Benchmarking SARS CoV-2 Infection in the Workplace to Support Continuity of Operations

Bart O. Iddins, MD, DVM, SM, Mark H. Waugh, PhD, Brandon Buck, BS, Tracey Cato, BS, David E. Graham, PhD, Kareem Attia, MS, Dan Jones, MLS, BS, Adam Partin, BS, Rania Shourbaji, MPH, MBA, and Christopher Wesh, BS

Objective: The COVID-19 pandemic jeopardizes continuity of operations of workplaces and the health and safety of workers. Exemplar workplace-related SARS-CoV-2 benchmarks are described and illustrated with empirical data. **Methods:** Benchmarks were collected over a 9-month period on a large workplace ($N = 5500+$). These ranged from quantitative indices associated with RT-qPCR targeted testing and random surveillance screening, surveillance for new variants of SARS-CoV-2, intensive contact tracing, case management, return to work procedures, to monitoring of antibody seropositive status. **Results:** Data and analyses substantiated effectiveness of interventions. This was evidenced in suppressed infection rates, rapid case identification and isolation, acceptance of the program by employees, documentation of presumptive immunity, and working relationships with senior management. **Conclusions:** These SARS-CoV-2 exemplar benchmarks provided an evidence-base for practice and contributed strategically to organizational decisions.

Keywords: COVID-19, pandemic response, SARS-CoV-2

Occupational medicine aspires to evidence-based decision-making and practice.[1] At root, evidence-based medicine (EBM) balances clinical expertise with external systematic evidence.[2] It is less well recognized, however, that the principles of EBM apply to management decisions as well as health care practice. Like in general medicine, aspirational EBM principles can inform business management. This is embodied in (1) seeking the best available systematic evidence, (2) applying careful logic, (3) encouraging experimentation and innovation, and (4) learning continuously from results.[3] We argue EBM occupational health can contribute and guide workplace management by use of health-related benchmarks and by embodying this type of strategic thinking.

From the Health Services Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee (Dr Iddins, Dr Waugh, Mr Buck, Ms Cato, Mr Attia, Mr Jones, Mr Partin, Ms Shourbaji, and Mr Wesh); University of Tennessee, Knoxville, Tennessee (Dr Waugh); Biosciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee (Dr Graham).

Ethical considerations and disclosure: Subject data reported herein represent summary internal quality metrics maintained by ORNL Health Services Division. The Department of Energy-Oak Ridge Institutional Review Board Committee (IRB) was consulted and determined that these data were "not human research since the focus is on quality improvement/assessment of the program using already collected data (August 18, 2020)."

The authors report no conflicts of interest.

Clinical significance: Occupational health services can support continuity of operations and protects health and safety of workers by deploying evidence-based benchmarks of SARS-CoV-2 infection, contact tracing, and antibody testing. A comprehensive anti-COVID-19 program requires investment of finances and labor but sustains continuity of operations during the pandemic.

Supplemental digital contents are available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.joem.org).

Address correspondence to: Mark H. Waugh, PhD, Oak Ridge National Laboratory, Oak Ridge, TN (waughmh@ornl.gov).

DOI: 10.1097/JOM.0000000000002188

Like the economy and the collective welfare of people, workplaces have been severely stressed by the coronavirus disease-19 (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. Conditions of high stress and a felt sense of urgency may lead to incompletely understood and potentially fear-based responses by medical and management personnel alike. These reactions are affected by unwitting cognitive biases which can endanger medical and business judgment.[3–5] Using EBM to guide occupational health practice and workplace consultation recognizes there is no one-size-fits-all approach to benchmarking but benchmarking through collecting data is essential. In support of this thesis, we describe exemplar workplace benchmarks of SARS-CoV-2 infection, illustrating and documenting how workplace continuity of operations can be supported during the pandemic.

EXEMPLAR WORKPLACE COVID-19 BENCHMARKS

A set of benchmarks was established by integrating public health-related pandemic interventions with disaster management and leadership principles.[6–8] All interventions and benchmarks were designed to support the health and safety of individuals as well as organizational decision making with continuity of operations the ultimate objective. The benchmarks were operationalizations of an articulated layered defense strategy against COVID-19.[9] Benchmarks were developed from the following:

1. Large-scale targeted testing and random surveillance of the workforce by Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR) for SARS-CoV-2 infection
2. Assertive contact tracing with rapid case isolation and quarantine of exposed employees
3. Evidence-based return to work (RTW) procedures
4. Occupational health case management and follow up
5. Monitoring of seropositive and seronegative SARS-CoV-2 antibody status over time
6. Continuous and reciprocal communication with employees and management

THE WORKPLACE, OCCUPATIONAL HEALTH CLINIC, AND MANAGEMENT SUPPORT

The Oak Ridge National Laboratory (ORNL; is the largest of the U.S. Department of Energy (DOE) Office of Science national laboratories. ORNL was established as a component of the Manhattan Project, the effort of the United States to develop atomic weaponry in World War II (WWII). ORNL has continued to support vital scientific and national security missions since WWII. Currently, these include two of the world's most powerful supercomputers and exaoscale computing, the Spallation Neutron Source facility, production of critical isotopes for medical and scientific research at the High-Flux Isotope Reactor (HIFR), neutron and materials science, and specific national security missions. ORNL employs over 5700 persons with an additional large contingent of contractor workers. Occupational categories include executives and managers, scientists and engineers, national security subject matter experts, federal oversight personnel, nuclear reactor operators, research and laboratory technicians, administrative support staff, skilled trade and craft workers, laborers, various service workers, hazardous material workers, and armed protective force and firefighter/emergency medical technician personnel.

The occupational health component of ORNL Health Services Division (HSD), includes physicians, psychologists, nurse practitioners, nurses, medical laboratory technologists, medical assistants, and skilled technicians and administrative support staff. HSD performs traditional occupational medicine activities such as RTW evaluation, fitness for duty, evaluation and certification for occupational programs, and managing emergent situations (eg, injuries, acute illness, exposure to hazardous or radioactive material, etc). Numerous specialized occupational programs are unique to the setting. Examples of regulation-driven occupational medicine programs include those for asbestos, Beryllium, Cadmium, nanoparticle, and fissile material workers as well as nuclear reactor operators, fire fighters, security police officers, Department of Transportation (DOT) drivers, and federally mandated certification of high reliability/safety-sensitive workers.

With the onset of the pandemic, HSD was required to rapidly expand the scope of operations to maintain occupational health services while implementing anti-SARS-CoV-2 interventions. Moreover, the occupational health clinic pandemic response was dynamic. HSD adjusted its activities in response to pandemic changes, fluctuations in workforce impacts, and the explosion of scientific information and technology associated with COVID-19. Continuity of operations was the overriding mission objective and clinic operations maximized a proactive disaster response posture rather than an ultra-lean budgetary footprint. At the height of pandemic operations, staffing reached 74 full time equivalent personnel, up from the pre-pandemic level of 23. Several of the HSD benchmarking operations required high levels of staffing. For example, SARS-CoV-2 sample collections, laboratory processing, contact tracing, and the telephone call center were labor intensive, and staffing fluctuated over time. Published human resource guides for medical setting staff-to-patient ratios and human resource calculators reference non-pandemic practice needs and thus do not necessarily speak to the current situation.[1,10] The call center handled thousands of telephone calls, the testing operations collected and processed more than 2000 nasopharyngeal swab samples some weeks, and thousands of contact tracing telephone interviews were performed. Clinic staffing expanded as the volume and range of interventions increased. Furthermore, staffing supported continuing traditional occupational medicine services during the pandemic. Some staff were assigned primarily to aspects of COVID-19 response, some to traditional occupational health services, but many performed dual roles. Thus, staffing was dynamic in terms of numbers and role assignment. It must be emphasized that the ORNL setting and mission are unique. Programmatic occupational health COVID-19 responses in smaller organizations or in those with a less comprehensive suite of responses would not necessitate staffing increases of this magnitude. Staffing needs should be individualized to the organization and mission scope.

