;28%-59%). Anosmia, fever and myalgia were identified as the only symptoms associated with HCW SARS-CoV-2 positivity. Among RT-PCR positive HCW, 40% (95%CI;17%-65%) did not show symptoms at the time of diagnosis. Finally, 5% (95%CI;3%-8%) of the COVID-19 positive HCW developed severe clinical complications, and 0.5% (95% CI; 0.02%-1.3%) died. HCW suffer a significant burden from COVID-19, with HCW working in hospitalization/non-emergency wards and nurses being the most infected personnel.

Keywords: 2019-nCoV; SARS-CoV-2; COVID-19; Health Care Workers; Medical Workers

Abbreviations
COVID-19: Coronavirus disease 2019
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
HCW: Healthcare workers
RT-PCR: Reverse transcription polymerase chain reaction
PPE: Personal protective equipment
HCQ: Hydroxychloroquine

INTRODUCTION

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 thousand deaths globally(1). Although SARS-CoV-2 infection has a lower mortality rate compared to infections caused by the severe acute respiratory syndrome (SARS) virus or Middle East respiratory syndrome (MERS) virus, its long incubation period and lower virulence have resulted in a large number of 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 due to asymptomatic coronavirus transmission, health care workers (HCW) represent an important but yet understudied population(6). HCW 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 (CDC) shows that, as of April 9th, 2020, 9,282 known coronavirus disease 2019 (COVID-19) cases were labeled as HCW in the U.S, with numbers probably underestimated (8).

Currently, there is no clarity regarding the prevalence of SARS-CoV-2 infection among HCW 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 HCW 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 health-care workers is critical for achieving optimal control of the pandemic. The present systematic review and meta-analysis aimed to identify, analyze, and quantify the prevalence, risk factors, clinical characteristics, and outcomes of COVID-19 among HCW.

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 PRISMA guidelines **(Web Table 1)** (13,14).

Data source and strategy

MEDLINE, EMBASE, LILACS, Cochrane, Web of Science, WHO COVID-19 database, Google scholar and 'Living Evidence on COVID-19', a database developed by the University of Bern (ISPM), were searched to identify relevant articles from inception until July 8th, 2020 without language restrictions. The following search terms related to the COVID-19 infection in HCW were used: coronavirus disease 2019, coronaviridae, SARS-

CoV-2, SARS coronavirus, 2019-nCov, prevalence, screening, clinical characteristics, clinical course, severity of illness, 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 (e.g., 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 HCW by using either 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 HCW. We excluded those articles that evaluated HCW with suspected but not laboratory-confirmed SARS-CoV-2 infection. Two independent reviewers screened the titles and abstracts according to the selection criteria.

Methods on Data extraction, Quality assessment and Living systematic review can be found in the Web Material ***(Web Appendix 2)***.

Data synthesis and analysis

Based on the extracted data of each study (performed by two 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 ORs with 95% confidence intervals (CI). 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, geographical location, HCW professions, the clinical setting, and the mean of daily new cases of SARS-CoV-2 per million inhabitants (obtained from the European Centers of Disease Control website. https://www.ecdc.europa.eu/en) in the country during the period in which the study was carried out were pre-specified as characteristics for assessment of heterogeneity and were evaluated using stratified analyses and univariate random-effects meta-regression. All analyses were conducted using STATA 15.1 (Statacorp, Texas, US, 2017). For main analysis, a p-value <0.05 was considered significant. To account for multiple testing, in the stratified analysis, we considered a p-value of 0.01 as significant.

RESULTS

The initial search yielded 4,107 studies, from which ninety-seven 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±11 years (8,15–58). Of the 97 studies, 70 studies reported data regarding the prevalence of SARS-CoV-2 infection in HCW (total screened HCW: 96,813) (15–18,22,24–26,28,30,33–35,35–39,41,42,42,43,49–98), 38 studies analyzed the clinical characteristics of infected medical workers (n=32,144) (8,19–21,23,27,29–32,34,44–46,50,52,57,59,64,65,68,71,74,77–80,93,99,99–107) and, thirteen studies evaluated risk factors for COVID-19 positivity among HCW(24,34,44,48,57,63,65,67,70,89,93,108,109).

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

Forty-six studies evaluated the prevalence of SARS-CoV-2 infection among HCW using RT-PCR. Of those, 31 studies were based in clinical facilities in Europe, nine in the USA, and six in Asia (15,16,18,22,24,26,28,30,34–36,38,39,41,43,44,50–54,57–59,62,64–68,70,71,74,75,78–84,86,87,92–95,110) **(Figure 2)**. The prevalence of SARS-CoV-2 infection ranged from 0.4% in the study of *Olalla et al* among 498 Spanish HCW to 57,06%% in the study of *Breazzano et al*, carried out in New York city. Among 75,859 HCW screened for COVID-19 using RT-PCR, the estimated pooled prevalence of SARS-CoV-2 infection was 11% (95% CI; 7%-15%; p-value for heterogeneity <0.001, I^2: 98%) (**Figure 3, Web Figure 1**). Furthermore, the prevalence among symptomatic HCW was the highest (19%. 95% CI; 12%-28%; p-value for heterogeneity <0.001, I^2: 99%), followed by the one observed in studies including both symptomatic and asymptomatic individuals (8%. 95% CI; 3%-16%; p-value for heterogeneity <0.001, I^2: 99%). Finally, asymptomatic HCW showed the lowest prevalence of SARS-CoV-2 infection (5%. 95% CI; 1%-13%; p-value for heterogeneity <0.001, I^2: 98%) **(Figure 3, Web Figure 1, Table 1)**. Among HCW with positive results, 48% (95% CI; 41%-56%; p-value for heterogeneity <0.001, I2: 98%) were nurses, followed by physicians (25%, 95% CI; 16%-35%; p-value for heterogeneity <0.001, I2: 99%) and other HCW (23%, 95% CI; 12%-36%; p-value for heterogeneity <0.001, I2: 99%). Most of the SARS-CoV-2 positive personnel were working in hospitalization/non-emergency wards during the screenings (43 %, 95% CI; 28%-59%; p-value for heterogeneity <0.001. I^2: 91%), followed by the operating rooms and surgery services (24%, 95% CI; 17% - 31%; p-value for heterogeneity: 0.05, I^2: 60%) (15,16,20,22,24–27,38,39,41–44,47,49,50,52–54,59–63,66,67,73,74,80,82–84,94,103,105,106) **(Web Figure 2 and Table 2)**.

