Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Sars-Cov-2 exposures of healthcare workers and acquisition of COVID-19

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Healthcare workers (HCWs) may be considered at a higher risk given their frequent contact and exposure to patients infected with SARS-CoV-2. As of June 1, 2022, the World Health Organization (WHO) reported 4 626 570 cases in HCWs from 150 reporting countries and territories with cases in HCWs generally following the population pattern waves [1]. The HCWs exposure to SARS-CoV-2 can occur during direct patient care in healthcare settings, during interactions with other HCWs, during work-related travel, and within the community and/or households [2]. Early in the pandemic, a systematic review found that SARS-CoV-2 acquisition among HCWs was more often associated with working in high-risk clinical settings, prolonged working hours, suboptimal hand hygiene, and improper use of personal protective equipment (PPE) [3]. However, more recent updates of this systematic review have identified household or community exposure to SARS-CoV-2 as the strongest risk factor with adjusted ORs varying from 2.55 to 8.98 [4]. In addition, more consistent use of full PPE measures and education/training in infection prevention and control (IPC) were associated with a protective effect [3,4].

A highly cited prospective, observational cohort study from early in the pandemic in 2020 found a higher frequency of COVID-19 test positivity in HCWs from the United States and the United Kingdom compared to the general population with higher frequency among those with reuse of or inadequate PPE [5]. The study did not appear to account for direct COVID-19 exposures among the general population, did not assess the level of training or adherence to the use of PPE, and was conducted at a time when HCWs were less prepared. Even though the authors tried to address differences in access to testing among HCWs and the general population with inverse probability weighting, selection bias was likely present. A smaller study done in the United Kingdom at the same time at a London teaching hospital observed that the rates of positivity amongst frontline HCWs paralleled the frequency of community-associated cases [6].

The matched case-control study reported by Belan et al. [7] that assessed HCW COVID-19 exposures and PPE use was unique because it included HCWs working across the spectrum of healthcare delivery (e.g acute care, long-term care facilities [LTCFs], and primary care). The strengths included its large size, nationwide scope, age, sex, and regional domicile matching, timing for inclusion, and prompt contact to reduce recall bias. Conditional multivariate analysis was conducted to adjust for multiple risk factors. The consistent associations across all healthcare settings and across similar at-risk HCW categories adds to the epidemiologic strength of association. The study was also conducted during a period with the more transmissible Alpha variant [8]. The strong association with the protective effect of previous COVID-19 infection and/or vaccination of the HCWs, which has been demonstrated in multiple randomized controlled trials (RCTs), provides further validation to the study [9,10]. The finding of exposure to infected persons outside

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the workplace as the highest independent risk factor for HCW SARS-CoV-2 acquisition and lesser risks from exposures to infected HCWs, COVID-19 patients, and working within a cluster of nosocomial cases are all biologically plausible findings. The identified risks to nurses and nurse's aides may be related to the amount of close contact, hands-on care provided and is consistent with a recent prospective cohort study that assessed the risk by HCW category [11]. An unexplained finding is the decreased risk of COVID-19 among HCWs in LTCFs with regular COVID-19 patient-facing activities. One might expect an increased risk in this setting, but it is possible that the HCWs in the LTCFs were previously immunized or infected during the initial wave of COVID-19. The findings from the multivariate analysis demonstrating a protective effect for the use of eye protection (goggles or face shields) has been reported in other studies and deserves more attention given recent reports of the human cornea supporting the presence of infectious SARS-CoV-2 [12]. The increased risk associated with the use of aprons is difficult to reconcile and observed only in the collated analysis but not in the individual subgroups. This may be a spurious finding or complicated by collinearity between components of PPE, which was not addressed. No data for compliance with hand hygiene were reported. The lack of any significant difference for risk associated with the use of surgical masks versus N95 respirators was present in all three health workplace settings, which added to the consistency of the association. A large multi-country WHO sponsored case-control study in HCWs, conducted between August 2019 and November 2021 involving 62 health facilities from 16 countries (1213 cases and 1844 controls) found prolonged patient contact (defined as < 1 metre distance for >15 mins) was significantly associated with SARS-CoV-2 infection (OR 1.4; 95% CI 1.0–1.8), and for those who had prolonged patient contact, inconsistent hand hygiene was significantly associated with infection (OR 2.7; 95% CI 1.7–4.2) in multivariate analysis [13]. This latter finding also requires more attention given the recent finding of the presence of infectious SARS-CoV-2 on human hands and within the immediate environment of infected COVID-19 patients [14].

