Antimicrobial Stewardship & Healthcare Epidemiology (2024), **4**, e190, 1–7
doi:10.1017/ash.2024.420

SHEA

Original Article

SARS-CoV-2 seropositivity among healthcare professionals in a rural state

Brianna Wright MD[1], Daniel Kang PhD[1], Allison Schuette MS[2], Melissa A. Ward MS[1], Matthew D. Krasowski MD, PhD[3], Aaron M. Scherer PhD[1], Daniel J. Diekema MD, MS[1], Joseph Cavanaugh PhD[2] and Loreen Herwaldt MD[1,4]

[1]Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, IA, USA, [2]Department of Biostatistics, University of Iowa College of Public Health, Iowa City, IA, USA, [3]Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA, USA and [4]Department of Epidemiology, University of Iowa College of Public Health, Iowa City, IA, USA

Abstract

Objectives: We evaluated SARS-CoV-2 anti-nucleocapsid (anti-N) seroconversion and seroreversion rates, risk factors associated with SARS-CoV-2 seroconversion, and COVID-19 risk perceptions among academic healthcare center employees in a rural state.

Methods: Among employees aged ≥18 years who completed a screening survey (n = 1,377), we invited all respondents reporting previous COVID-19 (n = 85; 82 accepted) and a random selection of respondents not reporting previous COVID-19 (n = 370; 220 accepted) to participate. Participants completed surveys and provided blood samples at 3-month intervals (T0, T3, T6, T9). We used logistic regression to identify risk factors for seropositivity at T0.

Results: The cohort was primarily direct patient caregivers (205/302; 67.9%), white (278/302; 92.1%), and female (212/302; 70.2%). At T0, 86/302 (28.4%) participants were seropositive. Of the seronegative participants, 6/198 (3.0%), 6/183 (3.3%), and 14/180 (7.8%) had seroconverted at T3, T6, and T9, respectively. The overall seroreversion rate was 6.98% at T9. At T0, nursing staff (odds ratio [OR], 2.37; 95% confidence interval [CI], 1.08, 5.19) and being within six feet of a non-household member outside of work (OR, 2.91; 95% CI, 1.02, 8.33) had significantly higher odds of seropositivity. Vaccination (OR, 0.05; 95% CI, 0.02, 0.12) and face mask use (OR, 0.36; 95% CI, 0.17, 0.78) were protective.

Conclusions: The seroconversion and seroreversion rates were low among participants. Public health and infection prevention measures implemented early in the COVID-19 pandemic – vaccination, face mask use, and social distancing – were associated with significantly lower odds of SARS-CoV-2 seropositivity among participants.

(Received 11 June 2024; accepted 8 August 2024)

Introduction

Many early studies of SARS-CoV-2 seropositivity rates and risk factors associated with seroconversion among healthcare professionals (HCPs) were cross-sectional studies of urban populations.[1–16] Some studies found that nursing positions, emergency department jobs, and contact with patients who have COVID-19 were associated with seroconversion.[4,7,11–13,15] Other studies found that exposure to someone with suspected or confirmed COVID-19 outside the hospital increased the risk of infection, but in-hospital exposures did not.[14,16,17] More recently, a few prospective cohort studies in the United States[18,19] assessed the duration of SARS-CoV-2 antibodies among HCP. For example, Wilkins *et al.* found that 48% (138/263) of participants with detectable anti-nucleocapsid antibodies at baseline were seronegative at their 6-month follow-up.[18] Similarly, Papasavas *et al.* found that the seroreversion rate among HCPs was 39.5% at a median time of 5.5 months.[19]

Some early studies assessed HCPs' reactions to the pandemic.[20,21] For example, Zhang *et al.* found that over 85% of HCPs feared becoming infected with SARs-CoV-2.[21] A cross-sectional study conducted in 2020 at two urban health centers found that 78.4% of healthcare personnel worried about contracting the virus from a patient, 97.3% were concerned that they would put their family or coworkers at risk, and 8.9% refused to care for patients with COVID-19.[22]

Thus, we have substantial information about seroprevalence and risk factors associated with seropositivity, but study results are conflicting and few studies have analyzed seroconversion rates over time among HCPs in rural areas. In addition, few prospective cohort studies have evaluated how either seroprevalence or perceptions of COVID-19 changed over time among HCPs in the United States. To address these gaps, we conducted a longitudinal cohort study of 302 employees at Iowa Health Care (IHC), which comprises the University of Iowa Hospitals and

Corresponding author: Loreen A. Herwaldt; Email: loreen-herwaldt@uiowa.edu
Cite this article: Wright B, Kang D, Schuette A, *et al.* SARS-CoV-2 seropositivity among healthcare professionals in a rural state. *Antimicrob Steward Healthc Epidemiol* 2024. doi: 10.1017/ash.2024.420

Clinics (UIHC) and the University of Iowa Carver College of Medicine, from October 2020 to May 2022. The UIHC, Iowa's only academic medical center, is a comprehensive healthcare center with 889 beds.

Methods and materials

Study population

One thousand three hundred seventy-seven adult (≥18 years) IHC employees completed a portion of the screening survey, of whom we invited all 85 who self-reported a previous positive COVID-19 test and 370 of those who did not have a positive COVID-19 test to participate. The final study population of 302 included 82 respondents who reported having had a positive COVID-19 test. After written informed consent, participants completed the baseline survey and had blood tested for SARS-CoV-2 antibody levels (See Supplemental Figure 1).