Stratification analysis, supported by meta-regression analysis, showed that the symptoms criteria (p-value=0.002) for performing SARS-CoV-2 RT-PCR screenings was significantly associated with SARS-CoV-2 infection prevalence among HCW (**Web Figure 3**), while no role of other factors was observed **(Web Figures 4 and Web Table 2)**.

Prevalence of antibodies against SARS-CoV-2 in HCW

Twenty-eight studies evaluated the prevalence of antibodies against SARS-COV-2 in HCW using serum antibody tests. The data regarding the sensitivity and specificity of the antibody detection kits used in each study are available in **Web Table 3**, with sensitivity ranging from 75% to 100%, and specificity being 80% and above. Among 27,445 HCW screened for the presence of antibodies, a pooled infection prevalence of 7% (95% CI; 4%-11%; p-value for heterogeneity < 0.001. I^2: 99%) was estimated. The prevalence of COVID-19 infection was similar after comparing studies regarding their screening criteria (p-value=0.543) and the mean of new daily cases of SARS-CoV-2 infection per million inhabitants in the country during the previous 2 weeks to the study initiation (p-value=0.787). **(Web Figure 5)**.

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

Eight studies analyzed the scenario of direct exposure of HCW to an individual or a group of SARS-CoV-2 infected patients without knowing their infection status. The studies comprised a total of 1126 HCW screened after in-hospital exposure, highlighting the lack of PPE use in 57.37% (n=646) of the exposed workers. From the studies including HCW 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, there was no single case of COVID-19 attributed to the exposure to the index case in the studies that included HCW with proper PPE use. In line with this trend, the study of *Chen et al* reported that adequate PPE use was associated with a reduced risk of seroconversion in HCW exposed to COVID-19 patients (OR, 0.127, 95% CI 0.017, 0.968)(42,49,60,63,69,71,75,91).

Clinical characteristics and outcomes of COVID-19 positive HCW

Thirty-seven studies, based on 31,866 COVID-19 positive HCW (69% women, mean age: 40.1±12.33), evaluated the clinical characteristics or outcomes of HCW infected by the SARS-CoV-2(8,19,19–21,23,27,29–32,32,34,44–46,46,50,52,57,59,64,65,68,71,74,77–80,93,99–107). Among the 11,772 positive HCW with data regarding comorbidities, the pooled prevalence of hypertension, cardiovascular disease, type 2 diabetes and chronic obstructive pulmonary disease was 7% (95% CI; 4%-10%; p-value for heterogeneity: 0.35, I^2: 10%), 3% (95% CI; 1%-8%; p-value for heterogeneity: 0.19, I^2: 39%), 4% (95% CI; 2%-7%; p-value for heterogeneity: 0.01, I^2: 63%) and 3% (95% CI; 1%-6%; p-value for heterogeneity: 0.01, I^2: 77%), respectively. Furthermore, based on data from 15 studies, including 12,089 HCW, the pooled prevalence of individuals diagnosed by RT-PCR that did not show symptoms at time of diagnosis was 40% (95% CI 17%-65%. p-value for heterogeneity < 0.001. I^2: 99%)(16,24,38,50,51,59,62,71,74,80,83,84,102,110,111) **(Web Figure 6)**.

Among symptomatic COVID-19 HCW, the most frequently reported symptoms were fever (57%, 95% CI; 50%-64%. 29 studies. p-value for heterogeneity < 0.001, I^2: 96%)and dry cough (57%, 95% CI; 50%-65%. 26 studies. p-value for heterogeneity < 0.001, I^2: 97%), followed by malaise (43%, 95% CI; 26%-61%. 1 studies. p-value for heterogeneity < 0.001, I^2: 96%) and myalgia (48%, 95% CI; 35%-62%. 10 studies. p-value for heterogeneity < 0.001, I^2: 92%) **(Table 3)**. Finally, eight studies reported the severity of the disease, including ICU admission(8,20,23,27,29,32,45,50). Among these, a pooled prevalence of 5% (95% CI; 3%-8%. p-value for heterogeneity < 0.001, I^2: 95%) for severe disease was estimated. Finally, eleven studies provided information regarding mortality in this population(8,19,23,32,50). An estimated 0.5% (95% CI; 0.02%-1.3%. p-value for heterogeneity < 0.001. I^2: 96%) of the total HCW reported as infected by the SARS-CoV-2 died because of complications of the disease.

Factors associated with SARS-CoV-2 infection in HCW

Fifteen studies analyzed the factors potentially associated with SARS-CoV-2 infection in HCW. From these, four studies provided sufficient data from infected and non-infected HCW to perform a meta-analysis for anosmia and five for fever, finding a significantly higher risk of COVID-19 with the presence of these symptoms (OR 28.37; 95%CI 9.45-85.16. p-value for heterogeneity = 0.002, I^2: 79% for anosmia and OR 4.86; 95%CI 2.83-8.37 p-value for heterogeneity < 0.001, I^2: 84% for fever) **(Web Table 4)**. Furthermore, the study of *Rudberg et al* also found a significantly higher risk of a positive RT-PCR result in HCW 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 (OR 3.06; 95% CI 1.24-7.56. p-value for heterogeneity = 0.001, I^2: 86%. three studies). Finally, the study of *Clemency et al* evaluated the predictive value of different symptoms for COVID-19 diagnosis, highlighting the loss of taste and smell, with a positive predictive value (PPV) of 0.5 and a negative predictive value (NPV) of 0.85, fever, with a PPV of 0.31 and a NPV of 0.83, and myalgia, with a PPV of 0.27 and a NPV of 0.80. On the other hand, no significant associations were found for fatigue (5 studies. OR 2.41. 95% CI; 0.92, 6.27. p-value for heterogeneity < 0.001, I^2: 92%)(24,44,57) and sore throat (4 studies. OR 0.55. 95% CI; 0.30, 1.01. p-value for heterogeneity: 0.02, I^2: 75%) **(Web Table 4)**(44,57).

