TO:
FROM: Delaware Initiative for Science and Ethics (DISE)
DATE:
RE: Asymptomatic PCR testing for SARS-CoV-2

Delaware Initiative for Science and Ethics (DISE) is a group of concerned medical doctors, chiropractors, paramedics, nurses, pharmacists, radiologists, physical therapists and other allied health professionals who interact directly with Delawareans. In conjunction with a group of dedicated researchers, we came together over mutual concerns related to healthcare policies and the desire to do more for our patients and community surrounding COVID-19.

One of the concerns of DISE and the reason for this letter is the continued polymerase chain reaction (PCR) testing for SARS-CoV-2 in asymptomatic patients at Bayhealth. Our understanding is that PCR testing is used for pre-procedure (surgery) testing or those awaiting transfer to certain skilled nursing/long term care facilities, as well as asymptomatic employees who have received either religious and/or medical exemptions from COVID-19 vaccination. We are writing to explain how PCR testing in asymptomatic populations is unnecessary, invalid, and not based on scientific evidence.

Molecular testing includes the use of nucleic acid amplification tests (NAAT) in which genetic material such as RNA is detected. PCR is a type of diagnostic test that uses the technique of NAAT. According to the Infectious Disease Society of American (IDSA) Guidelines for COVID-19 Diagnostics, molecular testing for SARS-CoV-2 has a variable sensitivity of 75-95%. Hence, there are likely to be false-negative test results, and repeat testing may be warranted. Alternatively, false-positive results would lead to unnecessary isolation, personal protective equipment (PPE) use and potentially cohorting with other positive patients.[1] Yet, PCR testing is relied on as a sole diagnostic test for confirmation for SARS-CoV-2 when there are great implications to both false-positive and false-negative results, knowing that both positive predictive value (PPV) and negative predictive value (NPV) are affected by the disease prevalence.

Additionally, per the IDSA guideline cited above, the IDSA panel suggests SARS-CoV-2 molecular testing in asymptomatic individuals (without known exposure to COVID-19) who are undergoing major time-sensitive surgeries. This is labeled as a conditional recommendation with very low certainty of evidence. The guideline goes on further to summarize the evidence for this recommendation by stating “The panel did not identify any studies that directly assessed a strategy of testing for SARS-CoV-2 versus no testing of asymptomatic individuals before undergoing major surgery.” Additionally, the panel “did not identify test accuracy studies directly assessing the performance of SARS-CoV-2 NAAT in asymptomatic individuals. However, based on existing evidence supporting that asymptomatic or pre-symptomatic patients **MAY** have similar viral loads and shedding as those who are symptomatic, the panel agreed that the test accuracy data from symptomatic patients should be applied to asymptomatic populations before surgery.”

Given the lack of any existing evidence that the practice of testing asymptomatic individuals for SARS-CoV-2 pre-surgery has a benefit or has been validated, and also considering that the conclusion of the panel is being based off of *possible* evidence, it becomes apparent that the process of testing asymptomatic individuals, has no scientific evidence. The IDSA guideline is exactly that, a *guideline*. Bayhealth needs to more closely examine the evidence, or lack thereof, before instituting their recommendations. Furthermore, this same lack of evidence in testing asymptomatic patients pre-surgery can also be applied to the testing of asymptomatic employees for which the IDSA guideline provides no recommendation for this population.

A similar parallel argument can be made while examining the process of testing for *Clostridioides difficile* infection (CDI), where it is not recommended to test asymptomatic patients or those who do not meet clinical criteria for a CDI. Not all patients who test positive for toxigenic *C. diff* however, have CDI. Hence, with the high sensitivity of the test, the challenge presents to determine which patients are carriers of toxigenic *C. diff* versus which patients have an active CDI. Also, the positive predictive value of NAATs for CDI is low to moderate depending upon disease prevalence and the limit of detection of the assay used. [2] Using a NAAT as a stand-alone test and relying on clinical symptoms to discern patients with CDI from asymptomatic carriers is not an optimal approach.[3] As supported by evidence from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), many hospitals who have adopted a NAAT test such as PCR for toxigenic *C. diff*, have also implemented pre-agreed institutional clinical criteria for stool testing to help reduce inappropriate testing, detection, and treatment of toxigenic *C. diff* in patients who don't truly have a CDI.[4]

Despite the use of the pre-agreed institutional clinical criteria with the stand-alone PCR *C. diff* test, there exist great implications to misdiagnosis as patients continue to be inappropriately diagnosed and treated for CDI leading to antibiotic resistance and increased costs. Institutions around the country have begun adopting a two-step diagnostic testing approach to curtail the overdiagnosis and overtreatment including both the PCR as well as a toxin test. It is unreasonable to continue to base a clinical diagnosis of CDI from a molecular test alone, when a patient could be toxin negative and hence would be considered negative overall for a diagnosis of CDI. If the PCR test is positive and toxin test negative, a patient has a low probability of changing from a carrier of toxigenic *C. diff* to a subclinical or full clinical infection and thus would not require treatment at that time.

Many parallels can be made between SARS-CoV-2 and toxigenic *C. diff* detection using PCR testing, where asymptomatic testing is not recommended and can have serious implications including overtreatment, overdiagnosis, overuse of PPE and antibiotic resistance. In conclusion, we strongly urge you to acknowledge this current lack of any evidence in testing for SARS-CoV-2 in asymptomatic surgical patients, patients awaiting transfer, as well as asymptomatic healthcare employees and to consider a practice change that is based on scientific evidence.

Thank you for your time and consideration of this letter.

Sincerely,

DISE

References:

1. IDSA Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing. https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/
2. McDonald LC, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018 Mar 19;66(7):e1-e48. doi: 10.1093/cid/cix1085. PMID: 29462280; PMCID: PMC6018983.
3. Planche T.D. et al. Differences in outcome according to *Clostridium difficile* testing method: a prospective multicentre diagnostic validation study of *C. difficile* infection. *Lancet Infect Dis.* 2013; 13: 936-945.
4. Crobach, M.J.T. et al. European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection. Volume 22, supplement 4, s63-s81, August 01, 2016.