SARS-CoV-2 Infection Among Symptom-Free Healthcare Workers

Ryan T. Demmer¹,², PhD MPH; Angela Ulrich¹, PhD; Talia Wiggen¹, BS; Ali Strickland³, MPH; Brianna Naumchik⁴, BS; Shalini Kulasingam¹, PhD; Steven D. Stovitz⁵, MD MS; Clarisse Marotz⁶, PhD; Pedro Belda-Ferre, PhD⁶; Greg Humphrey⁶, BS; Peter De Hoff⁷, PhD; Louise Laurent⁷, MD PhD; Susan Kline⁸, MD; Rob Knight⁶,⁹-¹¹, PhD;

Affiliations
¹Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN;
²Department of Epidemiology, Columbia University, New York, NY;
³Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, MN;
⁴Medical School, University of Minnesota, Minneapolis, MN;
⁵Department of Family Medicine and Community Health, Medical School, University of Minnesota, Minneapolis, MN;
⁶Department of Pediatrics, University of California San Diego, La Jolla, CA;
⁷Department of Obstetrics, Gynecology, and Reproductive Sciences, Sanford Consortium for Regenerative Medicine, University of California, San Diego, CA;
⁸Division of Infectious Diseases and International Medicine, Medical School, University of Minnesota, Minneapolis, MN;
⁹Department of Computer Science & Engineering, Jacobs School of Engineering, University of California San Diego, La Jolla, CA;
¹⁰Department of Bioengineering, University of California San Diego, La Jolla, CA;
¹¹Center for Microbiome Innovation, University of California San Diego, La Jolla, CA;

Corresponding Author
Ryan Demmer
1300 South 2nd Street
Suite 300
Minneapolis, MN 55454
demm0009@umn.edu

Word Count: 1169
Tables: 1
Figures: 2
KEY POINTS

Questions: What is the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among symptom-free healthcare workers (HCW) and what is the acceptability of self-collected nasopharyngeal swabs (NPS) for SARS-CoV-2 infection ascertainment?

Findings: SARS-CoV-2 was not detected in any of 489 HCWs studied. Self-collected NPS were well tolerated and over 95% of participants reported a willingness to repeat a self-collected NP swab in the future.

Meaning: The point prevalence of SARS-CoV-2 infection was likely very low in symptom-free Minnesota healthcare workers from April 20th and June 24th, 2020.
ABSTRACT

Importance: Current evidence suggests that transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is possible among symptom-free individuals but limited data are available on this topic in healthcare workers (HCW). The quality and acceptability of self-collected nasopharyngeal swabs (NPS) is unknown.

Objective: To estimate the prevalence of SARS-CoV-2 infection and to assess the acceptability of self-collected NPS among HCW.

Design: Cross-sectional convenience sample enrolled between April 20th and June 24th, 2020. We had >95% power to detect at least one positive test if the true underlying prevalence of SARS-CoV2 was ≥1%.

Setting: The metropolitan area surrounding Minneapolis and St. Paul, Minnesota.

Participants: HCW free of self-reported upper respiratory symptoms were recruited.

Exposures: Participants completed questionnaires regarding demographics, household characteristics, personal protective equipment (PPE) utilization and comorbidities.

Outcomes: A participant self-collected nasopharyngeal swab (NPS) was obtained. SARS-CoV-2 infection was assessed via polymerase chain reaction. NPS discomfort was assessed on a scale of 1 (no discomfort) – 10 (extreme discomfort). NPS duration and depth into the nasopharynx, and willingness to perform future self-collections were assessed.

Results: Among n=489 participants 80% were female and mean age±SD was 41±11. Participants reported being physicians (14%), nurse practitioners (8%), physician’s assistants (4%), nurses (51%), medics (3%), or other which predominantly included laboratory technicians and administrative roles (22%). Exposure to a known/suspected
COVID-19 case in the 14 days prior to enrollment was reported in 40% of participants. SARS-CoV-2 was not detected in any participant. The mean±SD discomfort level of the NPS was 4.5±2.0. 95% of participants reported that their self-swab was ≥ the duration of patient swabs they had previously performed, and 89% reported the depth to be ≥ the depth of previous patient swabs. Over 95% of participants reported a willingness to repeat a self-collected NP swab in the future.

Conclusions and Relevance: The point prevalence of SARS-CoV-2 infection was likely very low in symptom-free Minnesota healthcare workers from April 20\textsuperscript{th} and June 24\textsuperscript{th}, 2020. Self-collected NP swabs are well-tolerated and a viable alternative to provider-collected swabs to preserve PPE.
Current evidence suggests that nearly half of new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are due to transmission from asymptomatic or presymptomatic (i.e. symptom-free) individuals.1-4

Healthcare workers (HCW) have an increased risk of SARS-CoV-2 infection given their exposure to the virus while serving on the frontlines of the COVID-19 pandemic. HCW can inadvertently be a source of transmission since close contact with patients is often required for effective health care. However, it is also possible that the risk of infection among HCW in the healthcare setting might lower than that of the general population.5

Knowledge of the prevalence of infection among symptom-free HCW may help to determine the potential role HCW play in transmission, guide testing recommendations and inform infection modeling studies. However, to date there are limited data on this topic.

