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Coronavirus Disease 2019 (COVID-19) Seropositivity and Asymptomatic Rates in Healthcare Workers Are Associated with Job Function and Masking

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Background. Although the risk of exposure to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is higher for frontline healthcare workers, not all personnel have similar risks. Determining infection rate is difficult due to the limits on testing and the high rate of asymptomatic individuals. Detection of antibodies against SARS-CoV-2 may be useful for determining prior exposure to the virus and assessing mitigation strategies, such as isolation, masks, and other protective equipment.

Methods. An online assessment that included demographic, clinical, and exposure information and a blood sample was collected from 20 614 participants out of ~43 000 total employees at Beaumont Health, which includes 8 hospitals distributed across the Detroit metropolitan area in southeast Michigan. The presence of anti-SARS-CoV-2 IgG was determined using the EUROIMMUN assay.

Results. A total of 1818 (8.8%) participants were seropositive between April 13 and May 28, 2020. Among the seropositive individuals, 44% reported that they were asymptomatic during the month prior to blood collection. Healthcare roles such as phlebotomy, respiratory therapy, and nursing/nursing support exhibited significantly higher seropositivity. Among participants reporting direct exposure to a Coronavirus Disease 2019 (COVID-19) positive individual, those wearing an N95/PAPR mask had a significantly lower seropositivity rate (10.2%) compared to surgical/other masks (13.1%) or no mask (17.5%).

Conclusions. Direct contact with COVID-19 patients increased the likelihood of seropositivity among employees but study participants who wore a mask during COVID-19 exposures were less likely to be seropositive. Additionally, a large proportion of seropositive employees self-reported as asymptomatic. (Funded by Beaumont Health and by major donors through the Beaumont Health Foundation)

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Keywords. COVID-19; SARS-CoV-2; seropositivity; masking; healthcare workers.

During April 2020, at the height of the first wave of the Coronavirus Disease 2019 (COVID-19) pandemic in the United States, Michigan was disproportionately impacted with the third highest number of cases. By July 26, 2020, Michigan had more than 86 641 cases and 6400 deaths, with most cases distributed within the tri-county Detroit metropolitan area. Beaumont Health is the largest healthcare system in Michigan, consisting of 8 hospitals across the tri-county region (Supplementary Fig. 1) with more than 38 000 employees and 5000 private practitioners. During the peak of the pandemic, daily volumes exceeded 1200 COVID-19 inpatients. Several studies have documented the risk of infection among healthcare workers [1–3]. To assess COVID-19 exposure associated with different job functions at Beaumont Health, and to give our employees some peace of mind over fear of exposure to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), we embarked on a large-scale serological study. IgG levels usually develop within 21 days of infection, and higher levels of IgG are associated with more severe COVID-19 cases [4]. Serological status is useful in determining both infection and asymptomatic rates [5].

METHODS

Study Design and Sample Collection

The Beaumont Health Large-Scale Automated Serologic Testing for COVID-19 study (BLAST COVID-19 study, NCT04349202) was designed as a prospective cohort study,

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*A complete list of the BLAST COVID-19 study team members is provided in the Supplementary Material.

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and was approved by the Institutional Review Board at the Beaumont Research Institute. The entire employee population of Beaumont Health (approximately 43 000 individuals) was invited to participate in the study. To enroll, employees and nonemployed affiliated healthcare workers used their organizational credentials to access a web application, review the IRB approved information sheet, and provide consent. Following consent, demographic and job-related information from the employee database was automatically populated into the online questionnaire and verified. Participants were then required to answer an Employee Health Assessment (EHA) including questions about job function, exposure risk, patient contact, history of symptoms, prior COVID-19 diagnosis, medical history, and other relevant information (Supplementary Fig. 2). Blood draws were then scheduled at 1 of 9 locations across the health system between April 13, 2020 and May 28, 2020. Participants were required to be symptom-free for at least 72 hours prior to their scheduled blood draw. Excluded participants could re-enter the study after they met all health system requirements to return to work. A single serum separator tube was drawn, and antibody status was assessed using an automated SARS-CoV-2 IgG assay (EUROIMMUN, Lübeck, Germany) according to manufacturer's protocol (detailed methods in Supplementary Material). In general, the EUROIMMUN platform is among the best with respect to sensitivity and provides both qualitative and semi-quantitative measurements of SARS-CoV-2 antibodies [6–8]. Our internal validation demonstrated a specificity and sensitivity (16-day post PCR diagnosis) of 99.35% (95% CI: 97.93–99.86%) and 98.14% (95% CI: 97.75%–99.22%), respectively (data not shown). Participants were informed of their antibody test result via the employee health plan self-service application, but results were not included in their medical record to maintain confidentiality.