Importantly, as the pandemic emerged, the Medical Director was inserted into the ORNL senior management team. This ensured medical leadership guided administrative decisions at the highest level.[9] The COVID-19 layered defense strategy included RT-qPCR testing, contact tracing with isolation and quarantine, engineering controls, workspace ventilation assessments, social distancing with use of facial masks and sanitation, substantial use of work-from-home assignments, limiting the workplace census in response to fluctuating infection levels, and continuous communication of fact-based medical/health information to workers and to management.

BENCHMARK ONE: TARGETED TESTING AND RANDOM SURVEILLANCE BY RT-qPCR

The priority for HSD was to rapidly and accurately identify employees infected with SARS-CoV-2. This was imperative in order to protect the health and safety of workers as well as to support workplace continuity of operations. Rather than relying on relatively coarse screening measures such as temperature checks and self-reported symptoms, which have limited utility in granular medical decision-making,[11] HSD immediately implemented a Clinical Laboratory Improvement Amendments (CLIA) laboratory to support high-complexity RT-qPCR analysis of collected samples in order to ensure accuracy in case identification. Fully staffed walk-in and drive-through sample collection (testing) facilities were established. The workplace test sampling strategy spanned diagnostic testing of symptomatic and suspected exposed employees, frequent testing of mission-critical employees, and random sampling surveillance of the entire workforce. In addition, rapid testing capability (Cepheid Xpert Xpress ® SARS-CoV-2) enabled ORNL to provide very rapid assurance on infection status for occasional site visits by VIP personnel which included politicians and leaders from state and federal government as well as industry. Importantly, the comprehensive testing strategy including random sampling surveillance to identify asymptomatic and pre-symptomatic cases. These infections are less likely to be detected and can lead to large-scale spreading of infections.[12,13] Our procedure for random sampling surveillance evolved from a manual to a digitalized process over time. We obtained weekly listings of all workers who had ‘‘badged in’’ to a building on campus. Names were randomized and varying numbers of employees were selected daily for e-mail notification they had been identified for random testing. Up to 100 employees per day (approximately 10% of persons tested per day) received notification they had been randomly identified for testing. This number was flexed to ensure our testing capacity would not be overwhelmed because tests were also offered to employees for whom daily participation could not be predicted (eg, those working from home, symptomatic, or suspected exposed persons) and we maintained regular testing of many mission-critical personnel on a frequent basis.

Costs of materials and personnel associated with high-volume comprehensive RT-qPCR testing were substantial. Not all organizations can afford an operation of this scale. However, HSD argued that workplace continuity of operations would be well supported by data obtained from continuous benchmarking. Otherwise, for example, unchecked infection rates and/or wholesale quarantining of exposed persons could hamper critical missions and potentially trigger a regulatory mandated contraction or closure of operations. Company management concurred with HSD's recommendations and supported deployment of a comprehensive SARS-CoV-2 case identification strategy. An additional and highly important benefit of the program was that it fostered a sense of safety with workers, improving morale during the pandemic.

RT-qPCR Positivity and Case Rates

The COVID-19 testing program has conducted 36,222 RT-PCR tests and identified 598 SARS-CoV-2 infections for an overall new case rate of 1.46% (April 2020 to January 8, 2021). Over 39 weeks, the number of new case positives ranged from 0 to 72

[1] For example, survey results from Brown C, Shore E. AOHP 2016 Online Staffing Survey Results. SURE. YOU CAN LIFT HIM. BUT SHOULD YOU? 2016:2 Staffing Survey Results Dec 2016.pdf [https://aohp.org/aohp/Portals/0/MembersOnlyDocuments/survey result/Staffing Survey Results Dec 2016.pdf; last accessed 2/27/2021].[10]

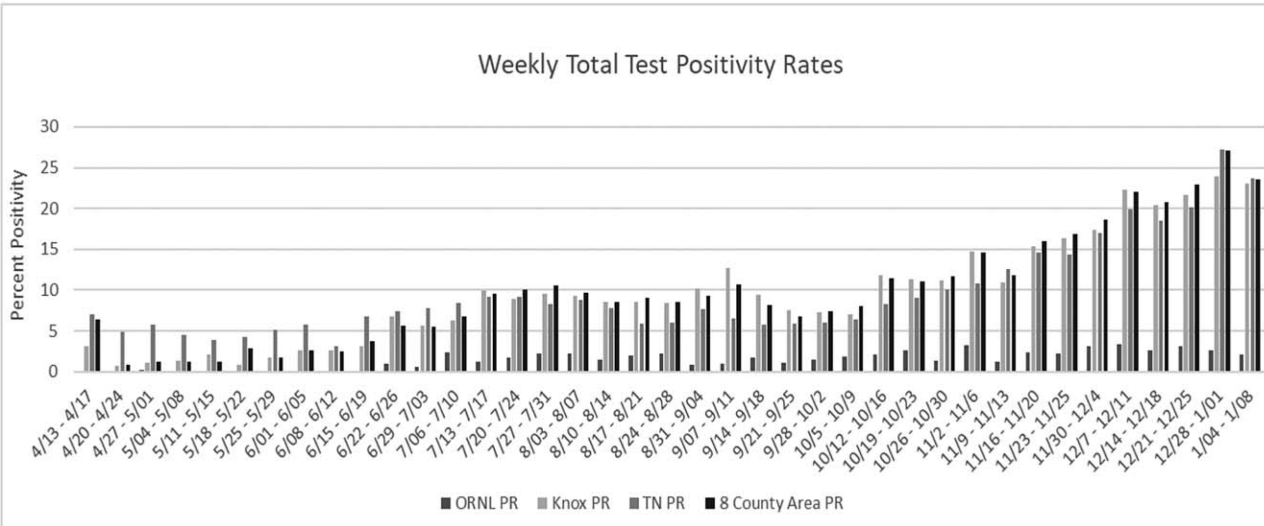

FIGURE 1. Total test positivity rate comparison for ORNL and reference groups. Note. ORNL, Knox County, Tennessee, and eight county surrounding region total test positivity rates over 39 weeks of COVID-19 testing. County and state data are from https://www.tn.gov/health/cedep/ncov/data.html. COVID-19, Coronavirus disease; ORNL, The Oak Ridge National Laboratory.

(mean = 15; standard deviation [SD] = 19). The number of tests administered ranged up to 2209 (mean = 906; SD = 591; 50th percentile = 799). As the infrastructure for high-volume testing expanded over time, the weekly number of tests increased (time and number tests: Pearson $r = 0.91$). The three most recent months averaged 1632 tests per week.

Weekly ORNL total test positivity (TTP) rates were compared with public health department published rates for Knox County, Tennessee, the state of Tennessee, and the eight-county region surrounding ORNL (see https://www.tn.gov/health/cedep/ncov/data.html). These comparisons, shared with Company management, evidenced in real time the success of the COVID-19 layered defense strategy (see Fig. 1).

