This is an Accepted Manuscript for *Infection Control & Hospital Epidemiology* as part of the Cambridge Coronavirus Collection.

DOI: 10.1017/ice.2020.455

**Article Type: Original Article** 

# Assessing COVID-19 Transmission to Healthcare Personnel: the Global ACT-HCP Case-Control Study

Running title: COVID-19 Transmission to Healthcare Personnel

Robert J. Lentz, MD<sup>1,2,3</sup>, Henri Colt, MD<sup>4</sup>, Heidi Chen, PhD<sup>5</sup>, Rosa Cordovilla, MD, PhD<sup>6</sup>, Spasoje Popevic, MD, PhD<sup>7</sup>, Sarabon Tahura, MBBS, FCPS<sup>8</sup>, Piero Candoli, MD<sup>9</sup>, Sara Tomassetti, MD<sup>10</sup>, Gerard J. Meachery, MD, BCh, FRCP<sup>11</sup>, Brandon P. Cohen, MBA, MHA<sup>12</sup>, Bryan D. Harris, MD, MPH<sup>3,13</sup>, Thomas R. Talbot, MD, MPH<sup>13</sup>, Fabien Maldonado, MD<sup>1,2</sup>

<sup>1</sup>Division of Allergy, Pulmonary and Critical Care, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>2</sup>Departments of Thoracic Surgery, Vanderbilt University School of Medicine, Nashville, TN, USA; <sup>3</sup>Department of Veterans Affairs Medical Center, Nashville, TN; <sup>4</sup>Division of Pulmonary Diseases and Critical Care Medicine (Emeritus), University of California, Irvine, CA, USA; <sup>5</sup>Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>6</sup>Department of Pulmonology, Interventional Pulmonary Unit, Salamanca University Hospital, Salamanca, Spain; <sup>7</sup>Department of Pulmonology, Interventional Pulmonology Unit, Clinical Center of Serbia, Belgrade, Serbia; <sup>8</sup>Department of Pediatric Respiratory Medicine, Bangladesh Institute of Child Health, Dhaka Shishu Hospital, Dhaka, Bangladesh; <sup>9</sup>Pulmonology Unit, Azienda Ospedali Riuniti Marche Nord, Pesaro, Italy; <sup>10</sup>Department of Experimental and Clinical Medicine, Interventional Pulmonary Unit, Careggi University Hospital, Florence, Italy; <sup>11</sup>Respiratory Medicine, Freeman Hospital, Newcastle University, Newcastle upon Tyne, UK; <sup>12</sup>HCA Healthcare, Ocala Health System, Ocala, FL, USA; <sup>13</sup>Division of Infectious Diseases and Department of Infection Prevention, Vanderbilt University Medical Center, Nashville, TN, USA

### Correspondence to:

Robert J. Lentz, MD
Division of Allergy, Pulmonary and Critical Care Medicine
1161 21<sup>st</sup> Avenue South
Nashville, TN 37232
robert.j.lentz@vumc.org
phone 615-936-1366
fax 615-322-0135

No element of this work has been previously presented, published, posted, or is currently submitted.

Abstract: 247/250 words Text: 2774/3000 words

Ref: 32

**ABSTRACT** 

Objective: To characterize associations between exposures within and outside the medical workplace

with healthcare personnel (HCP) SARS-CoV-2 infection, including the effect of various forms of

respiratory protection.

**Design**: Case-control study.

**Setting**: Data collected via online survey from international participants.

Participants: 1130 HCP (244 cases with laboratory-confirmed COVID-19, 886 controls healthy

throughout the pandemic) from 67 countries not meeting pre-specified exclusion (healthy but not

working, missing workplace exposure data, COVID symptoms without lab confirmation).

Methods: Respondents were queried regarding workplace exposures, respiratory protection, and extra-

occupational activities. Odds ratios for HCP infection were calculated with multivariable logistic

regression and sensitivity analyses controlling for confounders and known biases.

Results: HCP infection was associated with non-aerosol-generating contact with COVID-19 patients

(adjusted OR 1.4, 95% CI 1.04-1.9, p=0.03) and extra-occupational exposures including gatherings of ten

or more, patronizing restaurants or bars, and public transportation (adjusted ORs ranging 3.1-16.2).

Respirator use during aerosol-generating procedures (AGPs) was associated with lower odds of HCP

infection (adjusted OR 0.4, 0.2 to 0.8, p=0.005), as was exposure to intensive care and dedicated COVID

units, negative pressure rooms, and personal protective equipment (PPE) observers (adjusted ORs

ranging 0.4-0.7).

Conclusions: COVID-19 transmission to HCP was associated with medical exposures currently considered

lower-risk and multiple extra-occupational exposures, while exposures associated with proper use of

appropriate PPE were protective. Closer scrutiny of infection control measures surrounding healthcare

activities and medical settings considered lower risk, and continued awareness of the risks of public

congregation, may reduce the incidence of HCP infection.