As of May 28, 2020, a total of 21 699 Beaumont employees completed the EHA (Supplementary Fig. 3). Since some participants submitted multiple EHAs at varying times, only the most recent EHA submitted prior to the first blood collection was included in the study. The final sample size included 20 614 participants with both valid EHA and IgG serology results (Supplementary Fig. 3).

Data Aggregation and Statistical Analysis

Data from the EHA were matched with employee records and serology results from the SoftLab laboratory information system. Aggregated data were transmitted securely to a private Amazon Web Service cloud environment for validation and analysis (Supplementary Fig. 4). Data were stored in a PostgreSQL database using Amazon's Relational Database Service and backed up in Amazon's Simple Storage Service. The data were managed by Quire Inc. (Memphis, TN), who served as an honest broker under a Business Associates Agreement with Beaumont Health. Only de-identified data were transmitted to the research team for downstream analysis.

All data were summarized using either number and percent for categorical data or mean and standard deviation for continuous data. Bayesian estimates of percentages and credibility intervals were calculated using a beta-binomial posterior and Jeffreys prior. We used Pearson's chi-square test to evaluate the association between categorical variables. We used the likelihood ratio chi-square test to partition differences in any contingency table with more than two rows or columns based on planned comparisons. We compared all racial categories pairwise using the score test and the studentized range [9]. We used logistic regression to examine the relationship between seropositivity and age, using a linear relationship with age decade.

RESULTS

All data presented in the following sections, except for serology and job role, are self-reported in the EHA (Supplementary Fig. 2). As seen in Table 1, most of the participants were White (80.6%) and female (77.0%). The study also included 7.1% Asian/Pacific Islander, 6% Black, and 1.9% Hispanic. The mean age of all participants was 43.1 ± 13.0 years.

Most participants were negative for SARS-CoV-2 specific IgG antibodies (seronegative; 89.5%; 95% CI: 89.0%–89.9%), while 8.8% (95% CI: 8.4%–9.2%) of participants tested positive (seropositive), and 1.7% (95% CI: 1.6%–1.9%) had equivocal results. Of 268 participants who had equivocal results and were tested again ≥7 days later, 82.5% became seronegative and 29 (10.8%) became seropositive. Seroprevalence, based on adjusting seropositivity for specificity and sensitivity, was slightly lower than the seropositive rate, 8.1% (95% CI: 6.8%–8.9%; Supplementary Table 1 and Supplementary Material Methods). All results presented below showed similar trends for seroprevalence, with the seroprevalence being slightly smaller than the seropositivity.

Only 28.1% (95% CI: 26.6%–29.5%) of those who reported experiencing symptoms consistent with COVID-19 within 30 days prior to the blood draw were seropositive (Table 2). In contrast, among those who were asymptomatic, 4.7% (95% CI: 4.4%–5.0%) were seropositive (Table 2). Among the seropositive participants, 44.0% (95% CI: 41.7%–46.3%) reported no COVID symptoms during the previous 30 days (Table 2). Previous diagnosis of COVID-19 showed a stronger association with seropositivity, where 86.0% (95% CI: 82.7%–88.8%) of participants with a diagnosis being seropositive compared to 6.9% (95% CI: 6.5%–7.2%) of participants with no previous COVID diagnosis (Table 2).

Table 1. Demographic and Clinical Characteristics of Study Participants and IgG Against SARS-CoV-2 Spike Proteina