Similar to the findings of Belan et al. [7], a prospective cohort study at nine healthcare institutions from Switzerland found household exposure to be the strongest risk factor (adjusted hazard ratio 10.1; 95% CI 7.5–13.5) for both HCW SARS-CoV-2 swab positivity and seroconversion in a multivariate regression analysis [11]. This study also found no significant difference between the use of a filtering facepiece class 2 respirator versus the use of a surgical mask [11], which is consistent with the updated systematic review of observational studies for risk factors for COVID-19 among HCWs mentioned above, albeit recognizing the limitations of observational studies [4]. Other high-quality systematic reviews have not found any differences for an increased risk of transmission to HCWs for other respiratory viruses when comparing medical/surgical masks versus N95 respirators [15].

The study by Belan [7] has limitations that have been outlined by the authors, and there remain concerns over recall bias, self-reported compliance with PPE, lack of auditing, and no mention of filtering facepiece class 2 fit checking, although all HCWs in France should have been fit tested. An assessment of collinearity between the individual components of PPE was not mentioned and other intrinsic biases associated with a case-control design still exist (including lack of blinding of analysts to case or control status, contamination bias, ascertainment bias, detection bias, and non-responder bias).

Nonetheless, the findings from this study served as a reminder for HCWs for vigilance in their contacts outside the healthcare setting, maintaining distancing and other precautions with colleagues during workplace break periods, and strict adherence to the use of PPE and hand hygiene in interactions with patients known or suspected to have COVID-19. Important policy implications include the use of a screening programme for HCWs before workplace entry, avoidance of presenteeism, and the need for the use of eye protection as a component of the PPE used for the routine care of COVID-19 patients. The finding of no differences in HCW acquisition of SARS-Co-2 with the use of a surgical mask versus a filtering facepiece class 2 respirator is reassuring, although we await the results of RCTs to add a higher tier of evidence regarding this issue in the routine care of COVID-19 patients [16].

This pandemic has taught us important lessons, including the need for continuous risk assessment, the need for adequate training of all HCWs in the principles of IPC, strict adherence to hand hygiene, and the need for appropriate use of PPE in its totality, and not focusing on a particular component of the PPE. It has also reminded us of the necessity to conduct carefully done studies of meaningful size and high-quality design to enhance decision making. Real-time RCTs in IPC should be prioritized at the same level as trials in diagnostic testing, therapeutic interventions and vaccination.

Transparency declaration

JL holds funding from the University of Calgary Centre for Health Informatics that are used to provide in-kind analytical support for her COVID-19 research, not related to this manuscript. She has also used programme funding provided to the University of Calgary from the Public Health Agency of Canada, Canadian Nosocomial Infection Surveillance Programme to support professional development. TJ's competing interests are accessible at: https://restoringtrials.org/competing-interests-tom-jefferson. JMC holds grants from the Canadian Institutes for Health Research on acute and primary care preparedness for COVID-19 in Alberta, Canada and was the primary local Investigator for a Staphylococcus aureus vaccine study funded by Pfizer for which all funding was provided only to the University of Calgary. He is co-investigator on a WHO-funded study using integrated human factors and ethnography approaches to identify and scale innovative IPC guidance implementation supports in primary care with a focus on low-resource settings and using drone aerial systems to deliver medical supplies and PPE to remote First Nations communities during the COVID-19 pandemic. He also received support from the CDC to attend an Infection Control Think Tank Meeting. He is a member and Chair of the WHO Infection Prevention and Control Research and Development Expert Group for COVID-19 and a member of the WHO Health Emergencies Programme (WHE) *Ad-hoc* COVID-19 infection prevention and control Guidance Development Group, both of which provide multidisciplinary advice to the WHO and for which no funding is received and from which no funding recommendations are made for any WHO contracts or grants. He is also a member of the Cochrane Acute Respiratory Infections Working Group. No funding was received to support the writing of this Commentary.

Author contributions

JC and JL wrote the initial draft of the Commentary. Additional expertise on interpretation of the Belan study and assessment of bias and limitations was provided by TJ. All co-authors contributed to the final writing and editing of the Commentary.

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