We used the Roche Diagnostics Elecsys Anti-SARS-CoV-2 assay, which detects total antibodies (IgA, IgG, IgM) to the nucleocapsid protein (anti-N), to determine whether participants had been infected with SARS-CoV-2, and the DiaSorin assay, which detects IgG to the S1 and S2 subunits of the spike surface glycoprotein (anti-S) and is positive after infection and after vaccination. (See Supplemental Materials for further details about serologic testing).

Participants' visits occurred between 10/30/20 and 7/29/21 (baseline; T0), 2/11/21–12/2/21 (3-month follow-up; T3), 5/13/21–3/8/22 (6-month follow-up; T6), and 8/11/21–5/20/22 (9-month follow-up; T9). The UIHC's Core Clinical Laboratory performed SARS-CoV-2 antibody testing; the study coordinator entered serology results into a REDCap database.

Participants completed surveys online through a REDCap link; their answers were stored in the REDCap database. The baseline survey gathered information on possible worksite or community exposures, personal protective equipment (PPE) use at work and in the community, vaccination status, and COVID-19 perceptions. At follow-up visits, participants completed surveys that repeated some questions in the baseline survey and asked whether they had been tested for COVID-19 in the interim.

Analysis of risk factors for seropositivity at T0

To identify factors associated with seropositivity at T0, we conducted a five-step process using SAS 9.4 (SAS Institute, Cary NC). First, we assessed variable distributions; we removed variables if their distributions exhibited minimal variation across responses (eg, a very high percentage selected 'Yes' for a binary 'Yes'/'No' response) or if the number of participants who answered the questions was too small due to survey skip logic. Second, we removed variables that were not clinically or theoretically relevant as risk factors.

Third, we conducted a factor analysis on 12 items measuring participants' perceptions of COVID-19 and their attitudes toward risk behaviors to aggregate related items into three higher-level categories (ie, factors). The "Infection Likelihood" factor measured how likely participants thought they were to contract COVID-19; higher scores indicated the participants felt acquiring COVID-19 was more likely. The "Worry" factor measured how worried participants were about COVID-19; higher scores indicated they were more worried. The "Safe Behavior" factor measured participants' general risk-taking behavior, rather than COVID-19-related risk-taking behavior. Higher scores indicated that participants generally engaged in less risky or "safer" behaviors. (See supplemental materials for more details).

Fourth, we ran univariable logistic regression models with seropositivity status at T0 as the outcome measure; the predictor variables included the factor scores and the other potential seropositivity risk variables. We then removed variables not associated with seropositivity from our pool of potential risk factor variables. These four steps reduced our pool from 95 to 12 candidate variables: the three factors from the factor analysis, age, sex assigned at birth, role, unit where the participant worked, household size, children in the household, vaccination status, face covering use, and being within six feet of a non-household member outside of work (ie, did not practice social distancing). We used the Akaike information criterion (AIC) to determine variable representation (eg, continuous, quartiles, etc.).

Fifth, to test the relative influence of each potential risk factor with and without vaccination status in the model, we applied backward elimination regression with the other 11 candidate variables in two separate models, one with and one without vaccination status. We used an exclusion criterion that removed variables with P values exceeding 0.15. To illustrate the predictive utility of the model including vaccination status, we calculated the probability of being seropositive at baseline for three hypothetical subject profiles, which we created by specifying a set of factors resulting in the highest and lowest odds of seropositivity and a set resulting in intermediate odds.

Results

Of the 302 participants at T0, 286 (94.7%) returned at approximately 3 months, 266 (88.1%) at 6 months, and 264 (87.4%) at 9 months. Baseline sera from 248 (80.3%) participants were tested during the reflexive testing period. (See Supplemental Materials for details of serologic testing, including the definition of reflexive testing, and for a figure mapping study phases onto major pandemic events.)

Demographics

At T0, 92.1% of participants were white, and 49.7% were 31–50 years old. Most (205; 67.9%) participants had patient care roles: of whom, 56 (27.3%) were nurses or nursing assistants, 63 (30.7%) were physicians, and 19 (9.3%) were advanced practice providers (Table 1). Ninety-seven (32.1%) participants had non-patient care roles. At T0, about half of the participants had cared for patients with COVID-19 and for "persons under investigation" for COVID-19 but only 8.9% reported having contact with someone outside the hospital who had COVID-19. These percentages varied slightly during the study period (Table 2). Additionally, 130 (43%) participants had at least 1 COVID-19 vaccine at T0, and 9 participated in blinded vaccine trials before their T0 sera were obtained (Table 2).