One-way Analysis of Variance (ANOVA) of mean TTP rates showed highly significant mean differences ($F = 21.43$, df = 3, $P < 0.0001$) with a large effect size (eta^2 [η^2] = 0.29).[2] Of note, the ORNL, Knox County, Tennessee, and eight county region TTP rates increased over time reflecting the rise in infections locally and regionally (r ranged from 0.79 to 0.93; all $P < 0.0001$). However, particulars of the rate trends differed despite the shared increase over time. The degree of similarity of the trends can be indexed by an intraclass correlation coefficient (ICC) and treating the positivity rates as profiles compared for degree of exact correspondence. The mean absolute agreement, two-way random effects model ICC (2,39) for ORNL and Knox County, for ORNL and Tennessee, and ORNL and the eight-county region were poor (ICC = 0.20; 0.16, and 0.19, respectively). This documented that ORNL was dissimilar in rate trend relative to the highly similar trends between Knox County and Tennessee (ICC = 0.95), Knox County and the eight-county region (ICC = 0.99), and Tennessee and the eight-county region (ICC = 0.96). The ICC is a direct measure of effect size. The three reference groups shared about 90% common variance, in contrast to about 3% to 4% shared variance when they are compared to the ORNL positivity rate trend. These results documented both that (1) the ORNL TTP rate was much lower than in surrounding communities and that (2) the infection rate trend in ORNL differed and suggested the value of a particularized examination independent from the local and regional community rates.

Of note, the ORNL workforce differs from Knox County and Tennessee in several ways which could affect infection rates (eg, employment status, education level, and sociodemographic variable distributions). Thus, examining positivity rates in another large and occupationally diverse workforce is instructive. For example, Amazon.com published data from their massive workplace COVID-19 testing program. As of September 2020, Amazon.com reported administering 1,372,000 PCR tests for a TTP rate of 1.44.[14] The global TTP for ORNL (April 2020 to January 2021) was 1.46, not statistically different from that of the Amazon.com workforce (chi square = 0.099, df 1, $P < 0.75$). Thus, the ORNL and Amazon.com workforces, both of which include many different occupational types and a variety of employee demographic variables but are matched on being employment status, were similar in overall infection rates.

Interpreting COVID-19 testing result data must consider testing sampling strategies. Public health department COVID-19 data are often used to describe community infection rates, but they are known to under-estimate disease levels and sometimes by factors as high as 10 to 20 times.[15–19] In part, this is because health departments tend to test symptomatic and exposure-related cases. As well, their testing capacity and eligibility criteria for testing have varied over time. In contrast, the ORNL testing program deployed random surveillance, regular targeted-group testing, and symptom and exposure-based testing. This population sampling approach provided improved fidelity for estimates of disease levels.

COVID-19 has become a leading cause of death in the United States in 2020.[20] Thus, comparing death rates offers a (very) coarse and relative gauge of the success of HSD's program. ORNL has lost one employee to death from COVID-19, corresponding to a death rate of 0.17%. By comparison, as of January 19, 2021, the United States reported a death rate of 1.67%, the State of Tennessee 1.23%, and Knox County 1.03% (see https://www.tn.gov/health/cedep/ncov/data/downloadable-datasets.html). Death rates for some United States government agencies have been published: US Postal Service (2.5%), Veterans Affairs workers (2.14%), Department of Defense (0.20%), State Department (1%), and Food Safety Inspection Service (2%).[21] Regarding health workers, a recent study

[2] Kolmogorov-Smirnov tests confirmed TTP rates were distributed normally, permitting use of ANOVA.

reported a 0.3% death rate and a 4.5% positivity rate in Veterans Administration health workers.[22] In time, the Occupational Health and Safety Administration (OSHA) can be expected to clarify morbidity and mortality associated with the pandemic with publicly available data. However, at present, only a patchwork of reference group death rate data is available and estimates likely will change in time. With respect to the above, ORNL's workforce death rate is lower than these reference groups. Of note, predictors associated with death rates (eg, race, underlying health conditions, and other socioeconomic variables),[23] as well level of health care surveillance, likely vary across the above reference groups, rendering comparisons more illustrative than definitive.[3]

By benchmarking daily and weekly infection rates in real time HSD possessed dynamic indicators of the effectiveness of the COVID-19 layered defense strategy. This information was valuable to communicate to ORNL senior management so that these data played a role in decisions on workforce staffing, operations, assessing support needs ranging from engineering controls to budgetary shifts, and continuity of operations. This was particularly instrumental to management when case rates surged in the local community, but we determined more precise levels and patterns of infection in the ORNL workforce. For example, ORNL was able to flexibly adjust the onsite worker census based on particularized and accurate data. This was especially important during the 2020/2021 winter holiday season when management made several census level decisions.

Granular Analyses Support Medical and Business Decisions

Beyond overall effectiveness, testing program benchmarks provided granular data pertinent to medical and business decisions. For example, HSD determined that approximately 18% of infections were asymptomatic (107 of 598) at collection of a positive RT-qPCR result. The testing program built in quick turnaround times of results and they were often available in less than one day (mean = 0.57 day; SD = 0.70; median = 1; mode = 1). Because asymptomatic and pre-symptomatic cases pose major risks for spreading infection,[13,15] rapid case identification enabled infected individuals to be isolated quickly from the workforce. By performing continuous random and targeted surveillance of the workforce and deploying ring testing when needed to supplement case isolation and quarantines, HSD was able to identify emerging outbreaks in specific locations and occupational groups, mitigating further risks to the workforce.

Evidence showed some occupational categories were at greater risk for infection. For example, bargaining unit employees (occupational groups with collective bargaining agreements) had a statistically higher proportion of infection relative to non-bargaining unit workers (7.41% vs. 3.03%; $Z = 7.91$, $P < 0.0001$), although they represented but 41% of the workforce. These data indicated the need for high vigilance for infection and consistency in safety precautions in these occupational groups and settings. This was particularly crucial for the armed security force and the fire department/emergency medical technician personnel (who often work in close quarters). These groups evidenced high levels of infection (cumulatively greater than 33% and 42%, respectively). Accordingly, in consultation with senior management, HSD designed and implemented innovative workplace physical space and schedule arrangements to mitigate transmission risk for these mission-critical personnel.

[3] The ORNL workforce does not differ from the Knox County (population 470,313; 2019; https://www.census.gov/quickfacts/knoxcountytennessee) in terms of percentage of self-declared white race (82.9% vs. 82.2%; $Z = 1.35$, ns, $P < 0.18$), but the percentage of African Americans is lower (3.6% vs. 8.72%; $Z = -13.42$, $P < 0.00001$) and the percentage of Asian race is higher (10.4% vs. 2.15%; $Z = 36.66$, $P < 0.00001$).

The need for traditional occupational health services, including mandated certification programs for specialized workers, did not disappear during the pandemic. A key safeguard to clinic operations made use of rapid and accurate case identification by RT-qPCR. The doors to the clinic were kept locked, employee/patients were seen by appointment only (except in emergency), and entrance to premises was only by negative result from RT-qPCR testing obtained within 24 h. This substantially reduced infection potential within the clinic. Of note, only one health care worker (6% of total infected health care workers) was judged to have been infected on the job, and this occurred prior to implementation of the negative test entrance criterion. This safeguard protected health care workers and communicated safety to employees coming to the clinic.