Clinical trials identifier: not applicable

#### INTRODUCTION

Understanding the epidemiology of coronavirus disease 2019 (COVID-19) including risk factors associated with SARS-CoV-2 infection in healthcare personnel (HCP) is critical, as a substantial outbreak among HCP could dramatically disrupt patient care and threaten public health. Early reports suggested 19-29% of COVID-19 cases involve HCP with HCP more likely to have an occupational-related infection than other professions<sup>1–3</sup>. This aligns with data from the 2002-3 Severe Acute Respiratory Syndrome (SARS) epidemic in which HCP accounted for 21% of all global cases, most of which were believed to be nosocomial, raising similar concerns amid the COVID-19 pandemic<sup>4,5</sup>. Unlike SARS, however, COVID-19 achieved widespread community transmission around the world in early 2020, likely related to factors such as a propensity for asymptomatic and pre-symptomatic spread, placing HCP at risk for infection outside the workplace as well<sup>6-13</sup>.

This study assessed the degree to which exposures within and outside the medical workplace may be associated with HCP COVID-19 and investigated the association of different forms of respiratory protection on the odds of acquiring HCP infection. Explicit knowledge of exposures that place HCP at greater risk and what protective equipment reduces risk is of paramount importance to protect HCP. We hypothesized that healthcare activities capable of producing infectious aerosols would increase the odds of HCP infection while more protective respiratory PPE would reduce this risk.

### Study design and participants

This international case-control study used an online survey (Supplement A) to query HCP during a two-week period between April 20, 2020 and May 5, 2020. HCP were defined as individuals working in healthcare delivery settings. All data collected were anonymous and there was no direct investigator-to-respondent contact. The survey was conducted in REDCap<sup>14,15</sup>. Invitations to participate (Supplement B) were distributed by investigators from the United States, Spain, Italy, Serbia, and Bangladesh using HCP-oriented social media groups in WhatsApp, Facebook, Telegram, Reddit, and LinkedIn, as well as email. After survey completion, respondents were encouraged to recruit local colleagues to maximize the likelihood of drawing cases and controls from the same population. Participants were not recruited based on any studied exposures. Study protocol was approved as exempt research (VUMC IRB# 200677).

## **Variables and Exposures**

Respondents were required to confirm their status as HCP, then asked whether they had 1) been diagnosed with laboratory-confirmed COVID-19 ("cases"), 2) experienced an illness suspicious for COVID-19 after January 1, 2020 that was not laboratory-confirmed ("possible cases"), or 3) remained healthy while continuing to work ("controls"). Laboratory-confirmed COVID-19 was defined as report of a polymerase chain reaction (PCR) test detecting SARS-CoV-2. Cases and possible cases were asked the date of symptom onset and instructed to report their exposures during the 14 days prior to symptom onset. Controls were asked to complete the survey with respect to the 14 days prior to survey completion. A 14-day exposure window was chosen to correspond with the incubation period of SARS-CoV-2<sup>16</sup>.

The survey collected demographic data followed by questions about exposures to types of patients, healthcare settings, activities outside the workplace, and institutional policies regarding the use of PPE. Respondents exposed to laboratory-confirmed COVID-19 patients or persons under investigation for COVID-19 (COVID PUIs; defined as patients placed in precautionary isolation per local policy) were asked about specific exposures and respiratory protection used during the care of such patients. Intubation, extubation, open respiratory suctioning, bronchoscopy, nebulizer use, non-invasive positive pressure ventilation (NIPPV), tracheotomy, and cardiopulmonary resuscitation were considered aerosol-generating procedures (AGPs). Disposable N95/FFP2/FFP3 respirators (new or re-used), powered air purifying respirators (PAPRs), and reusable elastomeric respirators were considered respirator-level protection. "Prolonged contact" with patients was defined as 45 minutes or longer.

#### Statistical methods

Statistical analysis followed a pre-specified analysis plan. "Possible cases" and HCP healthy throughout the pandemic who had not worked in the 14 days prior to survey completion were excluded, as were surveys missing any demographic or workplace exposure data.

Descriptive statistics included mean and standard deviation for age and percent and frequencies for categorical variables. Between group comparisons were conducted with Wilcoxon rank sum and Pearson Chi-square tests for continuous and categorical variables, respectively. Odds ratios with 95% confidence intervals with respect to HCP COVID-19 were calculated for all exposures.

A multivariable logistic regression analysis was performed including pre-specified confounders age, gender, smoking status, presence of a baseline comorbidity, healthcare role, and world region.

Exposures involving COVID patients were additionally analyzed in a stratified manner according to the level of respiratory protection most frequently utilized during these exposures.

A pre-specified sensitivity analysis was performed to detect temporal bias with respect to the date of case illness onset, as we anticipated there would be incomplete overlap between case and control exposure time windows. Cases were grouped into the following cohorts and compared to controls: an "early sensitivity cohort" (symptom onset before April 1, 2020), "late sensitivity cohort" (onset on or after April 1, 2020), and "contemporaneous sensitivity cohort" (onset on or after April 20, 2020, the first day of survey data entry, therefore reporting over the same time period as controls).