Characteristic[a,b]	IgG Result: Negative (n = 18 441)	IgG Result: Equivocal (n = 355)	IgG Result: Positive (n = 1818)	% IgG Positive[c]	Entire sample (n = 20 614)
Race					[d]
White	14 630 (81.7%)	276 (80.7%)	1235 (70.1%)	7.65	16 141 (80.6%)
Asian/Pacific Islander	1233 (6.9%)	24 (7.0%)	162 (9.2%)	11.44	1419 (7.1%)
Black	949 (5.3%)	18 (5.3%)	236 (13.4%)	19.64	1203 (6.0%)
Hispanic	334 (1.9%)	7 (2.1%)	47 (2.7%)	12.21	388 (1.9%)
Other	545 (3.0%)	10 (2.9%)	64 (3.6%)	10.40	619 (3.1%)
Prefer not to answer	226 (1.3%)	7 (2.1%)	19 (1.1%)	7.71	252 (1.3%)
Gender (N = 20 428)— Female, no. (%)	14 107 (77.2%)	241 (68.3%)	1380 (76.6%)	8.78/9.01	15 728 (77.0%)[d]
Age—years	43.3 ± 13.0	41.1 ± 12.9	41.3 ± 13.0		43.1 ± 13.0[d]
BMI (n = 19 473)	27.8 ± 6.43	27.1 ± 6.08	28.9 ± 7.08		27.9 ± 6.70[d]
Chronic Conditions					
Diabetes—no. (%)	797 (4.3%)	10 (2.8%)	105 (5.8%)	11.56/8.70	912 (4.4%)[d]
Cardiovascular Disease—no. (%)	356 (1.9%)	6 (1.7%)	33 (1.8%)	8.46/8.83	395 (1.9%)
Chronic Lung Disease—no. (%)	639 (3.5%)	13 (3.7%)	58 (3.2%)	8.23/8.84	710 (3.4%)
Chronic Kidney Disease—no. (%)	73 (0.4%)	0 (0.0%)	5 (0.3%)	6.96/8.83	78 (0.4%)
Hypertension—no. (%)	2753 (14.9%)	27 (7.6%)	284 (15.6%)	9.28/8.74	3064 (14.9%)[d]
Immunosupressed—no. (%)	355 (1.9%)	3 (0.9%)	25 (1.4%)	6.64/8.86	383 (1.9%)
Any Chronic Condition—no. (%)	4036 (89.92%)	55 (1.24%)	397 (8.85%)	8.85	4488 (21.77%)
No Chronic Condition—no. (%)	14 405 (89.33%)	300 (1.86%)	1421 (8.81%)	8.81	16 126 (78.23%)
Use of ACEI / ARBs—no. (%)	672 (3.6%)	7 (2.0%)	59 (3.3%)	7.99/8.85	738 (3.6%)

[a] Percentages may not total 100 because of rounding. The full table of baseline characteristics is available in the Supplementary Material.

[b] All characteristics are self-reported.

[c] Percent IgG positive is shown the category of the characteristic shown in the table, and categories not shown in the table are shown following a "/."

[d] Statistically significant associations with IgG result.

Seropositivity decreased linearly with increasing age (Fig. 1A; $P < .0001$). Among seropositive participants, the proportion who were asymptomatic did not vary significantly across age groups, although the estimated linear relationship was positive (OR = 1.058 per decade, 95% CI:0.987–1.135, Fig. 1B). We observed racial differences in seropositivity rates with Black participants having a significantly higher seropositivity compared to all other races (Fig. 1C). Interestingly, seropositive Black participants had a significantly higher asymptomatic percentage as compared to White, Asian/Pacific Islander, and Hispanic races (Fig. 1D).

Among all participants, 42.5% (95% CI: 41.8%–43.2%) reported a direct exposure to COVID-19, defined by an interaction within 6 feet of a COVID-19 positive individual for more than 10 minutes. Among the COVID-19 exposed participants, 12.5% (95% CI: 11.8%–13.2%) were seropositive (Fig. 2A). In contrast, 6.1% (95%CI: 5.7%–6.6%) of those who were not exposed were seropositive (Fig. 2A).

Seropositivity varied across job categories (Fig. 2B and Supplementary Fig. 5). On average, participants in job categories involving direct patient care had a higher seropositive rate (9.5%; 95% CI: 9.1%–10.0%) than those who did not (7.0%;

Table 2. Association of IgG Result and Self-Reported COVID Symptoms or Diagnosis

COVID symptoms in previous 30 days	IgG Result: Negative	IgG Result: Equivocal	IgG Result: Positive	*P*-value[b]
No (n = 16 962)	15 880 (93.6%[a])	284 (1.7%)	798 (4.7%)	<.0001
Yes (n = 3622)	2536 (70.0%)	70 (1.9%)	1016 (28.1%)	
% of Positive cases that reported no symptoms			44.0%	
Previous COVID diagnosis				
No (n = 20 103)	18 378 (91.4%)	342 (1.7%)	1383 (6.9%)	<.0001
Yes (n = 506)	58 (11.5%)	13 (2.6%)	435 (86.0%)	
% of Positive cases that reported no previous diagnosis			76.1%	

[a] All percentages are for a given self-reported symptom/diagnosis category.

[b] *P*-value shown is the result of the Pearson chi-square test for association of the data shown.