Detection of Reinfection

Large scale continuous surveillance of the workforce by RT-qPCR testing identified four cases of suspected re-infection (0.64%; as of January 20, 2021). Reinfected cases of COVID-19 are rare and there is debate on case definition and whether some cases represent reinfection or relapse of illness.[24–26] The four cases HSD identified had RT-qPCR-confirmed second infections after the earlier prior RT-qPCR-confirmed first infection. At initial infection, two cases were asymptomatic (male; 41 and 48 years), one pre-symptomatic (male; 62 years), and one was symptomatic (male; 54 years). All were symptomatic at second infection which occurred after the following lengths of time since first infection: 7, 5, 4, and 4 months, respectively. These cases were quickly isolated, preventing contagion from these persons who might not have been expected capable of transmitting COVID-19. Identification of reinfection remains a critical if low incidence benchmark supporting safety of the workforce.

Surveillance for SARS-CoV-2 Variants

Although most mutations with the coronavirus are not of clinical consequence,[27] there is increasing concern about variants with potential increased transmissibility and pathogenesis.[28–30] One example is the mutation termed Variant of Concern 202012/01 (or 20B/501Y.V1) conventionally referred to as the B.1.1.7 variant, which is associated with apparent increased infectiousness.[31]

RT-qPCR cycle threshold (Ct) values were examined in ways beyond customary determination of positive or negative test result for SARS-CoV-2 infection. Knowledge of Ct values can support general clinical decision-making (eg, viral load is sometimes associated with disease severity)[32] and can inform RTW timing.[33] This granular information from RT-qPCR testing is unavailable with antigen testing and also enabled HSD to surveil for SARS-CoV-2 variants. This was done by manual inspection of Ct values, examining results for a "drop off" of the S gene Ct value as a proxy indicator for the B.1.1.7 variant. This variant can be detected by the Applied Biosystems TaqPath COVID-19 Combo Kit used by HSD for SARS-CoV-2 because a mutation in the S gene affects the binding of the primers or probes in the assay. This results in the S gene being undetected while the other two targets are detected, still yielding a positive result, and not affecting test sensitivity.

With this screening technique, HSD identified a S gene drop off in a positive SARS-CoV-2 case in December 2020 (S gene = undetermined; N gene = 20.50 Ct; ORF1ab gene = 18.99 Ct). This sample was sequenced by the Yale Center for Epidemiology and Public Health. Genomic analysis determined it was not an example of the B.1.1.7 variant but another emerging variant of unknown significance (B.1.375) which also shows the S gene drop off. This finding from sequencing is important in that it should not be assumed that any sample with S gene drop off signature is the B.1.1.7. Figure 2 shows the RT-qPCR amplification plot of Ct values for the S gene, N gene, and the ORF1ab gene from the TaqPath

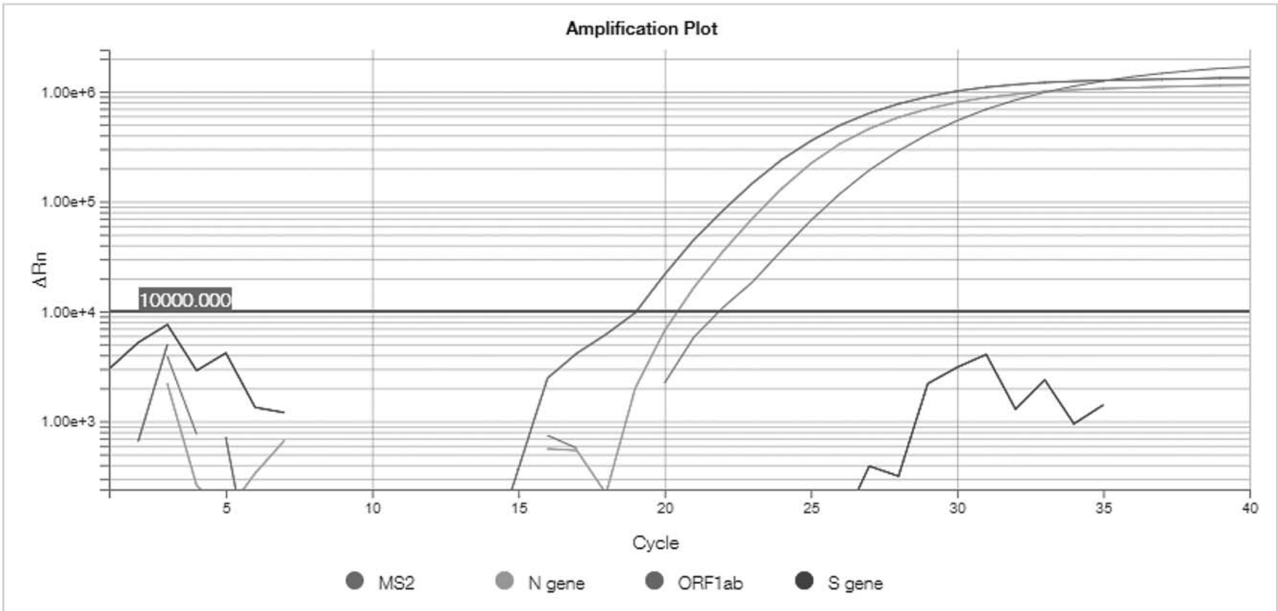

FIGURE 2. Amplification Plot of S gene Drop Off RT-qPCR Result. Note. A plot of fluorescence data produced by hydrolysis of probes bound to specific nucleic acid targets in an RT-qPCR assay shows exponential amplification of the bacteriophage MS2 extraction control as well as N and *ORF1ab* gene fragments in the sample. However, the S gene fragment is poorly amplified, and fluorescence values do not cross the threshold indicating a drop out. RT-qPCR, real-time quantitative reverse transcription polymerase chain reaction.

results for the identified S gene drop off case. Because the prevalence of the B.1.3.7.5 and B.1.1.7 variants at this time is low in the United States, using the S gene drop off as a proxy for B.1.1.7 leads to some false positives and confirmatory sequencing is required.

Space does not permit extended discussion of complexities of RT-qPCR testing for variants of concern, but the interested reader is referred to addendum text accompanying Supplemental Figure 1A (SF1A) and Supplemental Figure 1B (SF1B), http://links.lww.com/JOM/A891 which depict the S gene drop off and discusses further technical matters. Of note, gene typing was not available for specialized studies or tracking infection transmission patterns amongst employees. However, sequencer technology has been purchased and soon will be deployed in the clinic.

Surveillance for variants of concern is important because it enables occupational health services to offer timely, critical information to senior management. For example, should a variant of concern with virulent qualities be detected, appropriate workplace public health messaging can be recommended. This is a topic of great interest in the scientific community as well as the general public, including workers in the large workplace.

BENCHMARK TWO: ASSERTIVE CONTACT TRACING

The occurrence of a molecular test result positive for COVID-19 triggered a protocol for immediate case isolation and contact tracing for suspected workplace exposures. Contact tracing was led by an experienced occupational health physician with public health expertise supported by two lead BSN nurses and other nursing personnel. This team completed the Johns Hopkins online contact tracing course[4] and stayed abreast with evolving Centers for Disease Control (CDC) and World Health Organization (WHO) guidance on contact tracing, case definition, and isolation and quarantine recommendations.