#### **Role of the Funding Source**

This investigator-initiated study was not supported by specific funding.

#### **RESULTS**

A total of 1678 responses were received from 67 countries and 41 US states during the two-week study period. Five hundred forty-eight surveys were excluded from analysis based on pre-specified eligibility criteria, including 173 "possible cases" (Figure 1). Statistical analysis was performed on the remaining 1130 records, including 244 cases and 886 controls, of which 147 had non-exclusionary missing data.

Cases and controls were similar demographically, except for a higher proportion of cases among nurses (41%) than clinicians (20%) or respiratory therapists (6%, p<0.001, Table 1). Just over half of respondents were from Europe. Overall, respondent mean age was 42 years (range 19-73), 62% were female, and 74% were physicians or mid-level providers. About half of cases sought formal medical attention and 23% required hospital admission (Appendix Table 1).

#### Exposures to People in the Healthcare Workplace

Exposure to laboratory-confirmed COVID-19 patients was associated with HCP COVID-19 (OR adjusted 1.4, 95% CI 1.04 to 1.9, p=0.046). Non-AGP exposure to COVID-19 patients (n=634), but not participation in AGPs (n=321), was associated with HCP infection, which persisted in multivariate and temporal sensitivity analyses (Table 2). Cases and controls did not differ in the number of COVID-19 patients cared for (mean 19 vs. 22, mean difference 2.8, 95% CI -2.7 to 8.2, p=0.5). Workplace contact with an ill HCP colleague was associated with HCP infection (adjusted OR 4.4, 95% CI 3.2 to 6.0, p<0.001).

### Respiratory Protection and Specific Exposures to COVID-19 Patients

Respirators were used by 94% of respondents during AGPs and 72% during non-AGPs.

Respirator use in both AGPs and non-AGPs was associated with being a control (adjusted OR 0.4, 95% CI 0.2 to 0.8, p=0.005) while use of medical masks in both was associated with HCP infection (adjusted OR 7.4, 95% CI 2.8 to 20.0, <0.001, Table 3). Of those with only non-AGP contact, use of a medical mask was associated with HCP infection in the univariate but not adjusted or temporal sensitivity analyses. Re-use of disposable respirators during AGPs (vs. use of new disposable respirators) was not significantly associated with HCP infection (adjusted OR 1.6, 95% CI 0.7 to 3.5, p=0.29, n=254).

Prolonged contact with COVID-19 patients was associated with HCP infection in both univariate and temporal sensitivity analyses (Appendix Table 2). The odds of HCP infection were greater in those reporting prolonged continuous COVID-19 patient contact without a respirator (adjusted OR 2.3, 95% CI 1.1 to 4.9, p=0.04) versus those who wore respirators in this context (adjusted OR 0.8, 95% CI 0.5 to 1.5, p=0.6). Caring for COVID-19 patients in negative pressure rooms was associated with being a control (ORs ranging 0.4-0.7 across analyses). Most AGPs demonstrated ORs less than 1.0 though many did not meet statistical significance (Appendix Table 2).

#### Exposures to Specific Healthcare Settings

Working in ICUs, dedicated COVID ICUs, or dedicated COVID wards was associated with significantly lower odds of HCP COVID-19 (adjusted ORs ranging 0.5-0.7, 95% CIs ranging 0.3 to 0.96, p<0.05) than exposure to regular hospital wards (adjusted OR 1.4, 95% CI 1.0 to 1.9, p=0.05; Appendix Table 3). Skilled nursing or long-term care facility exposure also associated with HCP infection (adjusted OR 2.9, 95% CI 1.3 to 6.4, p=0.007).

## **Exposures Outside the Healthcare Workplace**

Exposure to ill household members, gatherings of more than ten people, restaurants or bars, and public transportation was associated with HCP infection (Table 4). Adjusted odds ratios ranging from 4.6 to 16.2 for the latter three exposures decreased over time in the temporal sensitivity analysis (contemporaneous cohort ORs ranging 3.1 to 4.7), though remained significantly associated with HCP infection (all p<0.05).

## **Exposures to Local Institutional Policies**

Working at facilities with policies recommending respirator use during AGPs (adjusted OR 0.4, 95% CI 0.3 to 0.7, p<0.001) and non-AGP contact (adjusted OR 0.6, 95% CI 0.5 to 0.9, p=0.008) were associated with being a control, while HCP at institutions with policies advocating extended use or reuse of disposable respirators did not associate with being a case or control (Table 4). HCP reporting they were always observed donning and doffing PPE by dedicated observers were more likely to be controls than those who reported PPE observers were never available (adjusted OR 0.4, 95% CI 0.3 to 0.7, p=0.001).

