Open Forum Infectious Diseases

BRIEF REPORT

When Should Healthcare Workers With Coronavirus Disease 2019 (COVID-19) Return to Work? An Analysis of Follow-up Antigen Test Results After a Positive COVID Test

Anthony Baffoe-Bonnie,[1,2,3,4] Mandy C. Swann,[1] and Hyun Sue Kim[2]

[1]Carilion Clinic Infection Prevention and Control, Roanoke, Virginia, USA, [2]Virginia Tech Carilion School of Medicine, Roanoke, Virginia, USA, [3]Carilion Clinic Infectious Diseases, Roanoke, Virginia, USA, and [4]Carilion Clinic Department of Medicine, Roanoke, Virginia, USA

A high percentage of healthcare workers (HCWs) who had met the Centers for Disease Control and Prevention criteria for returning to work 5 days after symptom onset remained positive for their return-to-work COVID-19 antigen test, suggesting continued infectiousness. Boosted HCWs were more likely to be antigen positive on their return-to-work test compared to unvaccinated HCWs, which merits further research.

Keywords. return-to-work antigen; healthcare worker; vaccination status; COVID-19.

The Centers for Disease Control and Prevention's (CDC) guidance for work restriction and the duration of isolation for healthcare workers (HCWs) after a coronavirus disease 2019 (COVID-19) infection has evolved throughout the pandemic [1]. Currently, the CDC outlines a continuum of options from conventional to contingency to crisis strategies for qualifying healthcare workers [1, 2]. This guidance aims to minimize HCW staffing shortages while mitigating the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in the healthcare setting. Under the contingency standards, HCWs with COVID-19 may return to work (RTW) after 5 days with or without a negative test with a face mask in both patient care and nonpatient care areas [1].

Multiple studies report a high rate of antigen positivity on day 5 after symptom onset [3, 4]. There is now accruing evidence suggesting a strong correlation between a positive COVID-19 antigen test and positive viral cultures or infectivity [5–7]. The implications of these findings merit continued research on the duration of isolation for HCWs and the population at large.

Our study describes the factors associated with a positive RTW antigen test after an initial positive SARS-CoV-2 polymerase chain reaction (PCR) test in symptomatic HCWs during the omicron variant and subvariant surges in southwest Virginia.

METHODS

We conducted a retrospective, cross-sectional study of employees of a healthcare system in southwest Virginia who tested positive for COVID-19 and completed RTW antigen testing between January 6, 2022 and July 6, 2022. Symptomatic employees who tested positive with a COVID-19 PCR test were instructed to isolate and follow an HCW RTW process outlined in Supplementary Appendix A. Upon meeting the criteria on day 5 or later, a single RTW COVID-19 antigen test (Quidel Sofia SARS Antigen FIA) was collected by trained personnel. Persons who were immunocompromised or had severe and/or critical COVID-19 were not eligible to utilize this protocol.

Demographics, COVID-19 vaccination history, COVID-19 PCR, and RTW antigen test data were obtained from administrative records. Supplementary Appendix B describes how we categorized the vaccination status of the HCWs.

Records where the completion of RTW antigen testing was performed between day 5 and day 11 after the initial positive PCR test (day 0) were included in the analysis. Categorical data were described as frequencies and percentages and compared by χ^2 tests. A logistic regression model was examined to identify characteristics independently associated with a positive RTW antigen test. Analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC).

Patient Consent Statement

This study was deemed exempt by our Institutional Review Board.