Of the 598 contact traces in the reporting period, 80% of the index cases were determined to have exposed 2 or fewer workers, with a range of 0 to 23 exposures. The modal number of exposures was 0 (48%) and the mean cumulative number of workplace exposures recorded on a weekly basis was 18 (SD = 21; range 0 to 76). Importantly, only 2% of the index cases were associated with more than 10 exposures. Consistent with the medical literature, most exposures and their case transmissions occur with but a few individuals; thus, identifying and isolating these high-risk cases is extremely important.[13,15] Success in reducing infections depends both on rapid case identification and rapid contact tracing with isolation/quarantine. Modeling has shown that immediate contact tracing (no time delay) can reduce onward transmission of infection by 80%, and completion within with 3 days is associated with 41% reduction in transmission.[34] The mean time from sample collection to test result was 0.57 days and a positive result triggered immediate deployment of the contact tracing team. A contact trace event ended only when all potential exposed individuals had been evaluated. At times, multiple contact tracers worked well into the evening hours until completion. With rapid implementation of this protocol, HSD substantially suppressed workplace infection transmissions. Of note, contact tracing was limited to evaluating workplace exposures and risks. The scope of operations was limited as we are an occupational health clinic serving a single large employer. Exposed and ill employees were advised to curtail risk of exposure to family and community contacts, but intensive contact tracing was focused on the workplace. All identified COVID-19 cases were reported to the State public health department, as required (along with all RT-qPCR and serology tests administered).

Contact tracing also revealed clues to the likely routes of exposure for infections. Analysis of data showed 46% of infections were determined to be associated with exposure to ill family members or relatives, 19% from other community sources (eg,

[4] https://www.coursera.org/learn/covid-19-contact-tracing?edocomorp=covid-19-contact-tracing.

church, restaurants, etc.), and 14% from vetted occupational exposures. Of the community exposures, 80% appeared associated with attending church or religious activities, restaurant dining, viewing or participating in athletics (including fitness centers), and shopping. This type of granular detail on exposures was valuable for informing company management and educating the workplace community about high-risk activities. Multiple communication channels were used to disseminate workplace public health messaging on risky activities.

High quality contact tracing is time-sensitive and extremely labor-intensive.[35] A given contact trace from an index case required rapid telephone interviews, and at times with numerous individuals, to determine exposure risks. The number of interviews needed to complete contact tracings far exceed the number of index cases ($N = 598$). The contact tracing team estimated approximately 3000 telephone call interviews were required. Over time, the contact trace team evolved several process enhancements. These spanned improvement in standardization of interview questions, evaluation of interviewer consistency, coordination of processes with an in-house dedicated COVID-19 telephone call center, documentation forms, and integration with the medical record. These improvements were unique to local needs and processes but not dissimilar to those described by the Mayo Clinic.[36]

The critical importance of the contact tracing program was communicated regularly to company management. Evidence of program performance was conveyed by benchmark metrics on number and type of exposure routes, work-related exposures, isolation/quarantine counts, and variation in these and other rates over time. Of note, HSD recommended a liberal quarantine policy. A low threshold to quarantine a suspected exposure was implemented, and many hundreds of workers were quarantined. This incurred significant costs to the company, not all offset by support from the Corona Virus Aid, Relief, and Economic Security Act, 2020 (CARES Act).[37] Creative management actions, in consultation with HSD, included using a dedicated building wherein exposed and quarantined workers (confirmed by molecular testing as not infectious) could perform duties outside their job descriptions. This arrangement supported other Company missions (eg, copying records for digitalization) and were executed with strict engineering controls to prevent worker-to-worker transmissions.

BENCHMARK THREE: RTW PROCEDURES

Return to work decisions following isolation occasioned by confirmed SARS-CoV-2 infection with molecular testing were anchored by, but not restricted to, the CDC RTW criteria.[5] HSD applied job and case-specific factors along with published CDC guidance for these decisions. Individuals were also quarantined from work based on suspected exposures determined from contact tracing and self-reported exposures. Of note, the CDC changed RTW guidance over time, including recommending symptom-based criteria over test-based criteria. In our population over the 39-week reporting period, the mean and median RTW time latencies were 24 and 22 days (SD = 11; range 2 to 86 days). Tailoring RTW decisions to CDC guidance buttressed by individualized health and safety factors, along with serial RT-qPCR testing, is a conservative strategy. In our data, the Spearman rho correlation[6] between RTW latency and mean Ct value was significant ($\text{rho} = -0.14$; $P < 0.001$; $N = 476$). That is, longer RTW latency was weakly associated with lower Ct values (higher viral load and likely more severe illness), a finding consistent with other RTW and PCR Ct reports.[33] Because RTW latencies could have changed over time due to evolving guidance from the CDC and local priorities, the relationship between RTW time and Ct values was examined after statistically removing variance due to time. The partial correlation remained significant ($r = -0.13$; $P < 0.006$; $N = 473$) when the longitudinal factor was controlled.

Adopting a flexible RTW strategy based on published authoritative guidance with enhanced health and safety factors is a conservative stance. HSD argued this approach ultimately would protect workers and the critical scientific and national security operations of ORNL. Of note, several exposed and quarantined employees who were test-negative upon quarantine and remained symptom-free during the 14-day period were identified as infected by COVID-19 testing prior to RTW. Thus, further potential workplace transmission was avoided. This is a costly and labor-intensive approach, and less stringent (or more flexible) RTW parameters may be appropriate in different settings. Organizations can determine the RTW protocol most appropriate for their setting based on occupational health professionals' recommendations, referencing published guidance (eg, CDC) and scholarly literature, in combination with the nature and needs of the workplace.[38,39] Importantly, RTW protocols can be dynamic. They may be adjusted according to evidence-based infection benchmarks and changing employer needs—while recognizing that not all occupational categories require the same approach. For example, ORNL determined that if all exposed but not infected firefighter/emergency medical technicians were quarantined during a large local occupational outbreak, continuity of operations would be acutely jeopardized. Accordingly, innovative engineering controls (eg, physical spacing, assessment of building ventilation, and shift-schedule management to reduce contact and exposure risk), enhanced testing surveillance, and temporary housing in a segregated building permitted these professionals to remain on-site and available for emergency operations while protecting other workers.

BENCHMARK FOUR: CASE MANAGEMENT

All employees diagnosed with COVID-19 (598) were followed with nursing case management.[40,41] This involved telephonic outreach to the ill employee and/or family member early in the course of illness and weekly case management contact until medically cleared for RTW. Evidence shows nurse case management improves case outcomes.[42] Occupational health case management was important in ways beyond enhancing recovery from COVID-19 and fostering RTW. Active case management provided guidance and solace to the ill employee and family members while indirectly demonstrating employer concern. Moreover, case management provided important documentary functions. Illness variables were tracked over time, yielding information on the course and burden of disease on the workforce. This involved assessing type, severity, and duration of symptoms which included anosmia/dysgeusia, cough, dyspnea, congestion/rhinorrhea, sore throat, fever/chills, myalgia, fatigue, headache, and GI symptoms. Complications of COVID-19 such as pneumonia and hypoxia also were tracked. Summary statistics were available to update company management on the collective status of ill employees. This also was useful for business planning regarding anti-COVID-19 expenditures, projected costs relative to Workers Compensation insurance, impacts on short- and long-term disability policy costs, and life insurance payouts for deceased employee and retiree beneficiaries.

Most ill employees suffered mild cases of COVID-19 or were asymptomatic. COVID-19 case definitions (and treatment options) have evolved during the pandemic, but mild illness is generally characterized by the ability to recover at home and not having symptoms or complications progressing to pneumonia or other respiratory tract disease, significantly compromised blood oxygen saturation, or need for hospitalization.[43–45] Of the 598 employees

[5] https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/returning-to-work.html.

[6] Ct values reported as undetermined (exceeding threshold of positivity for SARS-CoV-2) were imputed with values of 41 for the purpose of the present analysis.

diagnosed with COVID-19, 97% had mild disease or asymptomatic presentation, 12 employees developed pneumonia, 11 required hospitalization, and one died.