Ran et al. found that, among seventy-two HCWs in Wuhan, China, unqualified hand-washing (OR 2.64; 1.04-6.71), suboptimal hand hygiene before, patient contact (OR 3.10; 1.43-6.73,), and inadequate PPE (OR 2.82; 1.11-7.18) were risk factors for SARS-CoV-2 infection(34). Similarly, the study of *Wang X et al.* reported that in a sample of 493 HCW in Wuhan, China, the risk of COVID-19 in HCW using medical masks was significantly higher when compared to those using N95 respirators (OR: 464.82, (95% CI:97.73-infinite), despite this last group had a significantly higher exposure to infected patients (48). *Chaterjee et al* reported similar results, highlighting a higher risk of SARS-CoV-2 infection in HCW that never used PPE compared to those with usual protection usage (OR 3.72; 95% CI 2.12-6.52).

Moreover, the risk of aerosol-generating procedures for HCW was analyzed by the prospective multi-center study by *El-Boghdadly et al,* which evaluated 1718 HCW 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 (18–48) days. Furthermore, 10% of the HCW involved in tracheal intubation procedures in these cohort had subsequently the composite outcome(109).

The potential source of infection was studied by *García Basteiro et al,* observing that HCW with a larger household size tended to have more frequently detectable antibodies (IgM or IgA) against SARS-CoV-2; albeit non-significant (p=0.093)(24). The study of *Kluytmans et al.* reported that among 84 SARS-CoV-2 positive HCW in two hospitals in The Netherlands, only three percent reported having been exposed to an inpatient with confirmed COVID-19 before symptoms onset(30). Finally, *Sikkema et al.,* by investigating the genome sequences from infected HCW 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(93).

Interestingly, two studies evaluated the benefit of pharmacological prophylaxis with hydroxychloroquine (HCQ) to prevent SARS-CoV-2 infection among high-risk HCW, with both studies showing that the history of having taken maintenance doses of HCQ was associated with a significantly lower risk of COVID-19(70,108).

Study Quality

The majority of studies were of moderate (n=61 [62.9%]) quality, with 29.9% (n=29) being high quality, while of the rest of low quality (n=7, 7.2%). Web **Tables 5, 6, and 7** present a summary of the studies' quality evaluation.

Discussion

The current evidence shows that around a tenth of the total HCW in the screened hospitals have a diagnosis of acute SARS-CoV-2 infection, with half being nurses. To date, only 7% of the HCW have resulted to be positive for the presence of antibodies indicating SARS-CoV-2 infection. Furthermore, most of the SARS-CoV-2 positive personnel were working in hospitalization/non-emergency 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 fifteen studies that screened HCW irrespective of their symptoms and reported the clinical features of SARS-CoV-2 positive individuals, 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 HCW, while 0.5% of the infected HCW died because of complications of the disease.

Our findings show a higher prevalence of SARS-CoV-2 infection among HCW when compared to the data from the general population reported in the literature(112). This difference may be attributable to workplace exposures of the HCW; nevertheless, only a few studies analyzed the potential source of infection in this population, limiting the possibility of evaluating the impact of nosocomial vs. community-acquired infection. The study of *Folgueira et al.* reported that there were no significant differences in the infection rates between the groups of HCW working in high, intermediate, and low exposure risk settings(22). Furthermore, the study of *Hunter et al.* found no differences in the proportion of infected HCW when comparing the ones with patient-facing roles with those without this exposure(26). In addition, the results of the studies of *García-Basteiro et al, Kluytmans et al*, and *Sikkema et al* 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 HCW, mainly due to the rapid circulation of the virus in the community. Another reason could be the infection from asymptomatic carriers, considering that about a half of the SARS-CoV-2 infected HCW 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 HCW 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 the 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 WHO, at least 50% of patients dying from COVID-19 were residents in hospitals or nursing homes, highlighting the need to control the spread of infection in a health care setting. Our findings suggest that almost half of SARS-CoV-2 infected HCW 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 to asymptomatic individuals, highlighting the transmission potential of SARS-CoV-2 carriers despite their clinical status(114). On the other hand, the study of *Gao et al.* suggested potentially low infectivity of asymptomatic SARS-CoV-2 carriers, as none of the 455 contacts who were exposed to an asymptomatic COVID-19 virus carrier had a positive test(73). These results were in-line with the studies performed by *Ng et al.* and *Canova et al.*, in which none of the exposed HCW had a subsequent positive SARS-CoV-2 test(42,49). Nevertheless, the lack of infection among HCW 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.* were wearing a mask, reducing further the spread of the infection. Nonetheless, even if this low infectivity is confirmed by further studies, the potential of silent transmission still represents an enormous issue that needs to be addressed efficiently, especially in low and middle-income countries lacking medical resources (e.g. PPE and diagnostic capacity). Considering the results of the present study, in which almost half of the positive HCW by RT-PCR were asymptomatic, there is an urgent need to promote a process of continuous, systematic screening of all HCW in high-risk settings, 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(57).

To improve the screening performance and early detection of SARS-CoV-2 infection among HCW, the analysis of risk factors for COVID-19 positivity is of importance. In the present review, fifteen studies analyzed the symptoms and signs associated with SARS-CoV-2 infection among HCW. Fever (OR: 4.86, 95% CI; 2.38-8.37. I^2: 84%), anosmia (OR: 28.37; 95%CI 9.45-85.16I^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 HCW; 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 the study of *Yombi et al.,* which 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(57). Similar results were reported by *Chow et al.* in a cohort of HCW in King County, Washington. In this study, screening only for fever, cough, shortness of breath, or sore throat might have missed 17% of symptomatic HCW at the time of illness onset. The authors also mention that expanding criteria for symptoms screening to include chills and myalgia may still have missed 10%(21). According to the results of the present systematic review and meta-analysis, malaise (48%) and headache (36%) represent additional common symptoms with a high prevalence among positive HCW **(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(21,57). Specifically, screening for these symptoms could be useful in low- and middle-income countries with limited testing capacity. However, screening HCW by symptoms may still miss a significant proportion of COVID-19 cases; therefore, universal screening for all exposed HCW regardless of symptoms should be the standard strategy to reduce transmission of SARS-CoV-2 in a hospital setting.