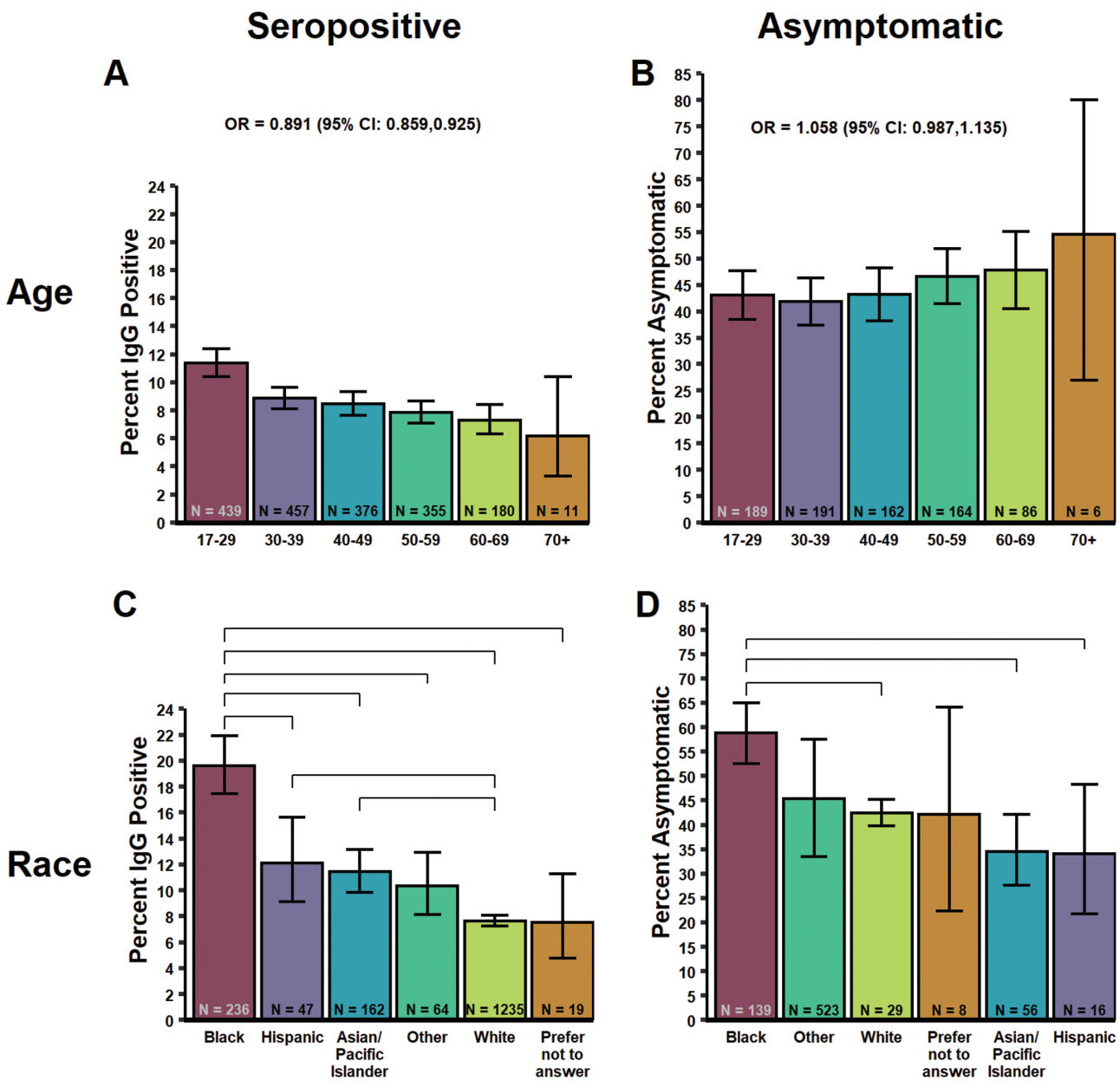

Figure 1. Comparison of seroconversion and asymptomatic rates across age and race categories. Logistic regression was used to examine the relationship between age decade and seropositivity or asymptomatic rate. Pairwise analysis of racial categories was performed using a score test and the studentized range [9]. The number of subjects (n) with the outcome shown for each category are indicated in the corresponding bar. Error bars represent credibility intervals calculated using a beta-binomial posterior and Jeffreys prior. Brackets above the bars indicate pairwise significance ($P < .05$).