Results from this international case-control study of more than 1100 HCP from over 60 countries characterizing important exposures associated with HCP COVID-19 may have immediate implications for infection control policies within and outside the healthcare setting. First, our results indicate nosocomial transmission to HCP was more likely during routine contact with COVID-19 patients rather than during AGPs. Second, significantly lower likelihood of HCP infection was associated with working in ICUs and COVID units, respirator use (in some contexts), and dedicated PPE observers, which reinforces the protective value of being familiar with and using appropriate PPE. Third, multiple exposures outside the healthcare setting were strongly associated with HCP infection, suggesting transmission of COVID-19 in the community remains a critical and underappreciated contributor to HCP infection.

Within the healthcare setting, AGPs have been implicated as major risk factors for nosocomial transmission of respiratory viral infections such as SARS-CoV-1<sup>17</sup>. Accordingly, attention has focused on practices believed to protect against transmission during these procedures, including use of respirators, negative pressure ventilation, and procedural techniques hypothesized to reduce aerosolization<sup>18–21</sup>.

Perhaps related to such attention, our results indicate participation in AGPs was not associated with HCP infection. Protective associations noted for respirator use during COVID-19 AGPs and work in ICUs and dedicated COVID units (the latter corroborated by a recent brief report utilizing PCR data<sup>22</sup>) suggest appropriate PPE and familiarity with its use and the risks involved in COVID-19 patient care are likely highly protective, which is further bolstered by the protective association with dedicated PPE observers. These data suggest providers can perform COVID-19 patient care including AGPs confidently with appropriate PPE including respirators, training, and supervision.

Routine non-AGP contact with COVID-19 patients, however, was associated with HCP infection in this study. Optimal respiratory protection during non-AGP contact with COVID-19 patients remains

uncertain. The World Health Organization recommends medical masks in this context while the US

Centers for Disease Control and Prevention advises respirators are preferred<sup>23,24</sup>. A meta-analysis of four
pre-COVID-19 randomized trials involving 4531 subjects suggested respirators and medical masks offer
similar protection from a variety of respiratory viral infections, though the certainty of this finding was
considered low<sup>25</sup>. Another meta-analysis of 44 observational studies involving protection from epidemic
betacoronaviruses indicated respirators may be more protective than face masks, but only includes a
single COVID-19-specific study related to this topic, which retrospectively compared respirator use to no
mask use<sup>26,27</sup>.

Our study represents the only COVID-19-specific data comparing respirators to other forms of respirator protection. Non-AGP medical mask use was not consistently associated with HCP COVID-19, but HCP infection was more likely with prolonged continuous contact (≥45m) while not wearing a respirator (adjusted OR 2.3 vs. 0.8 when respirator used). These results are consistent with a more nuanced view of respiratory viral transmission in which the distinction between large droplet and small-particle aerosol is better described as a spectrum than dichotomous mechanisms of infection<sup>28-31</sup>.

Respiratory viral transmission requires sufficient contamination of respiratory mucus membranes by virus-laden large droplets or deposition of virus-containing aerosol small-particles in the lower respiratory tract. Inhaled dose would be expected to increase with higher concentrations of aerosolized viral particles and longer duration of exposure, but decreases with effective filtration of inhaled air. This aligns with observed patterns of HCP infection in our study: AGPs increase the concentration of aerosolized virus and are associated with HCP infection unless highly effective filtration (a respirator) is utilized; negative pressure ventilation reduces aerosolized viral burden and is associated with protection from infection; prolonged non-AGP contact without a respirator might occasionally allow a sufficient inhaled dose and is associated with modestly increased odds ratio for HCP COVID-19. Our results suggest

medical masks are likely adequate during most non-AGP contact with COVID-19 patients, but respirators might be considered if very prolonged close contact is anticipated.

Some HCP in this study certainly acquired SARS-CoV-2 outside of the workplace. While several odds ratios corresponding to extra-occupational exposures decreased in magnitude in the temporal sensitivity analysis (due to the reduced frequency of these exposures over time as stay-at-home orders and business closures escalated), the ORs associated with gatherings of ten or more people, dining in a restaurant or patronizing a bar, and using public transportation remained high even in the contemporaneous sensitivity cohort, where they in fact exceed the ORs for all occupational exposures except AGP exposure without respirator protection. These results suggest extra-occupational exposures remain highly pertinent to HCP safety and indicate a continued risk in scenarios involving public congregation.

Finally, close contact with afflicted individuals in settings without the same PPE expectations as during patient care were associated with HCP infection, notably exposure to sick HCP colleagues and household members. Protective behaviors including social distancing outside the patient-provider relationship and not working while ill remain pertinent to HCP, particularly in light of a recent report noting 65% of HCP with COVID-19 worked while symptomatic<sup>32</sup>.

Strengths of this study include its large international sample of HCP, befitting of a pandemic with global consequences, which ensures good generalizability across a broad range of healthcare systems. Controls were matched as closely as possible to cases by design in which cases were asked to recruit local controls. The vast majority of analyzed responses (87%) contained complete data, and most (242 of 375) responses excluded by missing data criteria were nearly empty responses (lacking case-control or demographic information, ascertained at the start of the survey). Data on exposures and respiratory protections utilized were collected in a specific and detailed manner, and statistical analysis proceeded according to pre-specified analysis plan including multivariate and temporal sensitivity

analyses. This study also exemplifies a design in which medically oriented social media facilitated rapid and far-reaching HCP recruitment across a broad range of geographic origin and healthcare roles.