Seroprevalence

Of the 302 participants, 86 (28.4%) had a positive anti-N test result at their T0 visits, 74 of whom (86.0%) reported having had a positive COVID-19 test before study enrollment. Eight (9.8%) of the 82 participants who reported a prior positive COVID-19 result had a negative anti-N result. Four of 110 (3.6%) participants who reported that all of their pre-enrollment COVID-19 tests were negative were seropositive and 8 of 107 (7.5%; P not significant) participants who had not been tested for COVID-19 were seropositive. Seventy-seven of the 86 (89.5%) seropositive results were confirmed by positive anti-S tests and 9 (10.5%) were

Table 1. Demographics for healthcare professionals who participated in the initial screening survey and the baseline survey and serosurvey

Variable	Screening (n = 1377)	Baseline (n = 302)
Age (at time of consent), years		
19–30	281 (20.7%)	71 (23.5%)
31–38	319 (23.5%)	77 (25.5%)
39–50	347 (25.6%)	73 (24.2%)
51–69	409 (30.2%)	81 (26.8%)
Gender		
Female	1039 (76.6%)	212 (70.2%)
Male	316 (23.3%)	89 (29.5%)
Other gender	2 (0.1%)	1 (0.3%)
Race		
White	1275 (94.0%)	278 (92.1%)
Asian	44 (3.2%)	12 (4.0%)
Black	15 (1.1%)	4 (1.3%)
Native American	1 (0.07%)	0 (0.0%)
Hispanic or Latinx	50 (3.7%)	20 (6.6%)
Patient care roles[a]	787 (58.3%)	205 (67.9%)
Nurses/nursing assistants	279 (20.3%)	56 (18.5%)
Physicians/trainee physicians	179 (13.0%)	63 (20.9%)
Advanced practice providers	54 (3.9%)	19 (6.3%)
Non-patient care roles[b]	563 (41.7%)	97 (32.1%)
Researchers	151 (11.0%)	16 (5.3%)
Administrative/clerical staff	150 (10.9%)	24 (7.9%)
"Other" roles	142 (10.3%)	24 (7.9%)
Had prior COVID-19 PCR	689 (50.2%)	195 (64.6%)
Reported prior positive COVID-19 PCR	92/689 (13.4%)	82/195 (42.1%)

PCR, polymerase chain reaction.
[a]Top three responses in patient care roles.
[b]Top three responses in non-patient care roles.

considered indeterminant because the anti-S was negative. Seven of these 9 participants returned at T3 of whom 5 (71.4%) were confirmed to be positive (positive anti-N and anti-S) and 2 were negative (negative anti-N and anti-S).

Of the 86 participants with positive anti-N at T0, 71 (82.6%), 60 (69.8%), and 55 (64.0%) returned for the T3, T6, T9 follow-up visits, respectively. At T3, 2 participants (2.8%) had seroreverted to negative. At T6, 3 participants (5.0%) were seronegative (2 remained negative and 1 had seroreverted to negative [1.7%]). At T9, 6 (10.9%; 2 remained negative, 3 had newly seroreverted to negative, and 1 whose T0 result was indeterminant was negative) were seronegative. The overall seroreversion rate was 3.49% at T6 and 6.98% at T9.

Among the participants who were seronegative at T0, 6/198 (3.0%), 6/183 (3.3%), and 14/180 (7.8%) had newly seroconverted at T3, T6, and T9, respectively. Twenty-one of 26 (80.8%) seroconversions occurred during the Omicron surge (Figure 1).

COVID-19 sentiment

At T0 most participants thought their risk of acquiring COVID-19 either in the hospital or the community was low, and less than 20% worried that they or their household members would "catch COVID-19." However, 45% of participants were worried about spreading SARS-CoV-2 asymptomatically (Supplemental Table 1).

Figure 2 illustrates how the COVID-19 sentiment data changed over time. After vaccines were introduced, participants tended to report being less worried about spreading COVID-19, more willing to go to public places, and less likely to wear face coverings in the community. The direction of these changes reversed shortly after the Delta variant emerged but the responses did not return to their baseline levels. The sentiments of those who were seropositive at any time and those who remained seronegative during the study period diverged shortly before the Omicron variant emerged, with the latter group being more worried about asymptomatic spread, less willing to go to public places, and more willing to mask in the community than those who seroconverted.

Analysis of risk factors for seropositivity at T0

The final multivariable logistic regression model with vaccination status as a predictor (Table 3) revealed that nursing staff (ie, nurses or nursing assistants) (odds ratio [OR], 2.37; 95% confidence interval [CI], 1.08, 5.19) and participants who were within six feet of someone outside of work who was not in their household (OR, 2.91; 95% CI, 1.02, 8.33) had a significantly higher odds of being seropositive at T0 than other participants. Wearing a face covering in public (OR, 0.36; 95% CI, 0.17, 0.78), safer behavior in general ("Safe Behavior Factor") (OR, 0.73; 95% CI, 0.55, 0.95), thinking that they were more likely than not to acquire COVID-19 ("Infection Likelihood" Factor) (OR, 0.58; 95% CI, 0.41, 0.82), and being vaccinated (OR, 0.05; 95% CI, 0.02,0.12) were all associated with a significantly lower odds of being seropositive at T0.

On the basis of the modeling results, we developed low, intermediate, and high-risk participant profiles for the probability of being seropositive at T0 (Table 4). For example, participants with the lowest probability of being seropositive at T0 were those who were 31–38 years old, male, not a nurse or nursing assistant, and not within six feet of someone outside of work who did not live in their house and also reported always wearing a face covering in public, having the "safest" risk-taking behavior, feeling that acquiring COVID-19 was more likely than not, and having been vaccinated (Table 4). This model also confirmed that COVID-19 vaccine status had a strong protective effect; the odds of being seropositive were 20 times higher for unvaccinated than for vaccinated participants. For example, if we changed the value of the COVID-19 vaccination status variable from "vaccinated" to "unvaccinated" for a participant with an intermediate risk profile, the participant's estimated probability of being seropositive increased from 22% to 84%.