BENCHMARK FIVE: ANTIBODY MONITORING

SARS-CoV-2 antibody testing for immunoglobulin G (IgG) was offered to previously infected employees beginning in August 2020. Immunoassays were performed with the Beckman-Coulter Access-2 SARS-CoV-2 IgG antibody test applied to serum samples. Many employees diagnosed with COVID-19 agreed to serial monitoring of IgG levels. In the reporting period, 92% of the employees showed reactive IgG test results (seropositive immune status) within 35 days. The median time to seroreversion (non-reactive IgG test result after seropositive status) was 124 days. Supplemental Figures 2A and 2B (SF2A and SF2B), http://links.lww.com/JOM/A892 depict the Kaplan-Meir survival curves for achieving serological immunity within 35 days (SF2A) and cumulative seroreversion outcomes (SF2B). Analyses revealed that symptomatic, presymptomatic, and asymptomatic employee groups demonstrated significantly different median days to loss of IgG seropositivity (149, 150, and 92 days, respectively; $P < 0.0001$ by log-rank and $P < 0.0002$ by Wilcoxon test on the K-M curve).

These results show most employees with RT-qPCR-confirmed COVID-19 developed anti-SARS-CoV-2 IgG antibodies, and for those whose IgG decayed to non-reactive levels, this generally occurred at approximately 4 months. These results are consistent with findings from many studies.[46–48] Of note, decay of anti-SARS-CoV-2 IgG antibodies does not necessarily imply loss of immune protection because other immune components such as neutralizing antibodies, SARS-CoV-2-specific $CD4^+$ and $CD8^+$ T cells, and spike-specific memory B cells may provide durable protection.[49–52]

With respect to general pandemic anxiety in the workforce and personal apprehensions held by COVID-19 recovered employees, feedback from antibody testing was reassuring to employees and, in turn, company management. Antibody benchmarks furthermore were evidence that the pool of employees susceptible to infection was reduced.

In December 2020, SARS-CoV-2 vaccines with Emergency Use Authorization (EUA) by the FDA (ie, Pfizer-BioNTech [BNT 162b] and Moderna [mRNA-1273] vaccines) became available to HSD front-line health workers. As a facet of internal quality metrics, HSD initiated antibody testing for immunoglobulin M (IgM) and IgG at serial intervals for HSD personnel beginning 14 days after initial vaccination. These health workers were confirmed COVID-19 naïve by prior regular RT-qPCR testing. All HSD staff received weekly RT-qPCR tests from nasopharyngeal swab. Early data revealed that by day 28, 100% of the Pfizer (with boost) and Moderna (pre-boost) vaccinated employees achieved IgG reactive status, but signal-to-cut off (S/CO) ratios showed a wide range. Of note, by 386 days (3 weeks after Pfizer-BioNTech boost; $n = 24$; 2 weeks post boost for Moderna; $n = 10$), the pooled geometric mean IgG (38.64 S/CO) was over nine times that of the pooled mean IgG level at first blood draw (week 2 after first vaccine; 4.07 S/CO; $n = 57$). Thus, health workers demonstrated evidence of strong immunity. The IgM S/CO ratios at 20 days from vaccination were 59% reactive for Pfizer and 50% reactive for Moderna recipients. It is known that IgM response is quick and can decline within a short number of days.[51]

Tracking antibody kinetics and persistence post-vaccination is ongoing. Information from these measurements provide reassurance to HSD staff, of whom approximately 20% have previously tested positive for COVID-19 (and also received vaccination, at least 30 days post-infection, with a resulting very strong antibody increase). Importantly, these data also provide reassuring evidence for workers who may be vaccine hesitant.

HSD completed procedures to be a vaccine provider for the State of Tennessee. Vaccine distribution at the federal and state level is a work in progress and ORNL is yet to receive a vaccine supply. Plans and procedures for distributing up to 500 doses per day in tandem with the Drive Through COVID-19 testing operation have been established and vetted by the State of Tennessee. HSD also will conduct stratified sampling of a portion of employees receiving vaccination on site for purposes of benchmarking IgG status. This quality metrics initiative will provide immediate reassurance to the employee and the company alike. Once herd immunity is achieved (by prior infection and vaccination), on-site workforce operations are expected to increase. Nonetheless, HSD will conduct random surveillance of the workforce by RT-qPCR testing on an ongoing basis to surveil for potential asymptomatic or mild infections as well as provide testing for symptomatic and exposure-related cases.

BENCHMARK SIX: COMMUNICATION WITH EMPLOYEES AND MANAGEMENT

The importance of fact-based, frequent communication in disaster and pandemic situations cannot be underestimated.[9] This applies to communication within the occupational health clinic, with employees, and with management. HSD held daily synchronization sessions for the professional staff wherein important events and logistic issues were communicated. With senior management, multiple lines of communication were developed and protected. These included placement of the medical director in the senior leadership team of ORNL, daily (if not more often) face-to-face updates to ORNL executives, and open ‘‘on call’’ lines of communication between key HSD COVID-19 response staff and management. Frequent interaction with the Communication Department of ORNL was cultivated and occurred. This fostered effective professional communication about the pandemic information (supported by data) to be delivered to the workforce via multiple channels such as web-based publication, electronic mail, special alerts, signage, and established managerial chains of command. Members of HSD provided numerous virtual ‘‘town hall’’ information and educational sessions to various occupational sectors of the company. The Call Center established to support the COVID-19 response team fielded over 6500 telephone calls during the reporting period—illustrating the timely communication response by HSD, as well as intense employee interest in information.

One avenue of communication with the workforce was a customer satisfactory survey. Data were collected from a sample of employees ($N = 80$) presenting at drive-through testing during the month of November 2020. Four questions were asked (Question 1: ‘‘ease of scheduling,’’ Question 2: ‘‘ease of drive-through procedures,’’ Question 3: ‘‘skill of the medical staff,’’ and Question 4: ‘‘timely notification of results,’’ along with space for free-form comments. Each query was rated on a five-point Likert scale (5 = very satisfied, 4 = satisfied, 3 = neutral, 2 = somewhat dissatisfied, 1 = very dissatisfied). Results showed that the COVID-19 testing program was viewed very positively. The mean ratings for the four queries were: 4.79, 4.61, 4.81, and 4.79, for an overall mean rating of 4.62 out of 5. Several open-ended comments were offered. Examples included comments such as ‘‘staff are very professional and friendly, they do a great job,’’ and ‘‘they are doing an excellent job, they are heroes.’’

DISCUSSION

Occupational health professionals can contribute to workplace pandemic response through implementing relevant EBM benchmarks of SARS-CoV-2 infection and working tirelessly to communicate results with non-jargon based explanations and pointing out implications to organizational management. Importantly, the contribution of the occupational health professional includes modeling the practice of evidenced-based analysis for managers. In these ways, the occupational health professional contributes beyond the traditional stable of health and safety interventions, much of which often take place behind a wall of medical privacy and is thus effectively invisible to the organization. The ORNL COVID-19 layered defense strategy, underpinned by occupational health services, is an example of this process of using exemplar quantitative benchmarks of SARS-CoV-2 infection. The information from these benchmarks provided evidence upon which clarity, reassurance, and guidance could be delivered to management decision makers.

