Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Combination of antibody tests against SARS-CoV-2 for health care workers after vaccination

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The utility of SARS-CoV-2 serological testing for health care workers (HCW) is unclear [1–3]. In early 2021, nearly 10% of all documented SARS-CoV-2 infections in Canada were in HCWs (65,920 HCW cases from a total of 695,704 cases) [4]. This estimate was prior to the widespread vaccination efforts in Canada, prioritizing HCWs and other frontline workers for vaccination. William Osler Health System (Osler) is a large multi-campus tertiary care semi-academic community hospital comprising of 870 beds located in Brampton and north Etobicoke, Ontario and serving a catchment of approximately 1.3 million residents. As of July 2021, there have been more than 400,000 nucleic acid amplification tests (NAATs) for SARS-CoV-2 using reverse transcription polymerase chain reaction (RT-PCR) at our site. Of the 25,569 swabs collected on individuals who identified themselves as a healthcare worker the test positivity rate was 8.7% (n = 2240). Accordingly, we performed a seroprevalence study to estimate the prevalence of antibodies (Abs) against SARS-CoV-2 and characterize the Ab profile in HCWs after the initiation of vaccination efforts at Osler.

Briefly, all Osler HCWs from Jan/28/2021-Feb/28/2021 were informed with the exclusion criterion being an absence from the workplace in the last 30 days. After informed consent, a questionnaire was administered to obtain demographics (i.e., age, sex), work location, travel history, history of COVID-19 close contact, COVID-19 symptoms or test results and if participants received an mRNA SARS-CoV-2 vaccine (date of BioNTech/Pfizer vaccination). Blood was collected (Feb/01/2021-Mar/02/2021), with lithium heparin plasma stored at −70 °C prior to Ab testing. Two different anti-SARS-CoV-2-Abs, same cut-off of 1.0 were used in the study that targeted the receptor binding domain of the spike protein (Anti-S, Siemens Atellica Anti-SARS-Cov-2 total Ab) or the nucleocapsid antigen (Anti-N, Roche Elecsys Anti-SARS-CoV-2 total Ab). Data were analyzed by non-parametric methods or categorical with counts/percentages calculated with 95% confidence intervals (95%CIs). This study received ethics board approval (#20-0027).

There were 933 HCWs that provided consent; with 700 participants providing both the plasma sample and completed the questionnaire (study cohort). History of SARS-CoV-2 infection in the cohort was 8.4% (95%CI: 6.6–10.7). The cohort was mainly female (86%, 95%CI: 83–88) with the largest group of participants (16%, 95%CI: 13–18) working in Medicine with the median (interquartile) age of participants being 44 (34–52) years. Positive vaccination status for SARS-CoV-2 was reported in 501 participants (71%, 95%CI: 68–75) with anti-S Abs above the cut-off in 99.4% (95%CI: 98.2–99.9) in this group. Only three participants (no previous infection) in this group yielded anti-S-Abs below the cut-off with the most likely explanation for this discordance being blood collection too soon after vaccination (i.e., the lowest anti-S-Abs levels were associated to the shortest time from vaccination with results of 0.53, 0.60, and 0.74 obtained from samples collected 2-, 5- and 7-days post-vaccination, respectively, Fig. 1). Of the 199 participants without vaccination, 171 had no history of infection with 28 having a past history of SARS-CoV-2 infection. Of the 171 participants, 10 had anti-S Abs, 7 anti-N Abs, with 6 participants having both anti-S Abs and anti-N Abs above the cut-off, yielding a prevalence of dual positive Abs of 3.5% (95%CI:1.5–7.6) in this unvaccinated group. In the 28 unvaccinated HCWs with past infection, 25 had either/both anti-S Abs and anti-N Abs above the cut-off yielding a prevalence of 89.3% (95%CI: 72.0–97.1), which is lower than the overall vaccinated group (99.4%; 95%CI: 98.2–99.9) and even the vaccinated group with history of infection (n = 31 with all 31 HCWs positive for anti-S).

Intriguingly, prior to disclosing Ab results to the participants, 53% (95%CI: 49–56%) indicated that their results would be positive for SARS-CoV-2 Abs; however, Ab testing revealed 76% (95%CI: 73–79%) of the population as having anti-S-Abs and/or anti-N-Abs above the cut-offs. History of infection (n = 59) and vaccination alone (n = 470) would suggest 76% (95%CI: 72–79) of the population with Abs to SARS-CoV-2. This difference between self-reported versus measured Abs to SARS-CoV-2 suggests that HCWs may underestimate their Ab status and are also unclear on the serological response after either vaccination or infection.

In summary, the utilization of serological testing for SARS-CoV-2 appears most suitable for detecting past infection, vaccination, and neutralization status [1–3] but not other indications [5]. A combination of assays that detect Abs against different viral epitopes may be prudent as current vaccines only target the spike proteins of the virus. Recent or past infection with SARS-CoV-2 could be confirmed in vaccinated individuals by the presence of anti-N-Ab when NPS RT-PCR yields a negative result. The present study further confirms the utility of orthogonal serology testing and provides a framework for possible

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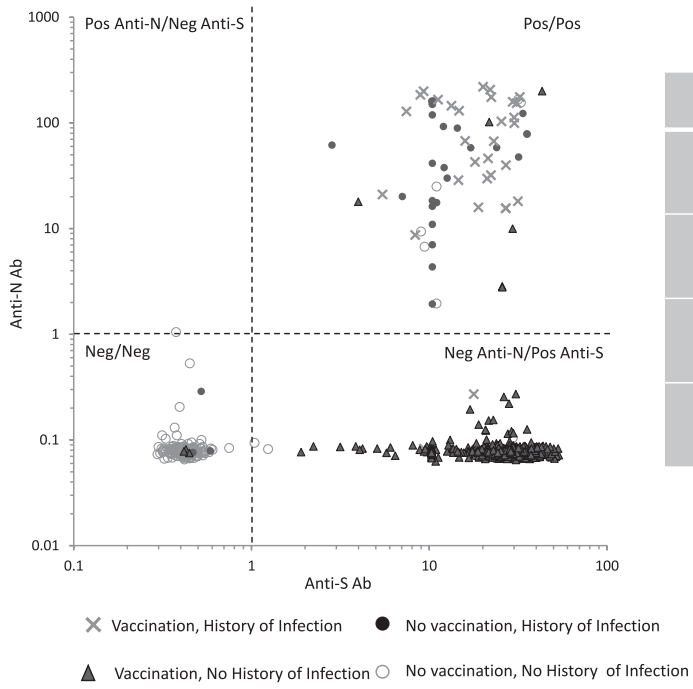

Group	Classification for Anti-N	Anti-S Reactive	Anti-S Non-Reactive
Vaccination, No History of Infection (n = 470)	Reactive	6	0
	Non-Reactive	461	3
Vaccination, History of Infection (n = 31)	Reactive	29	0
	Non-Reactive	2	0
No vaccination, History of Infection (n = 28)	Reactive	25	0
	Non-Reactive	0	3
No vaccination, No History of Infection (n = 171)	Reactive	6	1
	Non-Reactive	4	160

Fig. 1. Paired testing of the 700 HCWs with the anti-S-Ab assay (x-axis) and the anti-N-Ab assay (y-axis). Results were further classified based on history of infection and vaccination status with four different regions identified based on anti-N (negative/positive status) and anti-S (negative/positive status).

testing in HCWs after vaccination, with these data illustrating >99% of vaccinated HCWs having positive Abs to SARS-COV-2.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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