Fewer variables remained in the model that did not include vaccination status as a candidate variable (Table 3 and Supplementary Table 2). The results of this model were similar to those of the model that included vaccination status, but the associations were less strong. This model found that participants working in units caring for patients with COVID-19 or those who were under investigation for COVID-19 had significantly lower odds of being seropositive at T0 than those working elsewhere (OR, 0.42; 95% CI, 0.22–0.82).

Discussion

Our study of COVID-19 seroconversions and seroreversions is unique in that participants worked at an academic healthcare center in a rural state and were followed for approximately 19 months. In addition, we used factor analysis and logistic regression

Table 2. Serosurvey results for healthcare professionals who participated in the T0, T3, T6, and T9 follow-up surveys

Variable	T0 (n = 302)	T3 (n = 286)	T6 (n = 266)	T9 (n = 264)
Received COVID-19 vaccine	130 (43%)	257 (89.9%)	245 (92.1%)	246 (93.2%)
1 dose	22 (16.9%)	12 (4.2%)	2 (0.8%)	1 (0.4%)
2 doses	108 (83.1%)	235 (92.7%)	204 (76.7%)	131 (49.6%)
3 doses	–	10 (3.5%)	38 (14.3%)	113 (42.8%)
4 doses	–	–	–	1 (0.4%)
History of COVID-19 PCR test since last study visit	–	90 (31.5%)	55 (20.7%)	92 (34.8%)
Reported a positive result	–	9 (3.1%)	3 (1.1%)	11 (4.2%)
Overall SARS-CoV-2 antibody result				
Positive	77 (25.5%)	77 (26.9%)	70 (26.3%)	78 (29.5%)
Negative	216 (71.5%)	192 (67.1%)	177 (66.5%)	166 (62.9%)
Indeterminate	9 (3.0%)[a]	0	0	0
Filled out visit survey, did not return to clinic	–	17 (5.9%)	19 (7.1%)	20 (7.6%)
New positive anti-N since last study visit	–	6/198[b] (3.0%)	6/183[b] (3.3%)	14/180[b] (7.8%)
Positive anti-N[c]	5 (1.7%)	35 (12.2%)	70 (26.3%)	78 (29.5%)
Positive anti-S[d]	51 (16.9%)	213 (74.5%)	244 (91.7%)	244 (92.4%)
Household size, mean (range)	2.9 (1-8)	–	–	–
Children living in home	100 (33.1%)	–	–	–
Direct care to patients with COVID-19	149 (49.3%)	124 (43.4%)	102 (38.3%)	115 (43.6%)
Direct care to a patient under investigation	152 (50.3%)	105 (36.7%)	109 (41.0%)	110 (41.7%)
Close contact with a person with a confirmed COVID-19 outside the hospital	27 (8.9%)	17 (5.9%)	7 (2.6%)	20 (7.6%)

PCR, polymerase chain reaction.
[a]Indeterminate: positive anti-N and negative anti-S.
[b]Participants who had a negative anti-N at the prior visit.
[c]Until 3/22/2021, anti-S testing was performed only on specimens with a positive anti-N result. After this date, all specimens were tested using both Roche and DiaSorin assays. This count reflects the positive anti-N specimens obtained after this protocol change. See Supplementary Materials
[d]Positive anti-S count after protocol change in 3/2021.

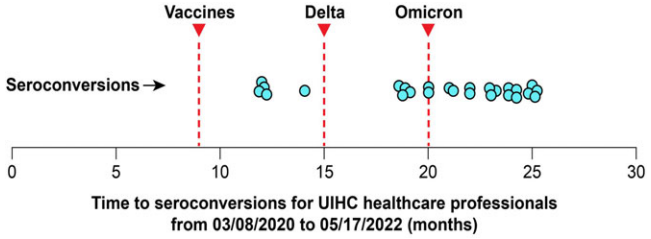

Figure 1. Seroconversions during Different Phases of the Pandemic. UIHC, University of Iowa Hospitals and Clinics. To assess COVID-19 seroconversion data in the context of vaccine availability and the circulating variants, we defined the time variable shown on the x-axis as the number of days since the first case of COVID-19 was identified in Iowa (March 8, 2020).

modeling to assess risk factors for seropositivity at T0. The modeling allowed us to develop participant profiles that identified staff who were at a higher or lower odds of seropositivity at T0.

During the baseline period, we found that persons with higher odds of seropositivity included those who were 19–30 years old, were female, and were nursing staff. Other studies[13,17,23] have found that staff aged 30 or younger were at higher risk than other groups. The younger respondents may have perceived COVID-19 to be less dangerous to their health and may have been more likely to congregate or visit public places than older respondents.[24,25] Our finding that nursing staff had an increased odds of seropositivity at T0 is consistent with some studies[4,23,26] but contrasts with others.[17,27] The study by Jacob *et al.* is an example of the latter.[17] Their early cross-sectional study of 24,749 healthcare workers across four US healthcare systems found that workplace factors, including nursing jobs, were not associated with seropositivity.[17] However, given nursing staff members' proximity to patients, they could be at higher risk of acquiring COVID-19 particularly if they do not have adequate access to PPE or if they do not use it correctly. The former was documented early in the SARS-CoV-2 pandemic[28,29] and the latter was a risk factor during prior outbreaks of respiratory viruses.[30]

The results of our multivariable model indicated that working in an intensive care unit (ICU) that cared for patients with COVID-19 or another COVID-19 unit, may have been a protective factor. This result is plausible given that the pandemic reached Iowa later than the coasts (Supplemental Figure 2), so our ICU staff were prepared and had adequate access to PPE during surges. Additionally, patients needing ICU admission for COVID-19 are usually past the early viral phase and are in the inflammatory phase when SARS-CoV-2 transmission is less likely because upper respiratory tract viral replication has declined.[31,32] This also may help explain why staff on COVID units and ICUs infrequently had work-related acquisitions as most were due to social interactions, or to patients who were admitted for other reasons during the pre-symptomatic or early symptomatic phase of infection, and thus were not initially recognized as transmission risks.