This data-driven approach relied on benchmark results from molecular testing and surveillance, screening for SARS-CoV-2 variants of concern, assertive contract tracing, case management of employees with COVID-19, and antibody monitoring of recovered and vaccinated employees. There are limitations, however, in the particulars of our methods and the generalizations available from these results. Most importantly, not all workplaces have the resources to deploy costly procedures to collect extensive benchmark data. Nor do all workplaces require a fully comprehensive COVID-19 layered defense strategy, and a growing literature provides guidance on graduated workplace initiatives.[39] For example, antigen testing sometimes is recommended for screening for COVID-19. Antigen screening is amenable to rapid scaling and has been used to good effect in schools, higher education, athletic teams, and businesses. Nonetheless, our results from RT-qPCR technology show there is advantage beyond increased test accuracy,[53] such as in providing capability for screening for the B.1.1.7 variant of concern via the S gene drop off pattern in Ct results. Workplace and occupational health pandemic responses ultimately will be individualized to the setting, and pooled sample testing by RT-qPCR is another way to economize resources while utilizing accurate detection technology.

The ORNL COVID-19 layered defense strategy and its elements are not without limitation. The occupational health pandemic response evolved over time, adapting itself to contingencies and needs. The suite of benchmarks (and personnel, material, and analytic approaches) was assembled and fine-tuned during clinical operations. Benchmarks went "live" at different times, and the need to learn on the go during high-tempo operations was the rule. Thus, the pandemic response informed by these benchmarks should be viewed with the lens of field research rather than representing ideal, methodologically rigorous methods such as in highly standardized, hypothesis-driven, and controlled research designs. Of note, a significant proportion of the published and preprint server literature related to the pandemic similarly makes use of convenience samples and clinical (field research) or modeling data. The SARS-CoV-2 pandemic was and remains a dynamic problem the world is confronting. We suggest diverse approaches, methods, and sources of information are relevant to increasing collective understanding of the pandemic and response repertoires.

We note that the January 21, 2021 Presidential Executive Order on Protecting Worker Health and Safety[54] gives reason to expect that financing, resources, and interest in occupational health pandemic initiatives will increase. This also means that opportunity for best practices in occupational health pandemic response, rather than making do with less, may be nearing.

Yet increased support for pandemic response carries risk that fundamentals could be eclipsed by well-intended enthusiasm and rapidly expanding resources. These fundamentals begin with the EBM approach to occupational health services. To extract the gain from EBM, workplace management needs to be assertively educated on what occupational health services can contribute. Smart, flexible thinking such as was John Snow's public health intervention at the Broad Street water pump in London in 1854[55] is needed now as much as in 1854. Bold, innovative ideas anchored by evidenced-based benchmarks are needed. Effective, responsive occupational health interventions for the twin audiences of workers and management derive from bootstrapping empirical data collected in real time. Furthermore, a critical context shift may be occurring in pandemic response. The arrival of SARS-CoV-2 vaccines may signal the end of the beginning of the pandemic, but it is not the end of the pandemic. Vaccine optimism, vaccine hesitancy, emergence and spread of SARS-CoV-2 variants less susceptible to current vaccines, and enthusiastic but inadequately grounded responses by people, professionals, employers, and the collective voices of nations expecting pandemic relief all pose risks.[56–58] These risks we suggest also are opportunities for occupational health services to demonstrate relevance, value, and to save lives.

ACKNOWLEDGMENTS

This work represents the opinions of the authors and not of the US DOE, ORNL, or UT-Battelle, LLC, on work authored by UT-Battelle, LLC under Contract No. DE-AC05–00OR22725 with the US Department of Energy. The US Government retains and the publisher, by accepting the article for publication, acknowledges that the US Government retains a non-exclusive, paid-up, irrevocable, worldwide license to publish or reproduce the published form of this manuscript, or allow others to do so, for US Government purposes. The Department of Energy will provide public access to these results of federally sponsored research in accordance with the DOE Public Access Plan (http://energy.gov/downloads/doe-publicaccessplan).

REFERENCES

1. Harris JS, Weiss MS, Haas NS, et al. Methodology for ACOEM's Occupational Medicine Practice Guidelines—2017 Revision. *J Occup Environ Med*. 2017;59:913–919.
2. Sackett DL. Evidence-based medicine. *Semin Perinatol*. 1997;21:3–5.
3. Pfeffer J, Sutton RI. Evidence-based management. *Harv Bus Rev*. 2006; 84:62.
4. Tversky A, Kahneman D. Judgment under uncertainty: heuristics and biases. *Science*. 1974;185:1124–1131.
5. Lechanoine F, Gangi K. COVID-19: pandemic of cognitive biases impacting human behaviors and decision-making of public health policies. *Front Pub Health*. 2020;8. doi.org/10.3389/fpubh.2020.613290.
6. World Health Organization. Risk communication and community engagement readiness and response to coronavirus disease (COVID-19): interim guidance, March 19, 2020. World Health Organization; 2020. Available at: https://apps.who.int/iris/bitstream/handle/10665/331513/WHO-2019-nCoV-RCCE-2020.2-eng.pdf retrieved 09-22-2020. Retrieved September 21, 2020.
7. Liu BF, Fowler BM, Roberts HA, Herovic E. Keeping hospitals operating during disasters through crisis communication preparedness. *Pub Rel Rev*. 2018;44:585–597.
8. Van Bavel J, Baicker K, Boggio PS, et al. Using social and behavioral science to support COVID-19 pandemic response. *Nat Hum Behav*. 2020;4:460–471.
9. Iddins BO, Waugh MH, Buck B. How did occupational and employee health services provide strategic input to organizational emergency contingency planning during the COVID-19 pandemic? A case study. *J Occup Environ Med*. 2021;63:e153–e155.
10. Moses XE, Walters KM, Fisher GG. What factors are associated with occupational health office staffing, job stress, and job satisfaction? *J Occup Environ Med*. 2016;58:567–567.
11. Gidnedgil CA, Fischer SH, Broten N. A framework for evaluating approaches to symptom screening in the workplace during the COVID-19 pandemic. Rand Corporation; January 15, 2021. Available at: https://doi.org/10.7249/PEA653-1. Accessed January 15, 2021.
12. Gandhi M, Yokoe D, Havlir D. Asymptomatic transmission, the Achilles' heel of current strategies to control Covid-19. *N Engl J Med*. 2020;382: 2158–2160.
13. Frieden TR, Lee CT. Identifying and interrupting superspreading events—implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020;26:1059–1066.
14. Case_Rates_Final_10012020.xlsx (d39w7f4ix9f5s9.cloudfront.net). Available at: https://d39w7f4ix9f5s9.cloudfront.net/87/16/c15991584983a89231fb7664e2fa/rates.pdf. Retrieved January 24, 2021.
15. Hellewell J, Abbott S, Gimma A, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *Lancet Glob Health*. 2020; 8:e488–e496.