The high number of nurses being SARS-CoV-2 positive in our study could be explained by the larger 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. The fact that more infected HCW were observed in hospitalization/non-emergency wards in the current study may suggest a difference in PPE use across the settings, being the compliance to this measures higher in the emergency departments and ICUs (where the subjective risk perception is higher) compared to non-COVID-19 wards(115–117). However, most of the studies did not report the total number of screened HCW per area/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 being the highest number of employees in the health care setting could explain the high nurse SARS-CoV-2 positivity among other positive HCW. If future studies confirm nurses being the most affected personnel and hospitalization/non-emergency 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 mortality among HCW. We found that COVID-19 among HCW is associated with approximately a 0.5% proportion of fatal cases. Although the mortality among HCW is lower compared to the rate of mortality in the general population reported in the literature, better overall health and care among HCW, different age demography, and other factors could explain these differences. Yet, due to exposure to numerous infected individuals exposures, HCW, if infected, could be characterized by higher viral load which is associated with worst clinical outcomes(12).

Strengths and limitations

To our knowledge, this is the first systematic review quantifying the burden of COVID-19 among HCW. However, limitations in the current 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 sub-group 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, and 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 based on 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 HCW was poorly studied in the included articles, therefore limiting the possibility of analyzing the impact of nosocomial vs. community transmission. 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, HCW represent a population with a significant burden from COVID-19. HCW exhibit a high prevalence of SARS-CoV-2 infection, with a significant proportion of the infected HCW being asymptomatic carriers, a condition that favors silent transmission both in the clinical and community contexts if preventive measures and other standard procedures are not implemented.

Declaration of interests

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Table 1. Characterization of studies describing SARS-CoV-2 prevalence in HCW using RT-PCR

First Author, Year (Reference No.)	Number of participants	Setting	Selection criteria	City, Country
Kluytmans et al (2020)(30)	86	Hospital, all services	HCW who fever or (mild) respiratory symptoms	Breda, The Netherlands
García-Basteiro et al (2020) (24)	583	Hospital, all services	All HCW who deliver care and services to patients, either directly as physicians or nurses, or indirectly as assistants, technicians, stretcher-bearers or other support staff (administrative officers, cleaning, kitchen, laundry, maintenance, etc.)	Barcelona, Spain
Breazzano et al (2020) (18)	2088	Hospitals at the city level. Data reported by each postgraduate director	Medical residents in universities of NYC. Screened according to symptoms.	New York City, NY, USA
Tosato et al (2020) (43)	133	Laboratory Department	All workers in the laboratory department.	Padova, Italy
Keeley et al (2020) (28)	1533	Hospital, all services	All HCW	Sheffield, UK
Tostmann et al (2020) (44)	803	Hospital, all services	HCW with symptoms suggestive of COVID-19	Nijmegen, The Netherlands
Reusken et al (2020) (35)	1097	Hospital, all services	HCW with respiratory any symptom, even mild respiratory complaints.	Noord-Brabant Province, The Netherlands
Hunter et al (2020) (26)	1654	Hospital, all services including ambulance service staff	Staff with compatible symptoms (ie, new continuous cough or fever)	Newcastle upon Tyne, UK
Ran et al (2020) (34)	72	Hospital, all services	All HCW	Wuhan, China
Solodky et al (2020) (39)	244	Hospital, Cancer Institute	Voluntary HCW	Lyon, France

Guery et al (2020) (37)	136	Long-term care facility	All HCW	Nantes, France
Treibel et al (2020) (41)	400	Hospitals at a city level	All HCW	London, UK
Roxby et al (2020) (38)	62	Long-term care facility	All HCW	Seattle, WA, USA
Lai et al (2020) (50)	335	Hospital, all services	All HCW	Wuhan, China
Graham et al (2020) (53)	70	Long-term care facility	Asymptomatic HCW	London, UK
Vahidy et al (2020) (54)	2887	Hospital, all services	Asymptomatic HCW	Houston, TX, USA
Olalla et al (2020) (58)	498	Hospital, all services	Asymptomatic HCW	Marbella, Spain
Yombi et al (2020) (57)	536	Hospital, all services	Symptomatic HCW	Brussels, Belgium
Khalil et al (2020) (51)	266	Hospital, all services	All HCW	London, UK
Contejean et al (2020) (52)	1344	Hospital, all services	Symptomatic HCW	Paris, France
Barrett et al (2020) (16)	546	Hospital, all services	All HCW that reported: (1) ≥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 (≥3 patients/shift) expected in the next three months.	Newark, NJ, USA
Bai et al (2020) (15)	118	Hospital, Neurosurgery Department	All HCW	Wuhan, China

Folgueira et al (2020) (22)	1438	Hospital, City-level	All HCW	Madrid, Spain
Antonio-Villa et al (2020) (59)	34263	Hospital, all services	All HCW	Mexico City, Mexico
Borras-Bermejo et al (2020) (62)	2655	Long-term care facility	All HCW	Catalonia, Spain
Cho JH et al (2020) (64)	278	Hospital, all services	Symptomatic HCW	South Korea
Clemency BM et al (2020) (65)	961	Hospital, all services	Symptomatic HCW	New York City, NY, USA
Fusco FM et al (2020) (66)	115	Hospital, all services	Asymptomatic HCW	Naples, Italy
Galán MI et al (2020) (67)	2590	Hospital, all services	HCW with positive IgG and symptoms in the past 14 days	Madrid, Spain
Albalate M. et al (2020) (68)	14	Hospital, all services	Symptomatic HCW	Madrid, Spain
Bhattacharya et al (2020) (70)	106	Hospital, all services	All HCW	Kollkata, India
Houlihan et al (2020) (74)	200	Hospital, all services	All HCW	London, UK
Lahner et al (2020) (78)	2115	Hospital, all services	All HCW	Rome, Italy
Lan et al (2020) (79)	592	Hospital, all services	All HCW	Massachussets, USA
Lombardi et al (2020) (80)	1573	Hospital, all services	All HCW	Milan, Italy
Ma et al (2020) (81)	33	Hemodialysis unit	All HCW	Wuhan, China