95% CI: 6.3%–7.6%; $P < .0001$). Of those directly involved in patient care, those with frequent patient contact (phlebotomy, respiratory therapy, and nursing) had a significantly higher rate (11.0%; 95% CI: 10.4%–11.7%) than those with intermittent patient contact [physicians or clinical support with patient contact (eg, physical therapists and radiology technicians); seropositivity = 7.4%; 95% CI: 6.7%–8.0%]. No other differences were observed among the remaining job categories. The asymptomatic rate also varied among job categories, with those involved in direct patient care having a lower asymptomatic rate (58.7%; 95% CI: 56.2%–61.3%) than those who did not (46.0%; 95% CI: 41.1%–51.0%; Supplementary Fig. 6). These results were not impacted by including potential confounders in a logistic regression (Supplementary Fig. 7), except for race slightly decreasing the odds ratio only for the comparison of those having frequent and those having intermittent patient contact.

Participants identified as being in 1 of 5 groups with differing potential risk of SARS-CoV-2 exposure based on contact with others, and seropositivity varied across these groups (Fig. 2C).

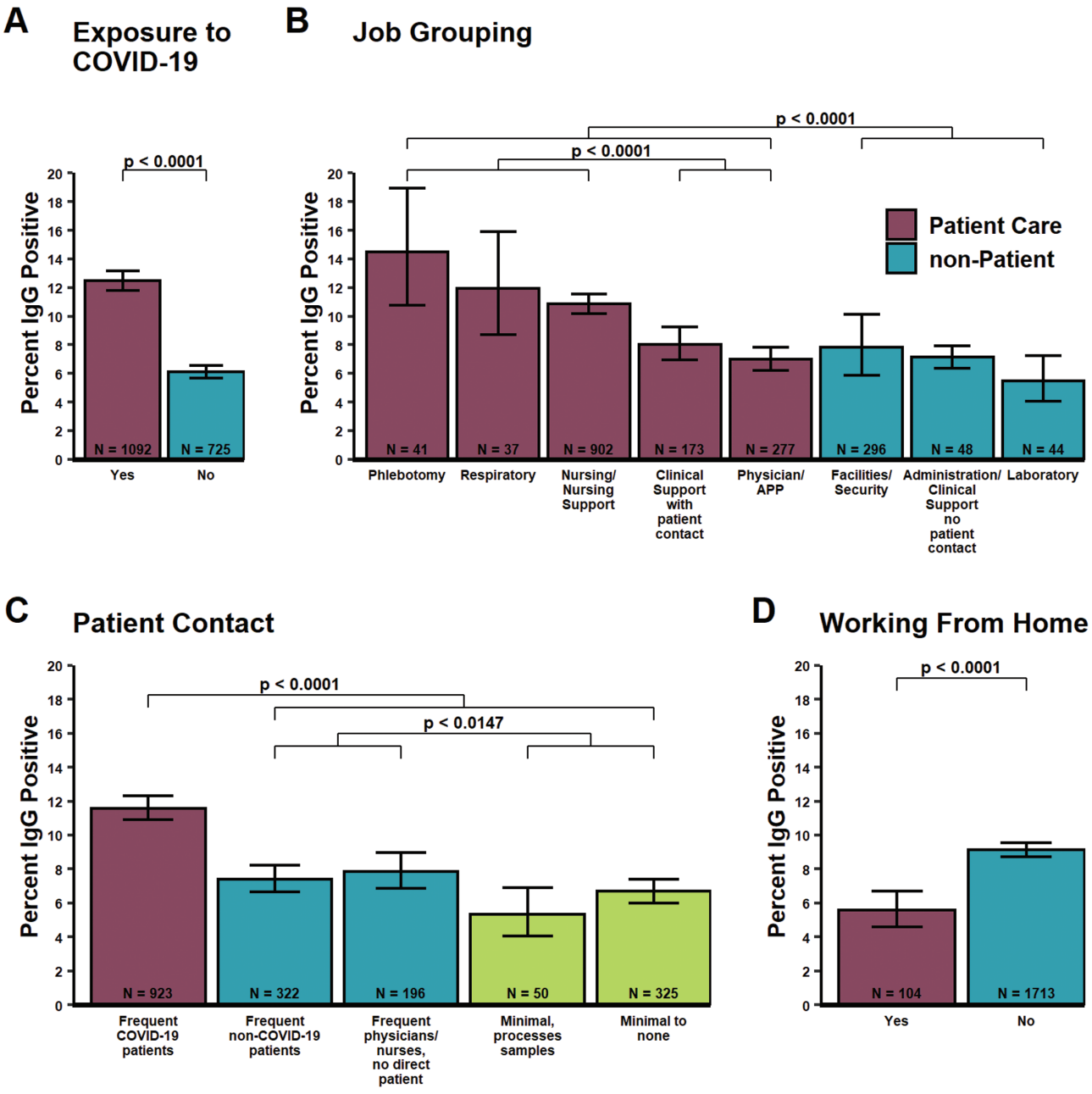

Figure 2. Seropositivity rate with respect to exposure, job category and patient contact. Job categories were classified first based on direct patient care (phlebotomy, respiratory, and nursing), patient care (physician and clinical support with patient contact), or nonpatient care (all others). Differences within each of the job categories were evaluated first and then compared between job categories. Patient contact groups include the following: frequent contact with COVID-19 patients, frequent contact with non-COVID-19 patients, frequent contact with doctors and nurses but not patients, no significant contact with doctors, nurses, or patients but handles patient specimens, and no significant contact with doctors, nurses, or patients. The number of subjects (n) with the outcome shown for each category are indicated in the corresponding bar.

Participants reporting frequent contact with COVID-19 patients had the highest seropositive rate (11.6% [95% CI: 10.9%–12.3%] vs 7.1% [95% CI: 6.6%–7.5%] for all others). Those who had frequent contact with either non-COVID-19 patients and those who had frequent contact with physicians or nurses but not patients (7.6%; 95% CI: 7.0%–8.2%) showed higher seropositivity than those reporting no significant contact with patients, physicians, or nurses; including those who handled patient samples (6.5%; 95% CI: 5.9%–7.1%). Seropositivity did not differ for those reporting frequent contact with non-COVID-19 patients (7.4%; 95% CI: 6.7%–8.2%) and those who had frequent contact with physicians or nurses (8.5%; 95% CI: 6.8%–9.0%). Seropositivity for those reporting no significant contact with patients, doctors, or nurses but who handle patient