Table 3. Multivariable model to assess risk factors for SARS-CoV-2 seropositivity at T0—includes vaccination status

Variables	OR (95% CI)
Age (years)	
19–30	reference
31–38	0.25 (0.10, 0.63)
39–50	0.94 (0.40, 2.22)
51–69	0.50 (0.21, 1.17)
Nurse or nursing assistant (ref = no)	**2.37** (1.08, 5.19)
Safe Behavior factor[a]	**0.73** (0.55, 0.95)
Sex assigned at birth (ref = female)	0.53 (0.26, 1.09)
Within six feet[b] (ref = no)	**2.91** (1.02, 8.33)
Wore a face covering (ref = not always)	**0.36** (0.17, 0.78)
Infection Likelihood factor[c]	**0.58** (0.41, 0.82)
Vaccination (ref = no)	**0.05** (0.02, 0.12)

CI, confidence interval; OR, odds ratio; ref, reference.
[a]A participant's overall risk-taking behavior in general, not specific to COVID-19.
[b]Were within six feet of a non-household member outside of work within the last week.
[c]How likely participants thought they were to contract COVID-19.

Table 4. Participant profiles at T0

	Best Case (Lowest Risk)	Intermediate Case (Intermediate Risk)	Worst Case (Highest Risk)
Age	31–38	39–50	19–30
Sex	Male	Male	Female
Nurse or nursing assistant	X[d]	✓	✓
Within six feet[a]	X	✓	✓
Always wore a face covering	✓	X	X
Safe Behavior factor[b]	Safest	Safer than Risky	Riskiest
Infection Likelihood factor[c]	Very Likely	Possible but Not Likely	Not at all Likely
Vaccinated	✓	✓	X
Probability of being seropositive	0.0001	0.22	0.99

[a]Were within six feet of a non-household member outside of work within the last week.
[b]A participant's overall risk-taking behavior in general, not specific to COVID-19.
[c]How likely participants thought they were to contract COVID-19.
[d]X = participant did not have the characteristic; ✓ = participant did have the characteristic.

Of note, participants with the lowest odds of seropositivity at T0 were those who always wore face coverings in public, were vaccinated, and were not within six feet of someone outside of work who did not live in their home. These results support the infection prevention and public health measures recommended throughout the pandemic.

Our seroconversion rates at T3 (3.0%) and T6 (3.3%) were low and were similar to that reported by Papasavas *et al.* (2.2% at 90–196 days).[19] Most seroconversions occurred during the Omicron surge, which began in November of 2021. By this time