RESULTS

A total of 1704 HCWs completed RTW antigen testing after a positive SARS-CoV-2 reverse-transcription-PCR test within this timeframe. Table 1 outlines the descriptive characteristics of the HCWs. Eighty-nine percent of the healthcare workers were either fully vaccinated or boosted at the time of their initial PCR test. Approximately two thirds (67.6%) of eligible HCWs completed RTW testing on day 5 or 6 after their initial positive PCR test. Of those, 53% were antigen positive. The

Received 27 December 2022; editorial decision 27 February 2023; accepted 28 February 2023; published online 3 March 2023

Correspondence: Anthony Baffoe-Bonnie, MD, Department of Medicine, Virginia Tech Carilion School of Medicine, 213 McClanahan Street SW, Roanoke, VA 24014 (abaffoe6@vt.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad114

Table 1. Descriptive Characteristics of Symptomatic HCWs Completing RTW Antigen Testing After a Positive SARS-CoV-2 RT-PCR Result

Characteristics	Positive Antigen Result [n = 816]	Negative Antigen Result [n = 888]	Total [n = 1704]	*P* Value
Gender				<.05
Male	200 (52.91%)	178 (47.09%)	378 (22.2%)	
Female	616 (46.46%)	710 (53.54%)	1326 (77.8%)	
Age Group, Years				<.01
18–29	184 (43.71%)	237 (56.29%)	421 (24.7%)	
30–39	232 (44.44%)	290 (55.56%)	522 (30.6%)	
40–49	164 (50.93%)	158 (49.07%)	322 (18.9%)	
50+	236 (53.76%)	203 (46.24%)	439 (25.8%)	
Vaccination Status				<.0001
Not vaccinated	67 (34.54%)	127 (65.46%)	194 (11.4%)	
Vaccinated[a]	313 (43.11%)	413 (56.89%)	726 (42.6%)	
Boosted 90+ Days	350 (55.91%)	276 (44.09%)	626 (36.7%)	
Boosted <90 Days	86 (54.43%)	72 (45.57%)	158 (9.3%)	
Days Since PCR Test				<.0001
05	464 (54.85%)	382 (45.15%)	846 (49.6%)	
06	239 (50.21%)	237 (49.79%)	476 (28.0%)	
07	105 (31.72%)	226 (68.28%)	331 (19.4%)	
08+	8 (15.69%)	43 (84.31%)	51 (3.0%)	

Abbreviations: HCW, healthcare worker; RT-PCR, reverse-transcription polymerase chain reaction; RTW, return-to-work; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Completion of primary series.

Table 2. Multivariable Logistic Regression of Factors Associated With a Positive RTW Antigen Test

Characteristics	Odds Ratio (95% CI)	*P* Value	Standard Error
Gender (ref = male)			
Female	0.84 (0.66–1.06)	.15	0.12
Age Group, Years (ref = 18–29)			
30–39	0.92 (.70–1.21)	.54	0.14
40–49	1.21 (.90–1.65)	.21	0.16
50+	1.31 (.99–1.74)	.06	0.14
Vaccination Status (ref = not vaccinated)			
Vaccinated[a]	1.41 (1.00–1.98)	<.05[a]	0.17
Boosted 90+ Days	2.21 (1.56–3.12)	<.0001	0.18
Boosted <90 Days	2.08 (1.34–3.24)	<.01	0.23
Days From Initial PCR Test (ref = Day 5)			
Day 6	0.85 (.68–1.07)	.16	0.12
Day 7	0.39 (.29–.51)	<.0001	0.14
Days 8+	0.16 (.08–.35)	<.0001	0.40

Abbreviations: CI, confidence interval; HCW, healthcare worker; PCR, polymerase chain reaction; ref, reference; RTW, return-to-work.

[a]Completion of primary series.

antigen positivity rate for HCWs testing on day 7 or later was 29.5%. (Supplementary Appendix C). Overall, almost half (48%) of the HCWs had a positive result on their RTW antigen test obtained between days 5 and 11 after the initial PCR test. In pairwise comparisons, gender, age, vaccination status, and days since initial positive PCR were all significantly associated with the RTW antigen test result (Table 1).