16. 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;180:1576–1586.
17. Bajema KL, Wiegand RE, Cuffe K, et al. Estimated SARS-CoV-2 seroprevalence in the US as of September 2020. *JAMA Intern Med*. 2020:e207976. doi: 10.1001/jamainternmed.2020.7976.
18. Wu SL, Mertens AN, Crider YS, et al. Substantial underestimation of SARS-CoV-2 infection in the United States. *Nat Commun*. 2020;11:1–10.
19. Shioda K, Lau MS, Kraay AN, et al. Estimating the cumulative incidence of SARS-CoV-2 infection and the infection fatality ratio in light of waning antibodies. *medRxiv [Preprint]*. 2020. doi: 10.1101/2020.11.13.20231266.
20. Woolf SH, Chapman DA, Lee JH. COVID-19 as the leading cause of death in the United States. *JAMA*. 2021;325:123–124.
21. Katz E. These federal agencies have seen the most COVID-19 deaths. Government Executive. May 21, 2020. Available at: https://www.govexec.com/workforce/2020/05/these-federal-agencies-have-seen-most-covid-19-deaths/165578/. Accessed March 17, 2021.
22. Oda G, Sharma A, Lucero-Obusan C, Schirmer P, Sohoni P, Holodniy M. COVID-19 infections among healthcare personnel in the United States Veterans Health Administration. *J Occup Environ Med.* 2020. Epub ahead of print.
23. Mehraeen E, Karimi A, Barzegary A, et al. Predictors of mortality in patients with COVID-19—a systematic review. *Eur J Integr Med*. 2020;40. doi: 10.1016/j.eujim.2020.101226.
24. Lumley SF, O'Donnell D, Stoesser NE, et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. *N Engl J Med*. 2021; 384:533–540.
25. Gousseff M, Penot P, Gallay L, et al. Clinical recurrences of COVID-19 symptoms after recovery: viral relapse, reinfection or inflammatory rebound? *J Infect*. 2020;81:816–846.
26. Yahav D, Yelin D, Eckerle I, et al. Definitions for coronavirus disease 2019 reinfection, relapse and PCR re-positivity. *Clin Microbiol Infect*. 2021;27:315–318.
27. van Dorp L, Richard D, Tan CCS, Shaw LP, Acman M, Balloux F. No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2. *Nat Commun*. 2020;11:5986.
28. Weisblum Y, Schmidt F, Zhang F, et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. *eLife*. 2020;9:e61312.
29. Plante JA, Liu Y, Liu J, et al. Spike mutation D614G alters SARS-CoV-2 fitness. *Nature*. 2020;1–6.
30. Mahase E. Covid-19: What new variants are emerging and how are they being investigated? *BMJ*. 2021;372:n158.
31. Galloway SE. Emergence of SARS-CoV-2 B. 1.1. 7 Lineage—United States, December 29, 2020–January 12, 2021. MMWR. *Morbidity and Mortality Weekly Report* 70.
32. Pujadas E, Chaudhry F, McBride R, et al. SARS-CoV-2 viral load predicts COVID-19 mortality. *Lancet Respir Med*. 2020;8:e70.
33. Domeracki S, Clapp RN, Taylor K, Lu CM, Lampiris H, Blanc PD. Cycle threshold to test positivity in COVID-19 for return-to-work clearance in health care workers. *J Occup Environ Med*. 2020;62:889–891.
34. European Centre for Disease Prevention and Control. Risk related to spread of new SARS-CoV-2 variants of concern in the EU/EEA – December 29, 2020. ECDC: Stockholm; 2020. Available at: https://www.sanitainformazione.it/wp-content/uploads/2020/12/valutazione-del-rischio.pdf. Accessed March 17, 2021.
35. Kretzschmar ME, Rozhnova G, Bootsma MC, van Boven M, van de Wijgert JH, Bonten MJ. Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study. *Lancet Pub Health*. 2020;5:e452–e459.
36. Breeher L, Boon A, Hainy C, Murad MH, Wittich C, Swift M. A framework for sustainable contact tracing and exposure investigation for large health systems. *Mayo Clin Proc*. 2020;95:1432–1444.
37. Coronavirus Aid, Relief, and Economic Security Act, S. 3548, 116th Cong., 2d Sess. (2020) (enacted). Available at: https://www.congress.gov/bill/116th-congress/senate-bill/3548/text. Accessed March 17, 2021.
38. Shaw WS, Main CJ, Findley PA, Collie A, Kristman VL, Gross DP. Opening the workplace after COVID-19: what lessons can be learned from return-to-work research? *J Occup Rehabil*. 2020;30:299–302.
39. Barnes M, Sax PE. Challenges of "return to work" in an ongoing pandemic. *N Engl J Med*. 2020;383:779–786.
40. Tahan HM. Essential case management practices amidst the novel coronavirus disease 2019 (COVID-19) crisis: Part 1: tele-case management, surge capacity, discharge planning, and transitions of care. *Prof Case Manag*. 2020;25:248–266.
41. Tahan HM. Essential case management practices amidst the novel coronavirus disease 2019 (COVID-19) crisis: Part 2: end-of-life care, workers' compensation case management, legal and ethical obligations, remote practice, and resilience. *Prof Case Manag*. 2020;25:267–284.
42. Sutherland D, Hayter M. Structured review: evaluating the effectiveness of nurse case managers in improving health outcomes in three major chronic diseases. *J Clin Nurs*. 2009;18:2978–2992.
43. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 case surveillance—United States, January 22–May 30, 2020. Morbidity and Mortality Weekly Report; 2020. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6924e2-H.pdf. Accessed March 17, 2021.
44. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. *N Engl J Med*. 2020;383:1757–1766.
45. National Institute of Health. Overview of COVID-19 Treatment Guidelines. Available at: https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section_43.pdf. Accessed March 17, 2021.
46. Staines HM, Kirwan DE, Clark DJ, et al. IgG Seroconversion and pathophysiology in severe acute respiratory syndrome coronavirus 2 infection. *Emerg Infect Dis*. 2021;27:85–91.
47. Marklund E, Leach S, Axelsson H, et al. Serum-IgG responses to SARS-CoV-2 after mild and severe COVID-19 infection and analysis of IgG non-responders. *PLoS One*. 2020;15:e0241104.
48. Self WH, Tenforde MW, Stubblefield WB et al. Decline in SARS-CoV-2 antibodies after mild infection among frontline health care personnel in a multistate hospital network-12 states, April–August 2020. Morbidity and Mortality Weekly Report, 69, 2020.
49. Rodda LB, Netland J, Shehata L, et al. Functional SARS-CoV-2-specific immune memory persists after mild COVID-19. *Cell*. 2020;184:169–183.
50. Smith DW, Sette A, Crotty S. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Infection* 1:31.
51. Isho B, Abe KT, Zuo M, et al. Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients. *Sci Immunol*. 2020;5. doi: 10.1126/sciimmunol.abe5511.
52. Peng Y, Mentzer AJ, Liu G, et al. Broad and strong memory CD4+ and CD8+ T cells induced by SARS-CoV-2 in UK convalescent individuals following COVID-19. *Nat Immunol*. 2020;21:1336–1345.
53. Pray IW. Performance of an antigen-based test for asymptomatic and symptomatic SARS-CoV-2 testing at two university campuses—Wisconsin, September–October 2020. Morbidity and Mortality Weekly Report, 69, 2021.
54. Executive Order on Protecting Worker Health and Safety | The White House. Available at: https://www.whitehouse.gov/briefing-room/presidential-actions/2021/01/21/executive-order-protecting-worker-health-and-safety/. Accessed January 29, 2021.
55. Cameron D, Jones IG, John S. The Broad Street pump and modern epidemiology. *Int J Epidemiol*. 1983;12:393–396.
56. Kreps S, Prasad S, Brownstein JS, et al. Factors associated with US adults' likelihood of accepting COVID-19 vaccination. *JAMA Netw Open*. 2020;3. e2025594.
57. Harrison EA, Wu JW. Vaccine confidence in the time of COVID-19. *Eur J Epidemiol*. 2020;35:325–330.
58. Bottemanne H, Morlaàs O, Fossati P, Schmidt L. Does the coronavirus epidemic take advantage of human optimism bias? *Front Psychol*. 2020; 11:2001.