While a case-control design is appropriate for a study intended to rapidly collect data from an international sample involving relatively rare individual events, this design has limitations. Confirming respondent SARS-CoV-2 status was not practical from a timing, logistic, or economic perspective given the diverse nature of this sample, so we relied on self-report of laboratory-confirmed COVID-19. A "possible case" group which was then excluded from the primary analysis was used to avoid these respondents from erroneously indicating they were laboratory-confirmed cases, and the large sample size limits the influence of any uncommon erroneous self-reports. Without serologic testing, the issue of asymptomatic infection remains, and some crossover of occult infection into the control group almost certainly occurred which would be expected to dampen the odds ratios. Recall bias is possible, although this is not dissimilar from other key studies used to assess HCP risk of SARS acquisition<sup>33</sup>. Controls were asked to report their most proximate exposures to limit recall bias. This design resulted in incomplete overlap in case and control exposure windows, addressed by pre-specified temporal sensitivity analysis. Geographic bias caused by differing levels of community illness and risk of exposure across different regions was addressed by including region in the multivariate logistic regression, though more local variations may still have had some impact. While we intended to capture comprehensive data relating to HCP infection risk, the possibility of unmeasured confounders is always present. Additionally, some exposures noted to be protective from infection, such as use of negative pressure rooms, might also be reflective of more advanced or affluent healthcare systems which may also reduce HCP infection in other ways (access to more or higher quality PPE, for example). Finally, as respondents self-selected into study participation, selection/collider bias is possible. This is among the reasons that case-control studies detect associations but do not imply causation, and we have been careful to discuss our results in a manner befitting the certainty level appropriate to this study design.

Results from this international case-control study highlight several occupational and extra-

occupational exposures associated with symptomatic COVID-19 among HCP. Attention should now shift

to currently less-scrutinized "lower risk" activities and hospital settings. Implementation of PPE observer

programs may help address occupational risk, while HCP should remain vigilant for potential exposures

outside of work which were more associated with infection than most healthcare exposures in this

study. These results have immediate implications for healthcare and public policy.

**ACKNOWLEDGEMENTS** 

The authors wish to acknowledge the COVIDBronch Initiative who participated in survey distribution as

well as the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR, via representative Dr. Rosa

Cordovilla), and the Malaysian Thoracic Society for their endorsement of this study to their

memberships. We dedicate this work to HCP who have become ill caring for COVID-19 patients, most of

all those who lost their lives in this service.

Guarantor statement: Robert J. Lentz and Fabien Maldonado had full access to all the data in the study

and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Author contributions**:

Study concept and design: RJL, HC, FM

Acquisition of data: RJL, HC, FM, RC, SP, ST, PC, ST, GJM, BPC

Analysis and interpretation of data: HC, RJL, HC, FM, BDH, TRT

Drafting of the manuscript: RJL, HC, FM, BDH, TRT

All authors participated in critical revision of the manuscript for important intellectual content and provided final approval to submit this version of the manuscript and have agreed to be accountable for all aspects of the work.

## Financial/nonfinancial disclosures:

No authors report any financial or non-financial conflicts of interest pertinent to this work.

## Funding/role of sponsors:

This study was supported by UL1 TR000445 (REDCap support). This investigator-initiated study was otherwise not supported by any funding.

#### REFERENCES

- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585
- 2. Lan F-Y, Wei C-F, Hsu Y-T, Christiani DC, Kales SN. Work-related COVID-19 transmission in six Asian countries/areas: A follow-up study. *PLOS ONE*. 2020;15(5):e0233588. doi:10.1371/journal.pone.0233588
- CDC COVID-19 Response Team, CDC COVID-19 Response Team, Burrer SL, et al. Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(15):477-481. doi:10.15585/mmwr.mm6915e6
- 4. WHO | Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. WHO. Accessed May 21, 2020. http://www.who.int/csr/sars/country/table2003\_09\_23/en/
- 5. Sepkowitz KA, Eisenberg L. Occupational deaths among healthcare workers. *Emerg Infect Dis.* 2005;11(7):1003-1008. doi:10.3201/eid1107.041038
- 6. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. *N Engl J Med*. Published online January 29, 2020. doi:10.1056/NEJMoa2001316
- 7. Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med*. 2020;27(2). doi:10.1093/jtm/taaa021
- 8. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill*. 2020;25(10):2000180. doi:10.2807/1560-7917.ES.2020.25.10.2000180
- 9. Furukawa NW, Brooks JT, Sobel J. Early Release Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic Volume 26, Number 7—July 2020 Emerging Infectious Diseases journal CDC. doi:10.3201/eid2607.201595
- 10. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). *Science*. 2020;368(6490):489-493. doi:10.1126/science.abb3221
- 11. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med*. 2020;382(12):1177-1179. doi:10.1056/NEJMc2001737
- 12. Peiris JSM, Chu CM, Cheng VCC, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *Lancet Lond Engl*. 2003;361(9371):1767-1772. doi:10.1016/s0140-6736(03)13412-5
- 13. Treibel TA, Manisty C, Burton M, et al. COVID-19: PCR screening of asymptomatic health-care workers at London hospital. *The Lancet*. Published online May 2020. doi:10.1016/S0140-6736(20)31100-4