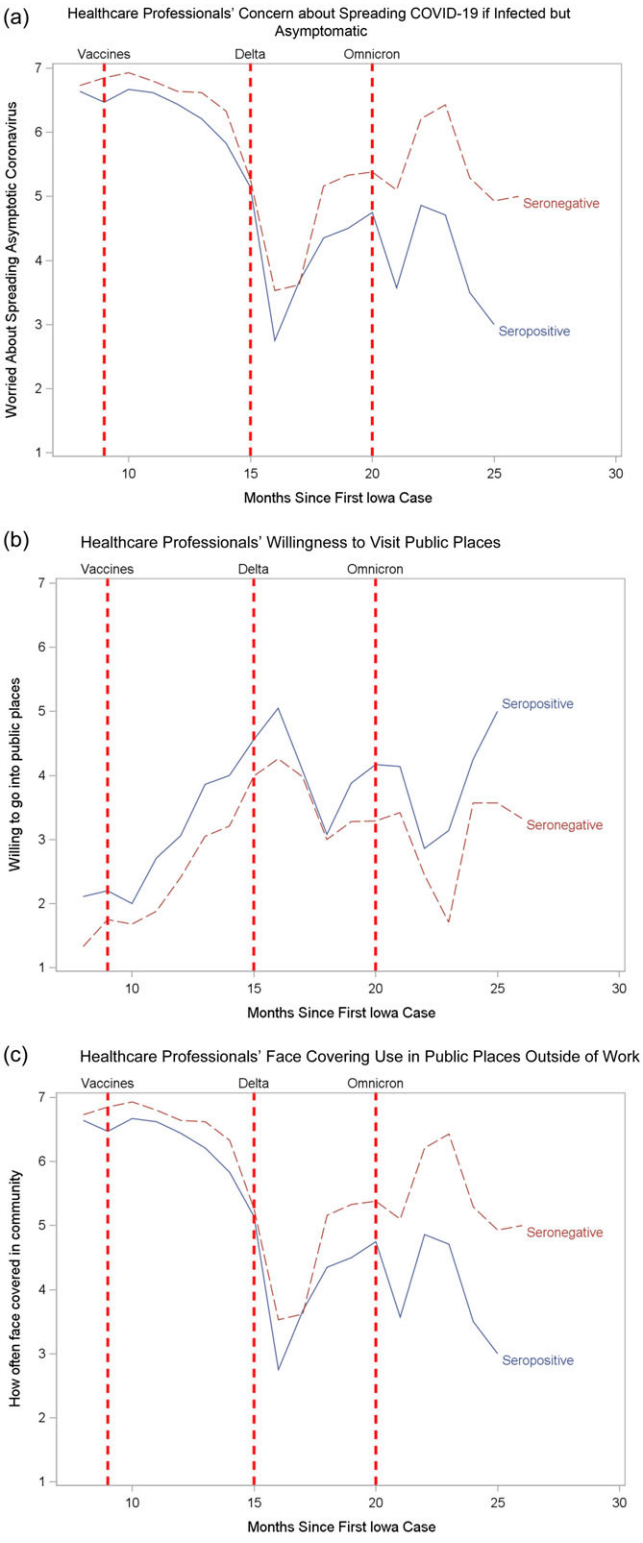

Figure 2. Changes in Healthcare Professionals' Perceptions of COVID-19 Over Time. (a). Healthcare Professionals' Concern about Spreading COVID-19 if Infected but Asymptomatic. (b). Healthcare Professionals' Willingness to Visit Public Places. (c). Healthcare Professionals' Face Covering Use in Public Places Outside of Work. To assess COVID-19 sentiment data in the context of vaccine availability and the circulating variants, we defined the time variable shown on the x-axis as the number of days since the first case of COVID-19 was identified in Iowa (March 8, 2020).

everyone was eager to resume their normal lives, 90% of UIHC's staff members were vaccinated, mask mandates had been lifted, and public places, including schools, were reopening. Participants may have been less vigilant in public and in the hospital because the severity of the disease caused by this variant was comparatively lower than that caused by prior variants.[33]

Participants' perceptions and behaviors varied with the pandemic phase and their serological status. For example, during the Omicron surge, respondents who were seropositive at any time were less worried than seronegative respondents about spreading the virus asymptomatically and about visiting public places. Similarly, a prospective cohort study by Shoemaker *et al.* found that participants who engaged in social activities similar to their pre-pandemic activities (ie, socializing at a home indoors with non-household members, visiting a store, and eating indoors at a restaurant) were significantly more likely to test positive for SARS-CoV-2 than those that did not.[34]

Lastly, we found that 3.49% and 6.98% of participants who had anti-N at T0 and returned for their 6- and 9-month follow-up visits, respectively, had seroreverted. Our 6-month seroreversion rate was slightly lower than the 4.3% seroreversion rate found by Fisher *et al.* at 6 months in 2020 (Beijing Wantai ELISA-based SARS-CoV-2 anti-S1 domain assay).[35,36] Our seroreversion rates were notably lower than those reported by Wilkins *et al.* (52% seroreversion at 6 months using the Abbott Architect or Alinity analyzers)[18] and by Papasavas *et al.* (39.5% seroreversion at a median of 5.5 months using Abbott Diagnostics anti-N IgG assays on the Architect analyzer).[19] Our results are similar to that described by Allen *et al.* who compared the Roche anti-N, Abbott anti-N, and Wantai ELISA anti-S1 assays.[37] The positivity rate among HCPs in the subset who had confirmed infection based on the Abbott IgG anti-N assay began to decline at 5.3 months, which was earlier than observed with the Roche and Wantai assays.[37]

Our study has several limitations. First, fewer participants enrolled than anticipated and some participants did not return for follow-up visits. In addition, the seroconversion rate was low. Consequently, we could not successfully build a longitudinal model to characterize risk factors for seroconversion over the whole study period. Also, relatively few employees from nonclinical services enrolled, so we could not assess differences between clinical and nonclinical services. Additionally, given staffing and COVID-19 policy constraints on human research, the baseline enrollment and testing period were extended longer than anticipated. Moreover, all data – except the anti-N and anti-S antibody test results – were collected via survey, which could introduce recall bias for some measures, and participants were not required to answer every question, which could lead to gaps in the data. Furthermore, our study population in this rural state was primarily direct patient caregivers who were white female nursing staff, which could decrease our findings' generalizability to urban or more diverse populations and limited our ability to evaluate whether results varied by occupation and ethnicity. Finally, socioeconomic and cultural factors, which we did not control for, may have influenced behaviors and perceptions during the pandemic and thus influenced seroconversion rates.

In conclusion, our study found that the public health and infection prevention interventions implemented early in the pandemic, including face mask use, vaccination, and social distancing, were associated with a significantly lower odds of SARS-CoV-2 seropositivity at T0 among employees working at an academic medical center in a rural state. These precautions are important, in part, because infected persons can transmit SARS-CoV-2 and other respiratory viruses when they are asymptomatic. In addition, these precautions are relatively easy and inexpensive to implement. However, they were politicized and many people, including some HCPs, have spread misinformation claiming these measures are ineffective and harmful.[38,39] Therefore, we must continue educating HCPs and the public about the ability of these measures to prevent spread of viral respiratory pathogens, including emerging viruses, thereby preventing illness, morbidity, mortality, and social disruption.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ash.2024.420.