Mani et al (2020) (82)	3477	Hospital, all services	Symptomatic HCW	Seattle,WA, USA
Jones et al (2020) (83)	4800	Hospital, all services	Symptomatic HCW	London, UK
Martin et al (2020) (84)	326	Hospital, all services	Symptomatic HCW	Brussels, Belgium
Paderno et al (2020) (86)	58	Otorrinolaringology Clinic	Symptomatic HCW	Brescia, Italy
Parcell et al (2020) (87)	1173	Hospital, all services	Symptomatic HCW	Tayside, UK
Shields et al (2020) (92)	554	Hospital, all services	All HCW	Birmingham, UK
Sikkema et al (2020) (93)	1796	Hospital, all services	Symptomatic HCW	Breda and tilburg, Netherlands
Bird et al (2020) (94)	152	Hospital, all services	Symptomatic HCW	Leicester, UK
Wee et al (2020) (95)	1642	Hospital, all services	Symptomatic HCW	Singapore
Brandstetter et al (2020) (71)	201	Hospital, all services	All HCW	Regensburg, Germany

HCW: Health care workers; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 2. Areas in which COVID-19 positive health care workers were laboring during RT-PCR screenings

Area/Setting	Number 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%
ICU	5	9	4% - 15%	68%

COVID-19: Coronavirus disease 2019; ICU: Intensive care unit.

Table 3. Prevalence of symptoms in COVID-19 positive health care workers

Symptom	Number 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%

COVID-19: Coronavirus disease 2019

Figure 1. Flowchart summarizing the study search and selection process.

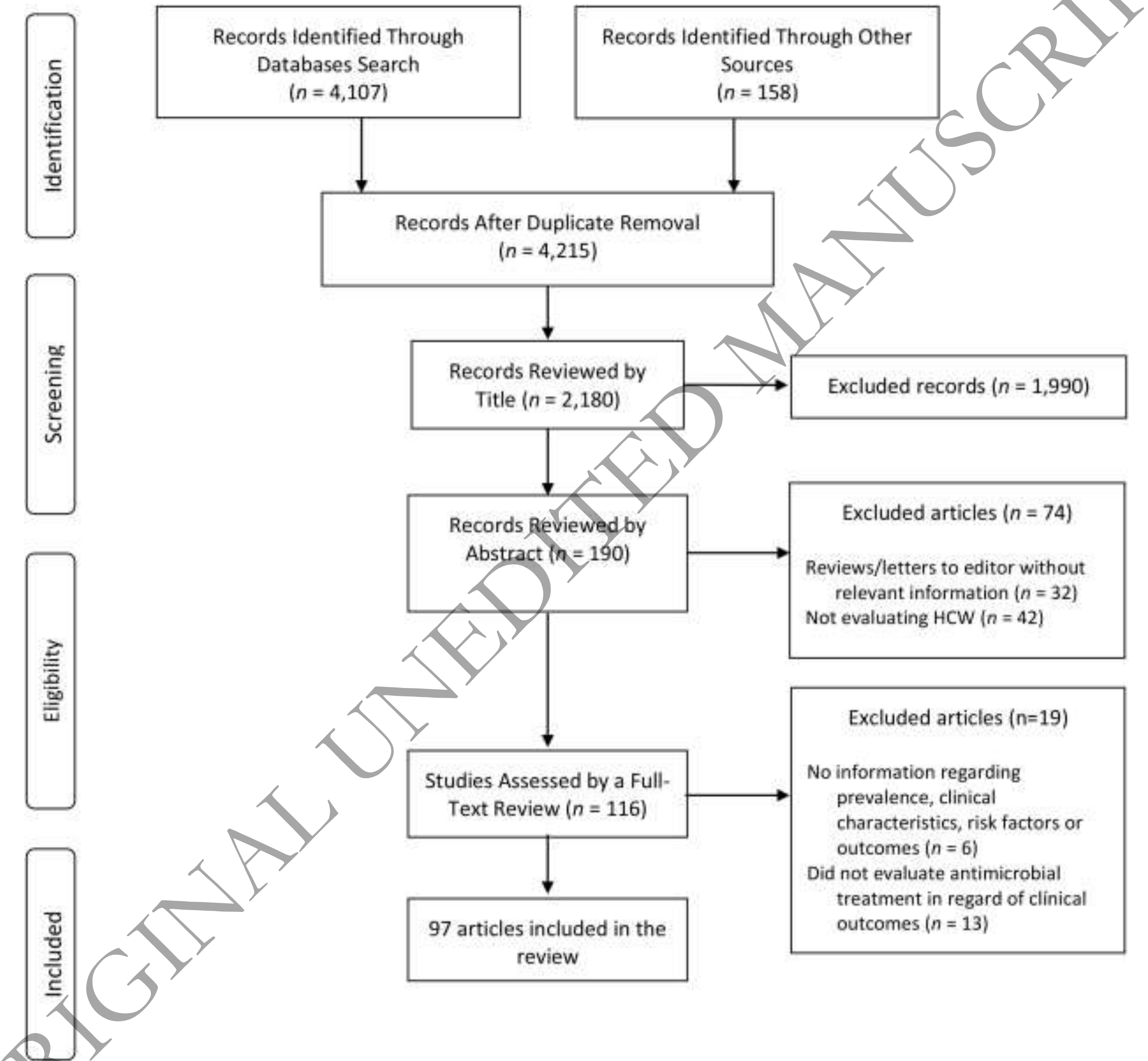
Legend. The PRISMA 2009 Flow Diagram, obtained from “Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097”

Figure 2. Geographical distribution of studies that reported data on SARS-CoV-2 prevalence in healthcare workers.