specimens (5.3%; 95% CI: 4.0%–6.9%) did not differ from those reporting no significant contact with patients, doctors, nurses, or patient specimens (6.7%; 95% CI: 6.0%–7.4%).

We explored whether the relationship between seropositivity and job category was largely determined by patient contact. Seropositivity was not the highest for those who reported contact with COVID-19 patients across all job categories (Supplementary Fig. 8).

As expected, participants working from home were significantly less likely to be seropositive 5.6%; 95% CI: 4.6%–6.7%) than those working in their normal manner (9.1%; 5% CI: 8.7%–9.6%; Fig. 2D).

We also examined the relationship of masks with seropositivity among those who reported an exposure to COVID-19 at work or elsewhere (Fig. 3 and Supplementary Fig. 9). Among those, 76.0% (95% CI: 75.1%–76.8%) reported wearing a mask of any type. Seropositivity in those wearing any type of mask (10.9%; 95% CI: 10.1%–11.6%) was significantly lower than for those not wearing a mask (17.5%; 95% CI: 16.019.2%, Fig. 3A). Additionally, seropositivity depended on mask type (P = .0314), with 10.3% (95% CI: 9.5%–11.1%) of those who used N95 or Powered Air Purifying Respirator (PAPR) masks being seropositive compared to other mask types (13.1%; 95% CI: 11.4%–14.9%; P = .0033). Those wearing either a N95 or PAPR mask were also more likely to be asymptomatic (Fig. 3B; 39.9%; 95% CI: 35.8%–44.1%) compared to those wearing either a surgical or other type of mask (28.1% 95% CI: 21.9%–34.9%).

DISCUSSION

This prospective cross-sectional study evaluated seropositivity at a large healthcare system with facilities distributed across the epicenter of the COVID-19 pandemic in Michigan (Supplementary Figure 1) between March and May 2020. Participants in our study included frontline workers such as nurses, respiratory therapists, and physicians who had direct contact with COVID-19 patients, as well as support staff and administrators who had minimal to no contact with patients. In fact, 1868 participants were working from home due to the pandemic. Thus, we posit that a health system of over 40 000 employees is a microcosm that represents the larger community and data regarding the spread of COVID-19, especially in employees outside of direct patient care, is reflective of the entire region. This study was designed to examine associations with seropositivity and cannot confirm causal relationships.