To address this question, we screened symptom-free HCW for SARS-CoV-2. Additionally, to preserve personal protective equipment (PPE), we implemented a protocol for self-collection of nasopharyngeal swabs (NPS) and surveyed participants about their perceived quality of a self-collected vs. provider collected NPS.
METHODS

Participants
A convenience sample of individuals working in Minnesota healthcare facilities located in the Minneapolis/St. Paul metropolitan area. Participants were identified via social media advertisements and enrolled from April 20th–June, 24th, 2020. Eligibility criteria were: i) employed or volunteering in a healthcare facility; ii) free of fever, chills, anosmia, pharyngitis, recently developed persistent cough, nasal congestion suspected to be unrelated to season allergies; iii) age 18-80 years; iv) not pregnant. A total of 489 participants provided self-collected NPS (Figure 1). The study was approved by the University of Minnesota Institutional Review Board. All participants provided informed consent.

Self-Collected Nasopharyngeal Swab (NPS)
Participants advanced a nylon flocked-tip NPS through the nasal passage (bilaterally) 3-4 inches into the nasopharynx and swirled the swab 360 degrees for 5 seconds. The swab tip was preserved in 95% ethanol, immediately placed on an ice bath, and transferred to a -80° freezer. Samples were shipped overnight on dry ice to UC San Diego.

Laboratory Assessment of SARS-CoV-2
Samples were processed within 48 hours of receipt at UC San Diego. Total nucleic acid was extracted from the swab heads using the MagMAX™ Microbiome Ultra Nucleic Acid Isolation Kit (A42357) and eluted in 100 µl nuclease-free H₂O. SARS-CoV-2
Screening was performed using the one-step Applied Biosystems TaqPath COVID-19 Combo Kit (A47814) following the manufacture’s protocol with the following exceptions: The reaction volume was scaled down to 3 µL with proportional reagent scaling and a replacement of ~94% of the water with participant RNA. Additionally, the MS2 phage spike-in control was diluted 160-fold to improve sensitivity through reducing competition for reagent material within the multiplex RT-qPCR reaction. Samples were prepared in 384 well reaction plates using a mosquito® HV Robotic Liquid Handler (SPT Labtech) and a mosquito® X1 (HV) Robotic Liquid Handler (SPT Labtech). The RT-qPCR was analyzed in a QuantStudio5 qPCR instrument (ThermoFisher Scientific). Positive controls for each SARS-CoV-2 target amplified as expected, as well as all MS2 sample controls. None of the negative controls amplified.

**Questionnaires**

Prior to the NPS, participants completed online surveys. After the NPS, participants were queried about their perception of the procedure relative to NPS they have performed on patients. They reported their level of discomfort with the self-swab on a scale of 1 (no discomfort) to 10 (the most discomfort they have ever experienced), their likelihood of repeating a self-collected NPS for clinical or research purposes.

**Statistical analysis**
Analyses were preformed using SAS version 9.4. Descriptive characteristics are reported as mean±SD for continuous variables and % (n) for categorical variables. Bivariate analyses, t-tests and Chi-Square tests assessed statistical significance.

We had >95% power to detect at least one positive test if the true underlying prevalence of SARS-CoV2 was ≥1%.
RESULTS

Among 489 participants enrolled, the mean age was 41±11 and 80% were female. All participants worked in facilities located in the seven-county Minneapolis and St. Paul metropolitan area. The average number of people living with participants was 2±1.4 and 12% reported living alone. The average number of children living with participants was 0.9±1.1 and 50% reported having at least one child at home.

The average time between NPS collection and laboratory testing was 36±18 (range=2-68) days. SARS-CoV-2 was not detected in any sample.

In the 14 days prior to enrollment, 40% of participants reported a known COVID-19 exposure. This proportion varied by venue (p<0.0001, Table 1) and role (p<0.01, Table 1). PPE use was high with only 1.4% of participants reporting no PPE use and this occurred among individuals without patient contact.