In the multivariate model, a positive RTW antigen result was more likely in HCWs boosted more than 90 days before infection (odds ratio [OR], 2.21; 95% confidence interval [CI], 1.56–3.12; $P < .0001$) and those boosted within 90 days of infection (OR, 2.08; 95% CI, 1.34–3.24; $P < .01$) compared to HCW who had not been vaccinated. A positive RTW antigen result was less likely on day 7 and later (OR, 0.39; 95% CI, .29–.51; $P < .0001$) compared to day 5 (Table 2). Neither gender nor age was predictive of a positive RTW antigen result in the multivariable model.

DISCUSSION

Our findings highlight that a majority of HCWs undergoing the RTW process had their test done by day 6 from the initial positive PCR test. Of those, more than half (53%) had a positive RTW antigen result. The high rate of positive RTW antigen result during this time frame is consistent with findings by other groups [3, 4, 8]. Current literature demonstrates that a negative antigen test obtained during this time frame is highly correlated with a negative viral culture and noninfectiousness [6]. In a newer but small study [9] of fully vaccinated or boosted young college students during the era of delta and omicron variants, the negative predictive value of the self-performed Abbott BinaxNOW rapid antigen test compared with culture growth at days 4 through 6 from initial diagnosis was 100%, making a negative rapid antigen test a reliable tool for determining when it is safe to return to normal activities after COVID-19.

There is an evolving understanding of what a positive RTW antigen test obtained after day 5 from an initial positive diagnostic PCR or symptom onset may mean. Lopera et al [7] demonstrated that a positive antigen test during the first 5 days after symptom onset was highly predictive of infectiousness and between 6 to 11 days moderately predictive of infectiousness, during the prevaccine, pre-omicron era. Bouton et al [9] noted a 50% positive predictive value when the antigen test was compared with culture growth at days 4 through 6 from initial diagnosis. In that study, 84% of participants had achieved culture conversion (no growth) by day 6 from initial diagnosis with 11% still positive beyond day 5. Boucau et al [10] noted a median time of 6 to 8 days from index PCR or symptom onset to culture conversion. Thus, a positive RTW antigen test after day 5 may or may not rule out infectiousness. Our study identifies a significant drop-off for RTW antigen positivity at day 7 and later among a large cohort of HCWs, offering a time point

where self-isolation could be discontinued. We anticipate that with the upcoming expiration of the COVID-19 public health emergency [11], there may be less access to RTW antigen testing due to cost. Thus, self-isolation through day 6 with continued masking until day 10 may be a strategy to limit transmission in both the healthcare and community setting.

In our study, HCWs who had received a booster vaccine were independently more likely to test positive on their RTW antigen test compared to their unvaccinated colleagues. In a smaller study, Landon et al [3] noted a similar finding of boosted HCWs more likely to have a positive RTW antigen test compared to their non-boosted peers. Both studies stand in contrast to one from the community, where unvaccinated individuals without prior infection were more likely to have a positive follow-up COVID-19 antigen test when compared to vaccinated or previously infected individuals [4]. The reasons for our finding of a higher proportion of positive RTW antigen in our boosted HCWs are unclear and may reflect a yet unaccounted-for performance characteristic of the lateral-flow antigen test or an unmeasured variable(s) of that population including possible differences in prior infection between the groups. Further probing of this finding is warranted given the recent signal seen in the Bouton [9] study where participants who had received a COVID-19 booster vaccination had a trend (albeit not significant) towards slower within-host viral load decay. The study by Boucau et al [10] looked at viral kinetics in the omicron era, but they did not find significant differences in the median duration of viral shedding among the 66 participants based on vaccine status. Both studies [9, 10] are limited by their small sample sizes, suggesting that they may not be adequately powered to identify this finding. There are ample data demonstrating that being up to date on COVID-19 vaccination is protective against severe disease and death from COVID-19 [12, 13]. Thus, this unexpected finding needs to be investigated further with prospective studies or by leveraging even larger data sets where viral cultures are performed.