- 14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
- 15. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. doi:10.1016/j.jbi.2019.103208
- 16. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med*. 2020;172(9):577-582. doi:10.7326/M20-0504
- 17. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol Generating Procedures and Risk of Transmission of Acute Respiratory Infections to Healthcare Workers: A Systematic Review. Semple MG, ed. *PLoS ONE*. 2012;7(4):e35797. doi:10.1371/journal.pone.0035797
- 18. Canelli R, Connor CW, Gonzalez M, Nozari A, Ortega R. Barrier Enclosure during Endotracheal Intubation. *N Engl J Med*. 2020;0(0):null. doi:10.1056/NEJMc2007589
- 19. McGrath BA, Brenner MJ, Warrillow SJ, et al. Tracheostomy in the COVID-19 era: global and multidisciplinary guidance. *Lancet Respir Med*. 2020;0(0). doi:10.1016/S2213-2600(20)30230-7
- 20. Odor PM, Neun M, Bampoe S, et al. Anaesthesia and COVID-19: infection control. *BJA Br J Anaesth*. Published online April 8, 2020. doi:10.1016/j.bja.2020.03.025
- 21. Angel L, Kon ZN, Chang SH, et al. Novel Percutaneous Tracheostomy for Critically Ill Patients with COVID-19. *Ann Thorac Surg.* Published online April 25, 2020. doi:10.1016/j.athoracsur.2020.04.010
- 22. Gagneux-Brunon A, Pelissier C, Gagnaire J, et al. SARS-CoV-2 infection: Advocacy for training and social distancing in healthcare settings. *J Hosp Infect*. 2020;0(0). doi:10.1016/j.jhin.2020.08.001
- 23. Rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages. Accessed May 21, 2020. http://www.who.int/publications-detail/rational-use-of-personal-protective-equipment-for-coronavirus-disease-(covid-19)-and-considerations-during-severe-shortages
- 24. CDC. Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings. Centers for Disease Control and Prevention. Published February 11, 2020. Accessed May 21, 2020. http://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html
- 25. Bartoszko JJ, Farooqi MAM, Alhazzani W, Loeb M. Medical masks vs N95 respirators for preventing COVID-19 in healthcare workers: A systematic review and meta-analysis of randomized trials. *Influenza Other Respir Viruses*. Published online April 21, 2020. doi:10.1111/irv.12745
- 26. Wang X, Pan Z, Cheng Z. Association between 2019-nCoV transmission and N95 respirator use. *J Hosp Infect*. 2020;105(1):104-105. doi:10.1016/j.jhin.2020.02.021

- 27. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *The Lancet*. Published online June 2020. doi:10.1016/S0140-6736(20)31142-9
- 28. Shiu EYC, Leung NHL, Cowling BJ. Controversy around airborne versus droplet transmission of respiratory viruses: implication for infection prevention. *Curr Opin Infect Dis*. 2019;32(4):372-379. doi:10.1097/QCO.000000000000563
- 29. Bahl P, Doolan C, de Silva C, Chughtai AA, Bourouiba L, MacIntyre CR. Airborne or droplet precautions for health workers treating COVID-19? *J Infect Dis*. Published online April 16, 2020. doi:10.1093/infdis/jiaa189
- 30. Bourouiba L. Turbulent Gas Clouds and Respiratory Pathogen Emissions: Potential Implications for Reducing Transmission of COVID-19. *JAMA*. Published online March 26, 2020. doi:10.1001/jama.2020.4756
- 31. Stadnytskyi V, Bax CE, Bax A, Anfinrud P. The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. *Proc Natl Acad Sci U S A*. Published online May 13, 2020. doi:10.1073/pnas.2006874117
- 32. Chow EJ, Schwartz NG, Tobolowsky FA, et al. Symptom Screening at Illness Onset of Health Care Personnel With SARS-CoV-2 Infection in King County, Washington. *JAMA*. Published online April 17, 2020. doi:10.1001/jama.2020.6637
- 33. Raboud J, Shigayeva A, McGeer A, et al. Risk Factors for SARS Transmission from Patients Requiring Intubation: A Multicentre Investigation in Toronto, Canada. *PLOS ONE*. 2010;5(5):e10717. doi:10.1371/journal.pone.0010717

#### **TABLES**

Table 1. Demographics of cases and controls.