The mean score for discomfort related to the self-collected NPS was 4.5±2.0 (range=1-10, Figure 2). Among the 62% (n=287) of participants who reported performing an NPS on a patient, 89% indicated that their self-swabbing depth was ≥ the depth of prior patient swabs, and 95% reported that their self-swab was ≥ the duration of previous patient swabs. Over 95% of participants reported a willingness to repeat a self-collected NPS in the future for either clinical or research purposes (Figure 2); 24% preferred a provider collected-swab, 57% preferred self-collection and 19% reported no preference.
DISCUSSION

We found that self-collection of NPS was acceptable to HCW, and that HCW perceive self-collection to be comparable in quality to provider-collected swabs. We did not detect any SARS-CoV-2 positive individuals among a sample of symptom-free HCW. Based on our power calculations, this strongly suggests that the prevalence of SARS-CoV-2 in our study sample of symptom-free HCW was <1%. This is consistent with results in the U.S. population and in MN specifically during the period these samples were collected. National seroprevalence estimates reported by the Centers for Disease Control, including Minnesota, ranged from 1%-7%, and the estimate from Minnesota during the period from April 20th – May 12th, 2020, was 2.2%. Low SARS-CoV-2 prevalence in HCWs, despite increased risk for exposure, is plausible since HCW are prioritized to receive PPE and are trained in infection control which likely translates into reduced infection risk.

Our findings from the self-collected NPS survey suggest that the method is acceptable to participants and that the depth and duration of swabbing in the nasopharynx is appropriate. The implementation of self-collection protocols could preserve PPE.

The sensitivity of our screening tests might have been low due to the use self-collected NPS, although recent studies report self-collection protocols to have acceptable sensitivity. Tests among symptom-free individuals could also have reduced sensitivity, however, prior studies in asymptomatic pregnant women and residents of long-term care facilities have successfully detected high SARS-CoV-2 prevalence. As this was a
convenience sample, it is not representative of all HCWs in Minnesota, nor is it representative of what future SARS-CoV-2 prevalence estimates might be among symptom-free HCW in settings with high community prevalence.

Our results suggest that the prevalence of SARS-CoV-2 infection was low in symptom-free Minnesota healthcare workers. Self-collected NP swabs are acceptable to participants and might be a future alternative to provider-collected swabs to preserve PPE. Ongoing monitoring of infection in healthcare workers will be important as the pandemic progresses and community transmission rises across the country.
REFERENCES

1. 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.
2. Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA.* 2020.
3. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N Engl J Med.* 2020.
4. Estimating the generation interval for COVID-19 based on symptom onset data. [https://www.medrxiv.org/content/10.1101/2020.03.05.20031815v1](https://www.medrxiv.org/content/10.1101/2020.03.05.20031815v1). Accessed.
5. Voytko L. Fewer NY Healthcare Workers Are Being Infected With COVID-19 Compared To Public, Cuomo Says. In *Forbes.*
6. Havers FP, Reed C, Lim T, et al. Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. *JAMA Intern Med.* 2020.
7. Altamirano J, Govindarajan P, Blomkalns AL, et al. Assessment of Sensitivity and Specificity of Patient-Collected Lower Nasal Specimens for Sudden Acute Respiratory Syndrome Coronavirus 2 Testing. *JAMA Netw Open.* 2020;3(6):e2012005.
8. Tu YP, Jennings R, Hart B, et al. Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. *N Engl J Med.* 2020;383(5):494-496.
9. Fassett MJ, Lurvey LD, Yasumura L, et al. Universal SARS-Cov-2 Screening in Women Admitted for Delivery in a Large Managed Care Organization. *Am J Perinatol.* 2020.
10. Sutton D, Fuchs K, D’Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. *N Engl J Med.* 2020;382(22):2163-2164.
11. Bigelow BF, Tang O, Barshick B, et al. Outcomes of Universal COVID-19 Testing Following Detection of Incident Cases in 11 Long-term Care Facilities. *JAMA Intern Med.* 2020.
Acknowledgements
This study was supported by funding from the University of Minnesota Office of the Vice President for Research and by the Minnesota Population Center (funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development Population Research Infrastructure Program P2C HD041023). Dr. Ulrich was supported by NIH grant T32AI05543315. We are also profoundly grateful for the study participants who have donated valuable time to advance our understanding about SARS-CoV-2 prevalence in healthcare workers. This study was also made possible by Prof. Jian Xu (Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Science), who generously donated nasopharyngeal swabs.
Table 1. General characteristics of n=488^1 Minnesota healthcare workers according to COVID-19 exposures within 14 days preceding enrollment. Enrollment occurred between April 20th, 2020 and June 24th, 2020.