This study was retrospective and in a single health system in southwest Virginia and may not be generalizable to other populations. There could be confounders that we did not account for given the retrospective nature of our study such as the history of prior infections. However, our control for many of the potential confounders and our large sample size for a HCW RTW antigen study are strengths of this study and improves on the available data to date. We did not conduct any viral cultures to determine virus viability in HCWs with a positive antigen test, and thus we cannot draw definite conclusions about their infectiousness.

CONCLUSIONS

A high proportion of HCWs have a positive RTW antigen for at least 6 days after their initial positive COVID-19 PCR test and are possibly contagious, even when symptoms are improving. Guidance during staffing shortages should evolve to reflect this growing body of evidence. Future studies should aim to understand the implications of vaccination status and RTW antigen results.

Supplementary Data

Supplementary materials are available at *Open Forum 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.

Acknowledgments

We thank Robin Strachman for her work with data abstraction.

Financial support. The authors would like to acknowledge Virginia Tech's Open Access Subvention Fund and the Carilion Clinic Department of Medicine for support of the article processing charges.

Potential conflicts of interest. All authors: No reported conflicts of interest.

References

1. Centers for Disease Control and Prevention. Strategies to mitigate healthcare personnel staffing shortages. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/mitigating-staff-shortages.html. Accessed 15 February 2023.
2. Centers for Disease Control and Prevention. Interim guidance for managing healthcare personnel with SARS-CoV-2 infection or exposure to SARS-CoV-2. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html. Accessed 10 February 2023.
3. Landon E, Bartlett AH, Marrs R, Guenette C, Weber SG, Mina MJ. High rates of rapid antigen test positivity after 5 days of isolation for COVID-19. medRxiv [Preprint]; 2022. doi: 10.1101/2022.02.01.22269931.
4. Lefferts B, Blake I, Bruden D, et al. Antigen test positivity after COVID-19 isolation—Yukon-Kuskokwim Delta Region, Alaska, January-February 2022. MMWR Morb Mortal Wkly Rep **2022**; 71:293–8.
5. Chu VT, Schwartz NG, Donnelly MAP, et al. Comparison of home antigen testing with RT-PCR and viral culture during the course of SARS-CoV-2 infection. JAMA Intern Med **2022**; 182:701.
6. Korenkov M, Poopalasingam N, Madler M, et al. Evaluation of a rapid antigen test to detect SARS-CoV-2 infection and identify potentially infectious individuals. J Clin Microbiol **2021**; 59:e0089621.
7. Lopera TJ, Alzate-Ángel JC, Díaz FJ, Rugeles MT, Aguilar-Jiménez W. The usefulness of antigen testing in predicting contagiousness in COVID-19. Microbiol Spectr **2022**; 10:e0196221.
8. Tande AJ, Swift MD, Challener DW, et al. Utility of follow-up coronavirus disease 2019 (COVID-19) antigen tests after acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among healthcare personnel. Clin Infect Dis **2022**; 75:e347–9.
9. Bouton TC, Atarere J, Turcinovic J, et al. Viral dynamics of omicron and Delta severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants with implications for timing of release from isolation: a longitudinal cohort study. Clin Infect Dis **2023**; 76:e227–33.
10. Boucau J, Marino C, Regan J, et al. Duration of shedding of culturable virus in SARS-CoV-2 omicron (BA.1) infection. N Engl J Med **2022**; 387:275–7.
11. U.S. Department of Health & Human Services. Fact Sheet: COVID-19 Public Health Emergency Transition Roadmap. Available at: https://www.hhs.gov/about/news/2023/02/09/fact-sheet-covid-19-public-health-emergency-transition-roadmap.html. Accessed 17 February 2023.
12. Arbel R, Hammerman A, Sergienko R, et al. BNT162b2 vaccine booster and mortality due to COVID-19. N Engl J Med **2021**; 385:2413–20.
13. Center for Disease Control and Prevention. Benefits of Getting A COVID-19 Vaccine. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/vaccine-benefits.html. Accessed 17 February 2023.