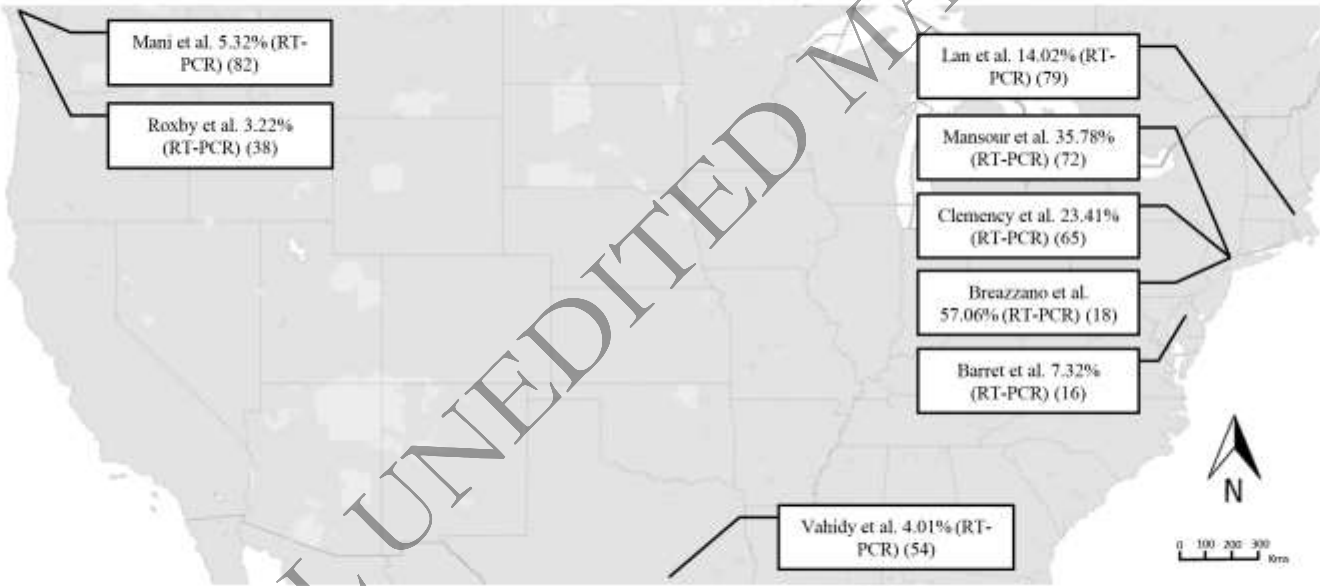
Legend: SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; %, percent.

Figure 3. SARS-CoV-2 infection prevalence in healthcare workers using RT-PCR

Legend: The results are presented as fractions. The overall summary estimates presented are calculated using random-effects models. HCW, health care workers; LTCF, long-term care facility; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; %, percent.

