Title

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In Reply: Navigating personal risk in rhinologic surgery during the COVID-19 pandemic

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Running Title: Personal Surgical Risk During COVID-19

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We read with great appreciation Dr. Bleier's and Dr. Welch's letter, in which they highlighted population-specific factors amongst rhinologic patients that may elevate the false negative rate (FNR) of SARS-CoV-2 viral RT-PCR testing, complicating reliance on a pre-procedural negative test result in risk assessment and decisions regarding personal protective equipment (PPE) utilization. [1] We agree with their note of caution and the importance of carefully considering those factors, FNR among them, that combine to produce the overall risk of viral transmission to healthcare workers and other patients. Consequently, the estimation of this overall risk, whether achieved through formal calculation or informal estimation, will benefit from attention to the relative contribution of

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additional factors and the added complexity of their interactions within a more comprehensive risk framework.

As the authors detail with respect to FNR and allude to regarding negative predictive value (NPV), a novel pandemic poses specific challenges in assessing risk, as the data about the virus and its regional prevalence evolves. The interpretation of a negative test result, for example, is more directly related to the NPV than the FNR, because the NPV takes into account disease prevalence, which can change by several orders of magnitude within a given time period or region. For example, a surgeon performing an elective sinus surgery in a patient with a negative RT-PCR test in San Diego County on June 15, with active cases at 81 per 100,000, would be at a much lower risk of exposure, all other things being equal, then one performing the same surgery on a patient from neighboring Imperial County where new cases were concurrently 1494 per 100,000.[2] Within a hypothetical locale with a caseload approaching 0 per 100,000, the NPV approaches zero as well, regardless of the FNR.

The analysis is further complicated when considering information other than the patient test results and the prevalence. If a patient is known to be asymptomatic, the probability of a patient still having the virus is not simply the test NPV, but rather a posterior probability conditioned upon both symptoms and test results, the calculation of which would require an application of Bayes' theorem. Adopting a simplified, informal notation, where we disregard the change of prevalence over time and location, and define the variables *D* for the disease state of a patient, *R* for the test result, and *S* for patient symptoms, the posterior probability is represented as

$$P(D \mid R, S) = \frac{P(R, S \mid D)}{\sum_{i \in \{\mathrm{T},\ \mathrm{F}\}} P(R, S \mid D = i) P(D = i)} P(D) \quad (1)$$

The *P(D)* in equation (1) is the prior probability of disease, namely the population prevalence, can vary by location, time, and patient demographics. Further exploration of the remaining terms in equation (1) is beyond the scope of this letter, but it illustrates some of the difficulty in integrating competing information without a formalized structure. For example, while acquiring samples during an asymptomatic period may increase the test FNR, as Drs. Bleier and Welch point out, treating only asymptomatic patients produces an opposing influence on the posterior probability, and judging exactly how these influences are likely to interact in the absence of a formal approach may produce misleading results (see, the *Monty Hall problem* for a classic example of this pitfall).[3]

In addition to evaluating the risk factors thoroughly, it may also be worth considering ways in which one could increase the sensitivity of RT-PCR testing in our patient population, thus directly working to mitigate the FNR. Oropharyngeal (OP) swabs could be considered as a complement to nasopharyngeal (NP) swabs for RT-PCR testing (sensitivity in days 0-7 of infection in mild disease: OP 61.3% 46/75 vs NP 72.1% 147/204)[4] and may increase sensitivity in this patient population, particularly when coupled with nasal cavity/nasopharyngeal swabs, as previously demonstrated in the diagnosis of influenza.[5]

Our profession has navigated provider exposure risks before, including from viruses such as hepatitis C and HIV, through the use of pre-operative testing, wearing additional gloves, needle handling techniques, and post-exposure prophylaxis. Dr. Bleier's research and innovations in source control

are a valuable step in mitigating the risk of transmission of COVID-19, along with appropriate use of PPE.[6,7] We agree with their conservative approach to minimize the risk of transmission during sinonasal procedures, but also hope to highlight the importance of considering other strongly influential variables, such as the prevalence of the disease, and how such variables interact to influence the posterior probability of a given patient having SARS-CoV-2, and the implications that this integrated risk assessment has on policy decisions.

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