	<b>Cases</b> , % (n)	Controls, % (n)
	n=244	n=886
Age*	41 (±10)	43 (±11)
Female gender	66% (161)	61% (544)
Clinical role		
Clinician†	68% (165)	75% (668)
Nurse	24% (59)	10% (86)
Respiratory Therapist	2% (5)	9% (81)
Other‡	6% (15)	6% (51)
Any existing medical condition	28% (68)	22% (199)
Asthma	9% (23)	7% (60)
HTN	11% (26)	10% (87)
DM	3% (8)	3% (26)
Current or former smoker	21% (51)	24% (208)
Region		
Europe	59% (144)	52% (465)
North America	19% (47)	24% (210)
Asia	16% (40)	16% (138)
Other	5% (13)	8% (73)
Institutional Setting		
Major Academic Hospital	36% (87)	37% (327)
Major Public Hospital	26% (64)	27% (241)
Local Public Hospital	12% (30)	10% (89)
Major Private Hospital	12% (28)	9% (78)
Others§	14% (35)	17% (151)

<sup>\*</sup>Mean (±standard deviation)

‡Includes administrative support staff, environmental services/custodial/janitorial, medical student or other clinical trainee, medical technician, emergency medical technician, medical laboratory staff, medical therapists, hospital transport staff

§Includes community/local academic hospital, community/local private hospital, Veteran's Affairs facility, military hospital, outpatient clinic, procedure center

<sup>†</sup>Physicians, mid-level providers such as nurse practitioners, or other analogous roles

Table 2. Odds ratios for HCP infection associated with exposures to people in the healthcare setting.

	Unadjusted	р	Adjusted	р	Contemporaneous Sensitivity Cohort	р
COVID-19 patient	1.4 (1.1 to 1.9)	0.02	1.4 (1.0 to 1.9)	0.046	2.4 (1.2 to 4.5)	0.01
AGP (n=321)	0.9 (0.6 to 1.2)	0.39	0.9 0.6 to 1.2)	0.44	1.0 (0.5 to 2.2)	0.97
Non-AGP (n=634)	1.5 (1.1 to 2.0)	0.009	1.4 (1.04 to 1.9)	0.03	2.2 (1.2 to 4.1)	0.01
COVID PUI	0.9 (0.7 to 1.3)	0.64	0.9 (0.6 to 1.2)	0.36	2.5 (1.0 to 6.1)	0.04
AGP (n=288)	0.8 (0.5 to 1.1)	0.09	0.8 (0.5 to 1.1)	0.12	0.7 (0.3 to 1.4)	0.31
Non-AGP (n=759)	1.0 (0.8 to 1.4)	0.86	1.0 (0.7 to 1.3)	0.76	2.1 (0.98 to 4.5)	0.06
Non-COVID patient	0.7 (0.5 to 1.0)	0.06	0.8 (0.6 to 1.1)	0.22	0.5 (0.2 to 0.9)	0.02
Sick colleague* (n=459)	4.9 (3.6 to 6.6)	<0.001	4.4 (3.2 to 6.0)	<0.001	4.8 (2.5 to 9.2)	<0.01

AGP = aerosol-generating procedure. PUI = person under investigation for COVID.

<sup>\*</sup>COVID symptoms or diagnosed with confirmed COVID-19

Table 3. Respiratory protection utilized most frequently during contact with COVID-19 patients.

			All Cases* - Unadjusted		All Cases - Adjusted		Early Sensitivity Cohort†		Late Sensitivity Cohort‡		Contemporaneous Cohort§		
During AGPs		During non-AGPs	n (all)	OR	р	OR	р	OR	р	OR	р	OR	р
Respirator	+	Respirator	242	0.4 (0.2 to 0.8)	0.003	0.4 (0.2 to 0.8)	0.005	0.2 (0.06 to 0.5)	<0.001	0.7 (0.3 to 1.5)	0.35	0.5 (0.1 to 2.4)	0.42
Respirator	+	Medical Mask	55	1.0 (0.5 to 2.1)	0.99	1.0 (0.4 to 2.3)	0.94	1.1 (0.3 to 3.9)	0.84	0.8 (0.3 to 2.1)	0.68	0.6 (0.06 to 5.2)	0.62
Medical Mask	+	Medical Mask	18	7.4 (2.8 to 20.0)	<0.001	9.1 (2.8 to 29.9)	<0.001	38.3 (7.7 to 189.9)	<0.001	3.9 (1.0 to 14.6)	0.04	4.7 (0.4 to 53.2)	0.21
(no exposure)	+	Respirator	208	1.1 (0.7 to 1.6)	0.67	1.2 (0.8 to 1.9)	0.43	0.8 (0.4 to 1.6)	0.48	1.3 (0.8 to 2.0	0.36	1.6 (0.7 to 3.4)	0.23
(no exposure)	+	Medical Mask	99	1.7 (1.1 to 2.7)	0.02	1.6 (0.9 to 2.6)	0.09	1.9 (0.9 to 3.9)	0.1	1.2 (0.6 to 2.1)	0.65	1.1 (0.5 to 2.9)	0.80

<sup>\*</sup>Median exposure windows Apr 14-28, 2020 (controls, n=886) and Mar 20-Apr 3, 2020 (all cases, n=244)

§Median case exposure window Apr 10-24, 2020 (n=54)

<sup>†</sup>Median case exposure window Mar 3-17, 2020 (n=101)

<sup>‡</sup>Median case exposure window Apr 3-17, 2020 (n=141)

Table 4. Odds ratios associated with extra-occupational and local institutional policy exposures.