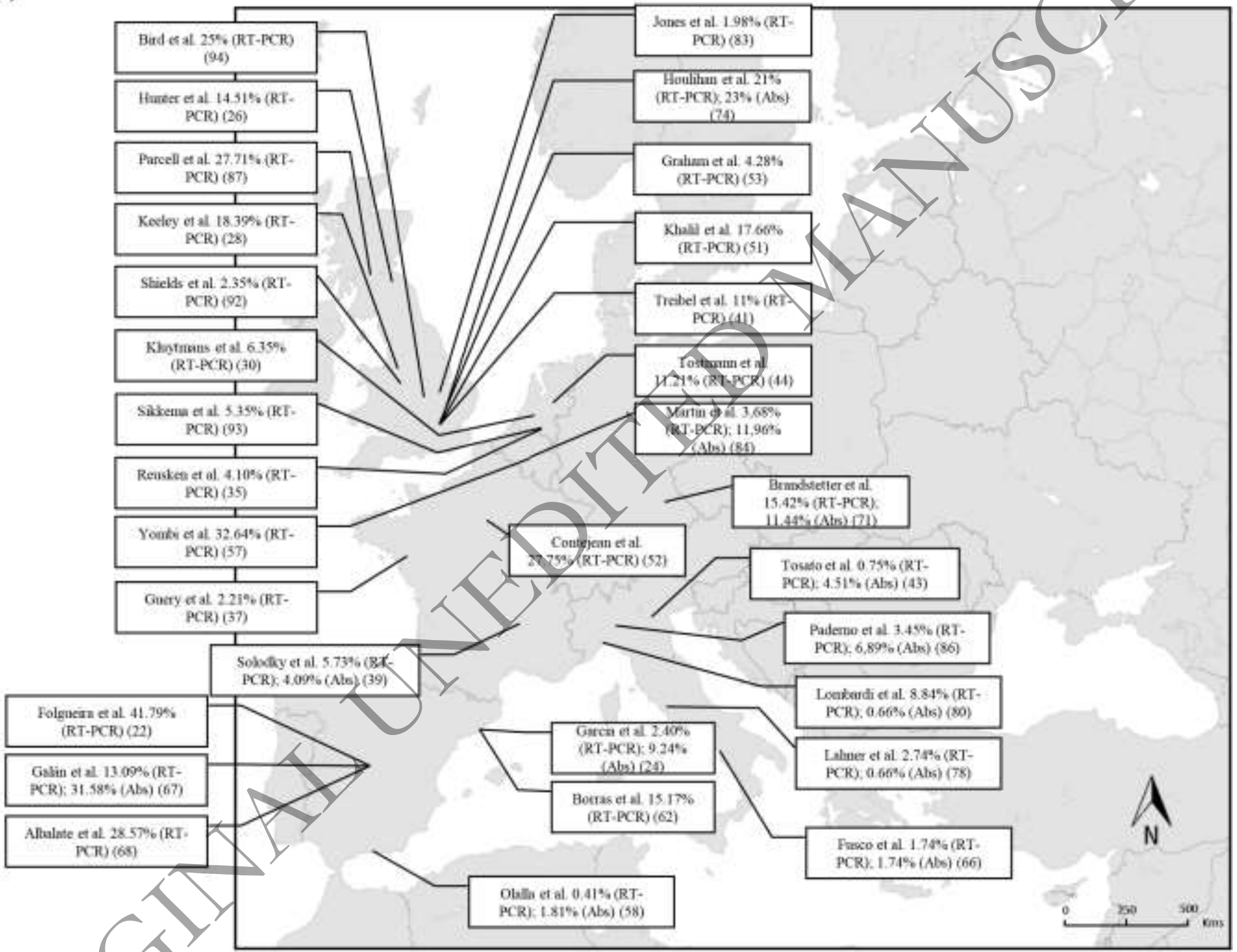

Identification
Screening
Eligibility
Included
Records Identified Through Databases Search (n = 4,107)
Records Identified Through Other Sources (n = 158)
Records After Duplicate Removal (n = 4,215)
Records Reviewed by Title (n = 2,180)
Excluded records (n = 1,990)
Records Reviewed by Abstract (n = 190)
Excluded articles (n = 74)
Reviews/letters to editor without relevant information (n = 32)
Not evaluating HCW (n = 42)
Studies Assessed by a Full-Text Review (n = 116)
Excluded articles (n=19)
No information regarding prevalence, clinical characteristics, risk factors or outcomes (n = 6)
Did not evaluate antimicrobial treatment in regard of clinical outcomes (n = 13)
97 articles included in the review

A)



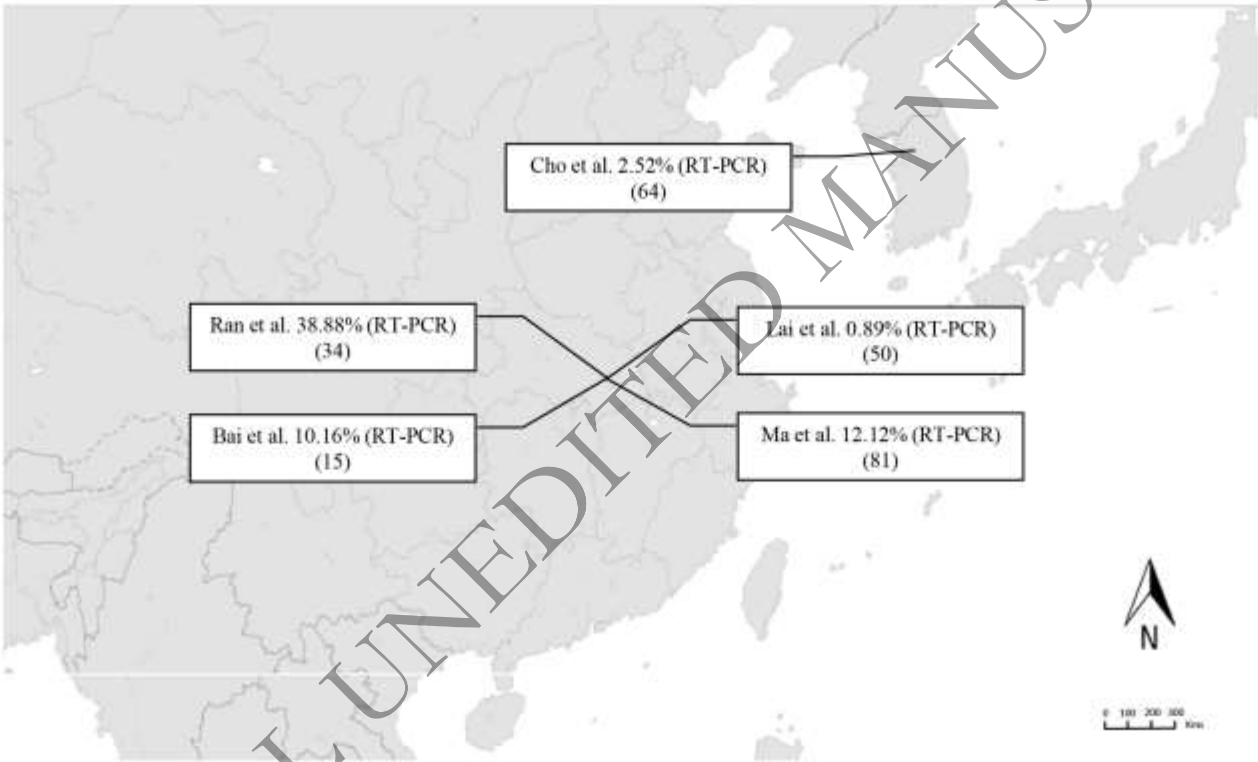
Mani et al. 5.32% (RT-PCR) (82)
Roxby et al. 3.22% (RT-PCR) (38)
Lan et al. 14.02% (RT-PCR) (79)
Mansour et al. 35.78% (RT-PCR) (72)
Clemency et al. 23.41% (RT-PCR) (65)
Breazzano et al. 57.06% (RT-PCR) (18)
Barret et al. 7.32% (RT-PCR) (16)
Vahidy et al. 4.01% (RT-PCR) (54)
N
0 100 200 300 Kms