As of May 28, 2020, the overall seropositivity rate across all job categories in the health system was 8.8%. This observation is consistent with other studies that reported seropositivity

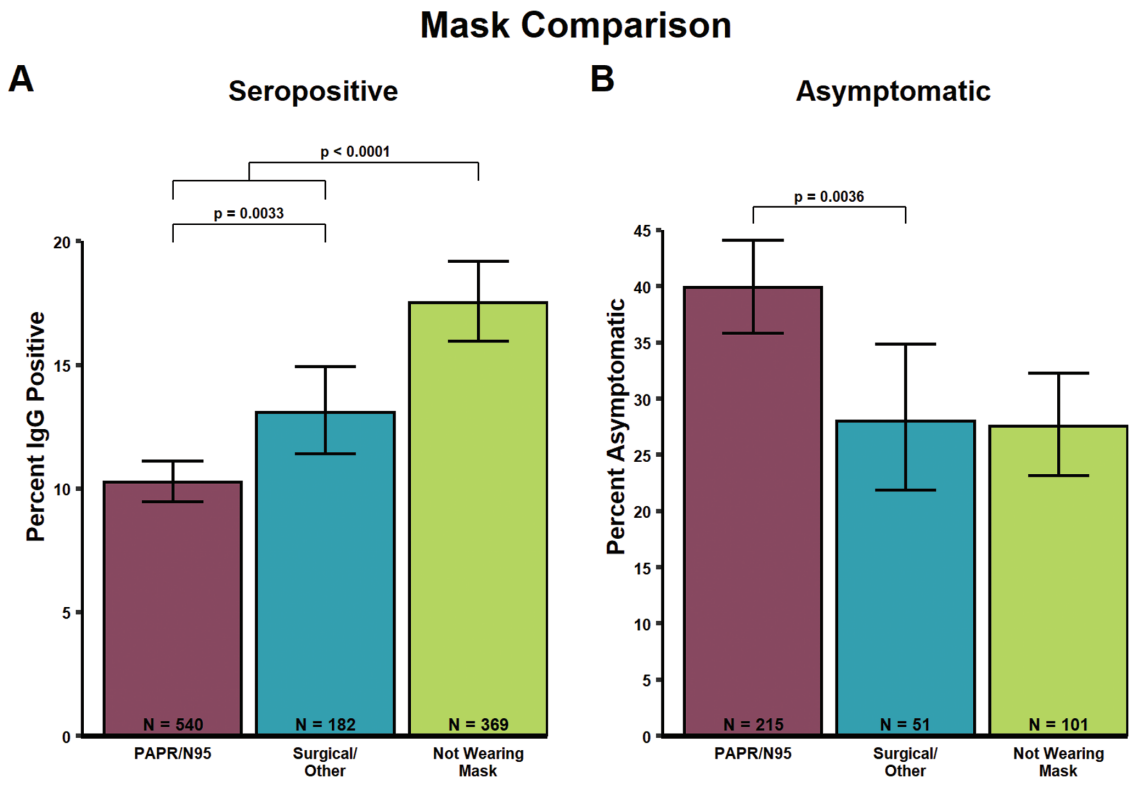

Figure 3. The relationship of mask type with seropositivity and asymptomatic rate among participants who were exposed to COVID-19 positive individuals by self-report. Masks were grouped into high-performing masks (PAPR + N95), other masks (surgical and other), and no mask of any type. The number of subjects (n) with the outcome shown for each category are indicated in the corresponding bar.

among healthcare workers in China (3.2%) [10], Spain (9.3%) [11], Belgium (6.4%) [12], Germany (1.6%-5.4%) [13], and the United States (7.6%) [14] within 3 months of caring for COVID-19. As expected, seropositivity was significantly higher in individuals who had direct contact with COVID-19 patients and significantly lower in individuals who worked from home (Fig. 2). The seropositive rate among those working from home (5.6%) likely is representative of the community rate for those who are sheltering at home and leaving only for necessary activities (physician visits, shopping).

The seropositive rate of 28.1% in participants reporting COVID-19 symptoms reflects our data being collected at the end of the respiratory virus season, and many respiratory viruses have symptoms that overlap with COVID-19. Anosmia and dysgeusia, which are more unique to COVID-19, had not yet been identified as symptoms of COVID-19 at the time data were collected. Out of 18 212 patients with symptoms who presented to our emergency center and were tested inhouse (March 16–April 30, 2020), 6318 were positive (34.7%); out of 1768 patients with symptoms who presented for drive-up testing (March 28–April 30, 2020), 501 were positive (28.4%). Thus, the seropositive rate in symptomatic participants in the study is consistent with the prevalence by PCR in patients presenting with symptoms of COVID-19.

The asymptomatic infection rate for SARS-CoV-2 across our population (44%) is important in helping determine the true rate of infection, particularly since PCR-based diagnostic testing can be variable and supply remains limited across the US. According to other studies, asymptomatic infection rates range globally between 18% to 42% in different populations [15–17]. Our estimate may include those who were oligosymptomatic and to a lesser extent presymptomatic.