	All Cases -	р	All Cases -	р	Early Sensitivity	р	Late Sensitivity	р	Contemporaneous	р
	Unadjusted		Adjusted		Cohort		Cohort		Sensitivity Cohort	•
Exposures outside work										
Person with known COVID-19	1.5 (0.95 to 2.5)	0.08	1.5 (0.9 to 2.5)	0.10	2.1 (1.2 to 4.0)	0.02	1.0 (0.5 to 2.1)	0.99	0.7 (0.2 to 2.9)	0.58
Person with COVID symptoms	1.2 (0.8 to 1.8)	0.42	1.1 (0.7 to 1.7)	0.75	1.9 (1.1 to 3.2)	0.02	0.7 (0.4 to 1.2)	0.2	0.2 (0.02 to 1.2)	0.07
Household member, known COVID-19	4.4 (1.9 to 10.3)	<0.001	3.8 (1.5 to 9.3)	0.004	4.1 (1.3 to 13.9)	0.02	3.6 (1.3 to 10.4)	0.02	4.2 (0.8 to 22.0)	0.09
Household member, COVID symptoms	3.0 (1.6 to 5.8)	<0.001	3.1 (1.5 to 6.3)	0.002	6.3 (2.8 to 14.2)	<0.001	1.6 (0.5 to 4.6)	0.42	1.4 (0.2 to 11.1)	0.76
Gathering of ≥10 people	4.6 (3.1 to 7.0)	<0.001	4.6 (3.0 to 7.1)	<0.001	8.6 (5.0 to 14.9)	<0.001	2.4 (1.4 to 4.4)	0.002	3.4 (1.5 to 7.8)	0.003
Patronized restaurant or bar*	15.8 (8.6 to 29.3)	<0.001	16.2 (8.6 to 30.5)	<0.001	45.3 (21.7 to 94.8)	<0.001	3.6 (1.5 to 8.8)	0.005	4.7 (1.5 to 15.1)	0.008
In-person retail shopping	0.9 (0.6 to 1.2)	0.35	0.9 (0.6 to 1.2)	0.36	1.0 (0.6 to 1.6)	0.93	0.8 (0.5 to 1.2)	0.21	1.2 (0.6 to 2.1)	0.66
Used public transportation	5.4 (3.5 to 8.2)	<0.001	4.4 (2.8 to 6.9)	<0.001	7.9 (4.3 to 14.4)	<0.001	2.7 (1.5 to 4.7)	<0.001	3.1 (1.3 to 7.0)	0.009
Institutional policies										
Respirator for AGP	0.4 (0.3 to 0.7)	<0.001	0.4 (0.3 to 0.7)	<0.001	0.3 (0.2 to 0.6)	<0.001	0.7 (0.4 to 1.2)	0.19	0.8 (0.3 to 2.1)	0.63
Respirator for non-AGP	0.6 (0.4 to 0.8	<0.001	0.6 (0.5 to 0.9)	0.008	0.6 (0.4 to 0.97)	0.04	0.7 (0.4 to 1.0)	0.06	1.0 (0.5 to 2.0)	0.93
Re-use of disposable respirators	1.1 (0.8 to 1.5)	0.6	1.1 (0.8 to 1.5)	0.74	1.0 (0.6 to 1.5)	0.82	1.1 (0.7 to 1.7)	0.6	1.5 (0.8 to 3.0)	0.22
No PPE doffing between patients†	0.9 (0.6 to 1.2)	0.33	0.9 (0.7 to 1.2)	0.5	0.8 (0.5 to 1.3)	0.3	1.1 (0.7 to 1.6)	0.73	0.7 (0.3 to 1.4)	0.28
In-person PPE training	1.3 (0.9 to 1.7)	0.13	1.1 (0.8 to 1.6)	0.44	2.1 (1.3 to 3.4)	0.001	0.7 (0.4 to 0.99)	0.05	0.8 (0.4 to 1.5)	0.41
PPE observers always utilized‡	0.4 (0.3 to 0.7)	<0.001	0.4 (0.3 to 0.7)	0.001	0.1 (0.04 to 0.5)	0.002	0.7 (0.4 to 1.2)	0.19	0.4 (0.1 to 1.5)	0.16

AGP = aerosol-generating procedure. PPE = personal protective equipment.

‡Compared to PPE observers never utilized.

<sup>\*</sup>Includes only dine-in or drink-in, not take-away.

<sup>†</sup>On dedicated COVID units.

Figure 1. Study Flow.