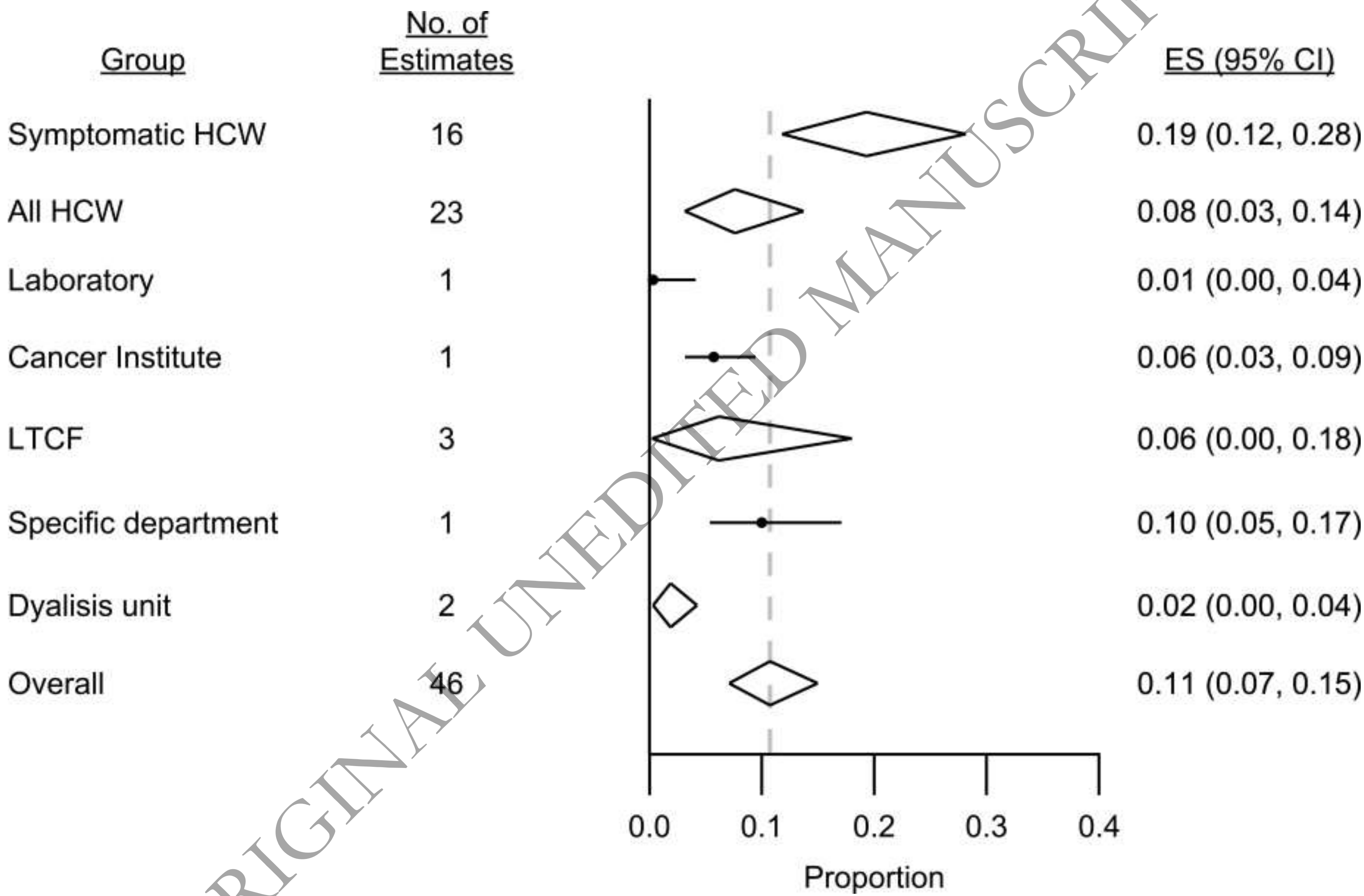
B)



Bird et al. 25% (RT-PCR) (94)
Hunter et al. 14.51% (RT-PCR) (26)
Parcell et al. 27.71% (RT-PCR) (87)
Keeley et al. 18.39% (RT-PCR) (28)
Shields et al. 2.35% (RT-PCR) (92)
Kluytmans et al. 6.35% (RT-PCR) (30)
Sikkema et al. 5.35% (RT-PCR) (93)
Reusken et al. 4.10% (RT-PCR) (35)
Yombi et al. 32.64% (RT-PCR) (57)
Guery et al. 2.21% (RT-PCR) (37)
Solodky et al. 5.73% (RT-PCR); 4.09% (Abs) (39)
Folgueira et al. 41.79% (RT-PCR) (22)
Galán et al. 13.09% (RT-PCR); 31.58% (Abs) (67)
Albalate et al. 28.57% (RT-PCR) (68)
Jones et al. 1.98% (RT-PCR) (83)
Houlihan et al. 21% (RT-PCR); 23% (Abs) (74)
Graham et al. 4.28% (RT-PCR) (53)
Khalil et al. 17.66% (RT-PCR) (51)
Treibel et al. 11% (RT-PCR) (41)
Tostmann et al. 11.21% (RT-PCR) (44)
Martin et al. 3.68% (RT-PCR); 11,96% (Abs) (84)
Brandstetter et al. 15.42% (RT-PCR); 11.44% (Abs) (71)
Contejean et al. 27.75% (RT-PCR) (52)
Tosato et al. 0.75% (RT-PCR); 4.51% (Abs) (43)
Paderno et al. 3.45% (RT-PCR); 6,89% (Abs) (86)
Lombardi et al. 8.84% (RT-PCR); 0.66% (Abs) (80)
Lahner et al. 2.74% (RT-PCR); 0.66% (Abs) (78)
Garcia et al. 2.40% (RT-PCR); 9.24% (Abs) (24)
Borras et al. 15.17% (RT-PCR) (62)
Fusco et al. 1.74% (RT-PCR); 1.74% (Abs) (66)
Olalla et al. 0.41% (RT-PCR); 1.81% (Abs) (58)
N
0
250
500
Kms

C)


Cho et al. 2.52% (RT-PCR)
(64)
Ran et al. 38.88% (RT-PCR)
(34)
Lai et al. 0.89% (RT-PCR)
(50)
Bai et al. 10.16% (RT-PCR)
(15)
Ma et al. 12.12% (RT-PCR)
(81)
N


Group
No. of Estimates
ES (95% CI)
Symptomatic HCW
16
0.19 (0.12, 0.28)
All HCW
23
0.08 (0.03, 0.14)
Laboratory
1
0.01 (0.00, 0.04)
Cancer Institute
1
0.06 (0.03, 0.09)
LTCF
3
0.06 (0.00, 0.18)
Specific department
1
0.10 (0.05, 0.17)
Dyalisis unit
2
0.02 (0.00, 0.04)
Overall
46
0.11 (0.07, 0.15)
0.0
0.1
0.2
0.3
0.4
Proportion