Seropositivity was related to individual job function, where roles such as phlebotomy, respiratory therapy, and nursing have significantly higher seropositivity. However, physicians and clinical support staff with patient contact were not different from participants with no patient contact. These results may reflect inherent risks based on the duration of exposure to COVID-19 patients and the type of contact. In general, nurses spend more time in patient rooms than physicians and often have more close and direct contact with the patients. Also, phlebotomists have close contact as they draw blood from patients. While policies to help control the spread of COVID-19, including drawing blood only once per day when possible were in place, the amount of contact where social distancing was not possible is likely higher for phlebotomy than for other jobs. Lastly, respiratory therapists, by nature of their job function, are directly involved in procedures more likely to cause aerosolization of COVID-19 and thus higher exposure. In addition, procedures such as intubation may compromise appropriate PPE donning and doffing. Taken together, job category and the risk of exposure show interesting differences (Supplementary Fig. 7). For nursing, those exposed to COVID-19 patients had the highest risk. In contrast, for phlebotomy and respiratory therapy, those with non-COVID-19 patient exposure had the highest risk. This may reflect decreased distancing between phlebotomists or respiratory therapists and the patients, along with use of only surgical masks and no eye protection with non-COVID-19 patients as opposed to N-95 masks and eye protection with COVID-19 patients. However, these results may be affected by the smaller sample sizes as the job categories were further subdivided into risk categories.

The impact of masks on acquisition of COVID-19 has received wide attention [18–20]. Our results are consistent with masks reducing the risk of acquiring COVID-19. Those wearing N95 or PAPR masks had the lowest seropositivity, and those wearing any mask had lower seropositivity than not wearing a mask (10.9% vs 17.5%, Fig. 3A). Still, our results may not simply reflect the effect of masks alone since employees who were wearing N95/PAPR masks were also likely using additional PPE, including gowns and eye protection.

Employees wearing an N95/PAPR mask also had a significantly higher asymptomatic rate. The potential effect of lowering the exposure dose of the SARS CoV-2 virus is also supported by the observation that employees with no known exposure or not having direct contact with patients are more likely to be asymptomatic (Supplementary Fig. 6). Prior studies also noted similar increased rates of asymptomatic COVID-19 with mask use [18, 20].

We also observed a negative relationship between age and likelihood of having IgG (Fig. 3A). Although this may suggest that younger individuals are likely to engage in risk-taking behaviors and not participate in social distancing, we did not observe any significant association between age and self-reported COVID-19 exposure or prior diagnosis. This raises the possibility that older individuals have a diminished immune response and are less likely to produce antibodies against SARS-CoV-2 spike protein; similar age-associated decreased immune response has been well described [21, 22].

Race has been a major factor in COVID-19 since the earliest days of the pandemic [23]. Black race has been disproportionally affected by COVID-19, and many health care systems note a larger number of Blacks admitted to the hospital and even higher mortality in this group [24, 25]. In our study, Black race had the highest seropositivity (19.6%), while White race had the lowest (7.7%). We also find that Black individuals have a higher likelihood of being asymptomatic. The reasons for these racial imbalances are likely multifactorial.

Several studies have examined seropositivity in healthcare workers [10–14, 26–30]. Moscola et al [30] showed a higher overall rate of seropositivity in a large study of healthcare personnel in New York, particularly in those at highest risk of exposure. This may reflect differences in prevalence since New York was affected more than Michigan. It also may reflect differences

in infection control policies, availability of PPE, or other measures aimed at mitigating risk.

Study limitations include that all data, except for actual serology and job role, were self-reported and may be subject to recall bias. Participation in the study was just over 50% and may be subject to selection bias, though it is difficult to evaluate if the bias would favor higher or lower rates of participation among those likely to be seropositive. Since IgG usually takes at least 2 weeks to develop, we may have missed recently infected participants. Our asymptomatic rates estimates may be inflated because of the 30-day time window imposed in the questionnaire. Although the study began 30 days after the first reported case of COVID-19 in Beaumont (March 13), we continued to collect blood samples until May 28. Therefore, some individuals reporting no symptoms may in fact have been symptomatic prior to the 30-day window.

In conclusion, this study establishes baseline seropositivity across a population of employees of a large healthcare system within the first 3 months of the COVID-19 pandemic in the United States. These findings support the appropriate use of PPE as a method of reducing the spread of SARS-CoV-2 and sets the stage for longitudinal analysis to determine duration of the humoral immune response to SARS-CoV-2 and the association between IgG and immunity against subsequent infections.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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