Acknowledgments. The authors thank our fellow University of Iowa Health Care, Stead Family Children's Hospital, and Carver College of Medicine colleagues, without whose generous participation this work would not be possible.

Financial support. This project was supported by a discretionary UIHC fund authorized by the UI Carver College of Medicine. AMS received additional support from a K01 award from the NIH National Institute on Aging (1K01AG065440-04). REDCap is maintained by the UI Institute for Clinical and Translational Science (NIH: UL1TR002537).

Competing interests. BW, DK, AS, MAW, MDK, AMS, and JC report no conflicts of interest relevant to this article. DJD reports research funding from BioMerieux, Inc. and Affinity Biosensors. LH reports having receiving povidone iodine product for unrelated clinical trials from 3M and from PDI.

References

1. Beh CC, Zulkufli NS, Loh LM, *et al.* SARS-CoV-2 seroprevalence and antibody trends in vaccinated, multi-ethnic healthcare employees. *Trop Biomed* 2021;38:552–560. doi: 10.47665/tb.38.4.098
2. Brousseau N, Morin L, Ouakki M, *et al.* SARS-CoV-2 seroprevalence in health care workers from 10 hospitals in Quebec, Canada: a cross-sectional study. *CMAJ* 2021;193:E1868–E1877. doi: 10.1503/cmaj.202783
3. Bryan A, Tatem K, Diuguid-Gerber J, *et al.* Cross-sectional study evaluating the seroprevalence of SARS-CoV-2 antibodies among healthcare workers and factors associated with exposure during the first wave of the COVID-19 pandemic in New York. *BMJ Open* 2021;11:e053158. doi: 10.1136/bmjopen-2021-053158
4. Plebani M, Padoan A, Fedeli U, *et al.* SARS-CoV-2 serosurvey in health care workers of the Veneto Region. *Clin Chem Lab Med* 2020;58:2107–2111. doi: 10.1515/cclm-2020-1236
5. Moscola J, Sembajwe G, Jarrett M, *et al.* Prevalence of SARS-CoV-2 antibodies in health care personnel in the New York city area. *JAMA* 2020;324:893–895. doi: 10.1001/jama.2020.14765
6. Jeremias A, Nguyen J, Levine J, *et al.* Prevalence of SARS-CoV-2 infection among health care workers in a tertiary community hospital. *JAMA Intern Med* 2020;180:1707–1709.
7. Self WH, Tenforde MW, Stubblefield WB, *et al.* Seroprevalence of SARS-CoV-2 among frontline health care personnel in a multistate hospital network - 13 academic medical centers, April-June 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1221–1226. doi: 10.15585/mmwr.mm6935e2
8. Mansour M, Leven E, Muellers K, Stone K, Mendu DR, Wajnberg A. Prevalence of SARS-CoV-2 antibodies among healthcare workers at a tertiary academic hospital in New York city. *J Gen Intern Med* 2020; 35:2485–2486.
9. Sydney ER, Kishore P, Laniado I, Rucker LM, Bajaj K, Zinaman MJ. Antibody evidence of SARS-CoV-2 infection in healthcare workers in the Bronx. *Infect Control Hosp Epidemiol* 2020;41:1348–1349. doi: 10.1017/ice.2020.437
10. Stubblefield WB, Talbot HK, Feldstein LR, *et al.* Seroprevalence of SARS-CoV-2 among frontline healthcare personnel during the first month of caring for patients with COVID-19—Nashville, Tennessee. *Clin Infect Dis* 2021;72:1645–1648.