| Variable                  | All^2 N=488 | Known/Suspected COVID-19 exposure^3 | P-value |
|---------------------------|-------------|--------------------------------------|---------|
|                           | Yes 194 (40%) | No 292 (60%)                        |         |
| **Age (years)**           | 41±11        | 38±0.7                               | <0.0001 |
| **Female**                | 411 (84%)    | 151 (77%)                            | <0.01   |
| **Race**                  |              |                                      |         |
| White                     | 442 (90%)    | 174 (90%)                            |         |
| Black                     | 7 (2%)       | 2 (1%)                               | 0.22    |
| Hispanic                  | 9 (2%)       | 4 (2%)                               |         |
| Other                     | 30 (6%)      | 14 (7%)                              |         |
| **Role**                  |              |                                      | <0.01   |
| Physician                 | 70 (14%)     | 23 (12%)                             |         |
| Nurse Practitioner        | 37 (8%)      | 14 (7%)                              |         |
| Physician’s Assistant     | 19 (4%)      | 8 (4%)                               |         |
| Nurse                     | 251 (51%)    | 111 (57%)                            |         |
| Paramedic/EMT             | 14 (3%)      | 12 (6%)                              |         |
| Other                     | 97 (18%)     | 26 (14%)                             |         |
| **Setting**               |              |                                      | <0.0001 |
| Emergency Department      | 74 (15%)     | 55 (28%)                             |         |
| Inpatient ICU             | 93 (19%)     | 58 (30%)                             |         |
| Inpatient Other           | 137 (28%)    | 50 (26%)                             |         |
| Ambulatory Clinic         | 101 (21%)    | 11 (6%)                              |         |
| Emergency Transport Vehicle | 9 (2%)  | 7 (4%)                               |         |
| Other                     | 74 (15%)     | 13 (6%)                              |         |
| **PPE use last 14 days**  |              |                                      |         |
| N95 respirator            | 159 (33%)    | 107 (55%)                            | <0.0001 |
| Surgical mask             | 347 (71%)    | 117 (60%)                            | <0.0001 |
| N95+surgical mask         | 193 (40%)    | 112 (58%)                            | <0.0001 |
| Face shield               | 87 (18%)     | 38 (20%)                             | 0.59    |
| PAPR                      | 18 (4%)      | 14 (7%)                              | <0.01   |
| None                      | 7 (1.4%)     | 0 (0%)                               | 0.09    |
| **Comorbidities**         |              |                                      |         |
| Asthma                    | 68 (14%)     | 28 (14%)                             | 0.82    |
| COPD                      | 1 (0.2%)     | 0 (0%)                               | 0.71    |
| T1 Diabetes               | 3 (0.6%)     | 2 (1%)                               | 0.63    |
| T2 Diabetes               | 13 (3%)      | 5 (3%)                               | 0.97    |
| History of Myocardial Infarction | 1 (0.2%) | 1 (0.5%) | 0 (0%) |
|---------------------------------|----------|----------|-------|
| Immuno-compromised              | 17 (3.5%)| 5 (3%)   | 12 (4%)|

COPD: Chronic obstructive pulmonary disease. Continuous data presented as \(^1n=489\) received a NPS but survey data were not available for one participant. \(^2\)mean±SD or \(^3\)mean±SE; All categorical data presented as number (%). One participant did not complete the questionnaire and was excluded from the table.
Figure Legends

Figure 1. Participant Flow Diagram.

Figure 2. Participant perceptions of a self-collected nasopharyngeal swab. a) Histogram showing the distribution of responses to the following question: ‘On a scale of 1 to 10 how much discomfort did you experience during your self-swab (1 = no discomfort and 10 = the most discomfort you have ever experienced)?’; b) response patterns to questions about the future likelihood of performing a self-collected nasopharyngeal swab for research vs. clinical diagnostic purposes.
**Figure 1. Participant Flow Diagram.**

**Initiated Screener**
N=795

**Eligible**
N=759 (95% of screened)
- Ineligible
  - n=2 not a healthcare worker
  - n=10 prior COVID-19 dx
  - n=17 pregnant
  - n=7 symptomatic

**Completed Consent**
N=599 (79% of eligible)
- Incomplete consent
  - N=160
- Unable to attend in-person visit for nasopharyngeal swab
  - N=110

**Completed Nasopharyngeal Swab**
N=489
(81% of consented)

**Completed Nasopharyngeal Swab Questionnaire**
N=462 (94% of swabbed)
a) Self-Reported Participant Discomfort

In the future how likely would you be to perform a self-collected nasopharyngeal swab, if asked for research purposes?

In the future how likely would you be to perform a self-collected nasopharyngeal swab, if asked for clinical diagnostic purposes?

b)
Figure 2. Select results from participants responses to a survey asking about their perceptions of a self-collected nasopharyngeal swab. a) Histogram showing the distribution of responses to the following question: ‘On a scale of 1 to 10 how much discomfort did you experience during your self-swab (1 = no discomfort and 10 = the most discomfort you have ever experienced)?’; b) response patterns to questions about the future likelihood of performing a self-collected nasopharyngeal swab for research vs. clinical diagnostic purposes.