11. Amendola A, Tanzi E, Folgori L, *et al.* Low seroprevalence of SARS-CoV-2 infection among healthcare workers of the largest children hospital in Milan during the pandemic wave. *Infect Control Hosp Epidemiol* 2020; 41:1468–1469.
12. Grant JJ, Wilmore SM, McCann NS, *et al.* Seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a London NHS Trust. *Infect Control Hosp Epidemiol* 2021;42:212–214.
13. Iversen K, Bundgaard H, Hasselbalch RB, *et al.* Risk of COVID-19 in health-care workers in Denmark: an observational cohort study. *Lancet Infect Dis* 2020;20:1401–1408. doi: 10.1016/S1473-3099(20)30589-2
14. Paderno A, Fior M, Berretti G, *et al.* SARS-CoV-2 infection in health care workers: cross-sectional analysis of an otolaryngology unit. *Otolaryngol Head Neck Surg* 2020;163:671–672. doi: 10.1177/0194599820932162
15. Rudberg A-S, Havervall S, Månberg A, *et al.* SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. *Nat Commun* 2020;11:5064.
16. Steensels D, Oris E, Coninx L, *et al.* Hospital-wide SARS-CoV-2 antibody screening in 3056 staff in a tertiary center in Belgium. *JAMA* 2020;324: 195–197. doi: 10.1001/jama.2020.11160
17. Jacob JT, Baker JM, Fridkin SK, *et al.* Risk factors associated with SARS-CoV-2 seropositivity among US health care personnel. *JAMA Netw Open* 2021;4:e211283. doi: 10.1001/jamanetworkopen.2021.1283
18. Wilkins JT, Hirschhorn LR, Gray EL, *et al.* Serologic status and SARS-CoV-2 infection over 6 months of follow up in healthcare workers in Chicago: a cohort study. *Infect Control Hosp Epidemiol* 2022;43:1207–1215. doi: 10.1017/ice.2021.367
19. Papasavas P, Olugbile S, Wu U, *et al.* Seroprevalence of SARS-CoV-2 antibodies, associated epidemiological factors and antibody kinetics among healthcare workers in Connecticut. *J Hosp Infect* 2021;114:117–125.
20. Billings J, Ching BCF, Gkofa V, Greene T, Bloomfield M. Experiences of frontline healthcare workers and their views about support during COVID-19 and previous pandemics: a systematic review and qualitative meta-synthesis. *BMC Health Serv Res* 2021;21:1–17.
21. Zhang M, Zhou M, Tang F, *et al.* Knowledge, attitude, and practice regarding COVID-19 among healthcare workers in Henan, China. *J Hosp Infect* 2020;105:183–187.
22. Ottolenghi J, McLaren RA, Jr., Bahamon C, Dalloul M, McCalla S, Minkoff H. Health care workers' attitudes toward patients with COVID-19. *Open Forum Infect Dis* 2021;8:ofab375. doi: 10.1093/ofid/ofab375
23. Jespersen S, Mikkelsen S, Greve T, *et al.* Severe acute respiratory syndrome coronavirus 2 seroprevalence survey among 17 971 healthcare and administrative personnel at hospitals, prehospital services, and specialist practitioners in the Central Denmark Region. *Clin Infect Dis* 2021;73: e2853–e2860.
24. Moore RC, Lee AY, Hancock JT, Halley MC, Linos E. Age-related differences in experiences with social distancing at the onset of the COVID-19 pandemic: a computational and content analytic investigation of natural language from a social media survey. *JMIR Hum Factors* 2021;8:e26043.
25. Luo Y, Cheng Y, Sui M. The moderating effects of perceived severity on the generational gap in preventive behaviors during the COVID-19 pandemic in the US. *Int J Environ Res Public Health* 2021;18:2011.
26. Rudberg A-S, Havervall S, Manberg A, *et al.* SARS-CoV-2 exposure, symptoms and seroprevalence in health care workers. *Nat Commun* 2020;11:5064
27. Howard-Anderson JR, Adams C, Dube WC, *et al.* Occupational risk factors for severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection among healthcare personnel: A 6-month prospective analysis of the COVID-19 Prevention in Emory Healthcare Personnel (COPE) Study. *Infect Control Hosp Epidemiol* 2022;43:1664–1671.
28. Schoberer D, Osmancevic S, Reiter L, Thonhofer N, Hoedl M. Rapid review and meta-analysis of the effectiveness of personal protective equipment for healthcare workers during the COVID-19 pandemic. *Public Health Pract (Oxf)* 2022;4:100280.
29. Ran L, Chen X, Wang Y, Wu W, Zhang L, Tan X. Risk factors of healthcare workers with coronavirus disease 2019: a retrospective cohort study in a designated hospital of Wuhan in China. *Clin Infect Dis*. 2020;71:2218–2221.
30. Lau JT, Fung KS, Wong TW, *et al.* SARS transmission among hospital workers in Hong Kong. *Emerg Infect Dis* 2004;10:280.
31. Cheng HY, Jian SW, Liu DP, Ng TC, Huang WT, Lin HH. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. *JAMA Intern Med* 2020;180:1156–1163. doi: 10.1001/jamainternmed.2020.2020
32. Braun KM, Moreno GK, Buys A, *et al.* Viral sequencing to investigate sources of SARS-CoV-2 infection in US healthcare personnel. *Clin Infect Dis* 2021;73:e1329–e1336. doi: 10.1093/cid/ciab281
33. Chatterjee S, Bhattacharya M, Nag S, Dhama K, Chakraborty C. A detailed overview of SARS-CoV-2 omicron: its sub-variants, mutations and pathophysiology, clinical characteristics, immunological landscape, immune escape, and therapies. *Viruses* 2023;15:167.
34. Shoemaker H, Li H, Zhang Y, *et al. Association Between Behavior and Risk of COVID-19 in A Cohort of Healthcare Personnel*. Oxford University Press, US. 2023:ofad500.
35. Fisher BT, Sharova A, Boge CL, *et al.* Evolution of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) seroprevalence among employees of a US academic children's hospital during coronavirus disease 2019 (COVID-19) pandemic. *Infect Control Hosp Epidemiol* 2022;43: 1647–1655.
36. Sikkens JJ, Buis DTP, Peters EJG, *et al.* Serologic surveillance and phylogenetic analysis of SARS-CoV-2 infection among hospital health care workers. *JAMA Netw Open* 2021;4:e2118554. doi: 10.1001/jamanetwork open.2021.18554
37. Allen N, Brady M, Carrion Martin AI, *et al.* SARS-CoV-2 antibody testing in health care workers: a comparison of the clinical performance of three commercially available antibody assays. *Microbiol Spectr* 2021;9:e0039121. doi: 10.1128/Spectrum.00391-21
38. Smith R, Chen K, Winner D, Friedhoff S, Wardle C. A systematic review of COVID-19 misinformation interventions: lessons learned: study examines COVID-19 misinformation interventions and lessons learned. *Health Affairs* 2023;42:1738–1746.
39. Ferreira Caceres MM, Sosa JP, Lawrence JA, *et al.* The impact of misinformation on the COVID-19 pandemic. *AIMS Public Health* 2022; 9:262–277. doi: 10.3934/publichealth.2022018