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We have concerns about the study by Loeb et al. 2022 “Medical Masks Versus N95 Respirators for Preventing COVID-19 Among Health Care Workers – A randomized trial”¹ – from an interdisciplinary standpoint including, occupational hygiene, occupational medicine, bioengineering, ethical, medical science, and clinical perspectives. Therefore, in line with other comments objecting to this study¹, we request that the journal rescind this study.

Our concerns include:

- a) Ethical issues, including violation of equipoise
- b) Lack of interdisciplinary involvement, in particular - occupational hygiene expertise
- c) Study design
- d) Results
- e) The dangers of misinterpreting the results of this study

Ethical issues

A [letter](#)² to the Canadian Government, Responsible Conduct of Research, Tri-council Federal Office from occupational health and safety professionals from around the world, noted:

“Our fundamental concern about the ethics of this study is that it exposes healthcare workers to COVID-19 infection by allowing them to wear surgical masks when engaged in patient care versus the respirators to which they would otherwise be entitled (19 April 2021)”.

We believe that the study violated the principle of equipoise, which requires that a subject be enrolled in a trial only if there is true uncertainty about which of the trial arms is likely to benefit the participants³. In this case, there was, at the time of the study, sufficient evidence, amplified since that time,⁴⁻¹⁶ to demonstrate that N95 respirators are superior to surgical masks for protection from inhalable aerosol transmissible diseases, including coronavirus 2 causing severe acute respiratory syndrome (SARS - 2).

Equipoise in our opinion, should be assessed by means of a thorough literature review, along with input from different disciplines, including occupational hygienists and occupational physicians who have expertise in aerosol science.

Interdisciplinary input is key to determining whether there is in fact equipoise¹⁷ along with proper study design along with interpretation of results.

Failure to demonstrate a 100% excess in risk is a limitation and is not surprising if the outcome were rare and the population were at high risk already, such as the elderly or where co morbidity was more frequent such as a potentially fatal cancer. However, COVID-19 is common, occurs with community transmission, as well as occupational, and is being studied in a health-conscious profession. Therefore, allowing a 100% excess risk, before declaring the intervention as being inadequate, means tolerating a 200% risk ratio for the attack rate of a disease.

For a disease with chronic consequences, in a population functioning at times, at limits of endurance, interacting with patients, and performing a critical function for the community – allowing a risk ratio up to 200% is unacceptable.

In addition, had there been an interdisciplinary approach, it is likely, that the study design would have “more precisely” accounted for and analysed all risk factors including community and staff to staff transmission.

Lack of an interdisciplinary approach, including absence of occupational hygiene expertise

The implementation of effective personal protection for workers requires the involvement of a range of experts. Although doctors and nurses are the experts in ill patient care, protection of workers from physical, chemical, and biological hazards falls within the domain of occupational/industrial hygiene, a profession that has a certification scheme ¹⁸. In studies like this one, it is important that there be input from different disciplines, such as respiratory protection specialists, into the study design, implementation, and interpretation.

Occupational hygienists are skilled and certified professionals in the field of personal protective equipment (PPE). Certified / registered occupational hygienists are very familiar with the Canadian national standard on respiratory protection, CAN/CSA-Z94.4-18 ¹⁹, which covers the selection, use, and care of respirators. Unfortunately, these standards were not referenced in this study, nor were any occupational hygienists included in the study design or as co-authors. We feel that the absence of the occupational hygiene perspective from this study contributed to flaws in the design, implementation, and analysis of the results. The inclusion of at least one professional from the occupational health and safety sector would have ensured compliance with the CSA standard ¹⁹ including minimum requirements for using N95 respirators.

Study Design

The study in question started out as a “[randomized controlled trial](#) (RCT)” from the original study design, but later morphed into a “randomized trial” ¹.

We concur with the comment by Brosseau, L ²⁰,

“Without a control (no mask), it is impossible to conclude that surgical masks or respirators were effective”.

Furthermore, we are of the view that basing the study design on a randomized trial, with or without a control group, in this type of study is not only ineffective, it is unethical, because it could potentially put health care workers at risk.

Although the medical field insists that the only way to demonstrate clinical effectiveness is through RCTs, that is simply not how the rest of the world works. We don't use RCTs to determine if one bridge design vs. another works - that would be unethical!

Many medical devices are not tested with RCTs before they are deployed in medical settings. Respirators are medical devices from the perspective of the US Food and Drug Administration (FDA), which readily admits on its website that respirators and surgical masks are different, and that the former

protects the wearer from inhalation hazards and the latter does not. In addition, a proper face fit test is required for a respirator, whereas for surgical mask there is no requirement ²².

This randomized trial seeks to determine the efficacy of surgical masks as personal protective equipment (PPE), compared to filtering face piece respirators (or N95s), for protection against inhalable particulate matter (airborne particles $\leq 100\mu\text{m}$) ²¹. among healthcare workers across 29 health care facilities in four countries.

A more thorough literature search would clearly have revealed that sporadic wearing does not provide sufficient protection for workers. Jansenn et al. (2013) ²³ reports the impact on effective protection being greatly reduced for non-wear time > 10%.

In addition, lessons from China, after the start of the pandemic, would have revealed that nurses were better protected, with lower rates of infection, by means of the proper use of personal protective equipment (PPE) including as a minimum use of an N95 ²⁴⁻²⁵.

Randomised trials that compare filtering face piece respirators (FFRs) (N95s) to surgical masks are doomed to fail when minimal protocol requirements for the use of FFRs are not respected or even considered. A randomized clinical trial would have a limited scientific value if the administering protocol for one of the drugs were administered incorrectly to demonstrate its ineffectiveness. As we noted above, there is no evidence that the standard for respirator use, CSA Z94.4 ¹⁹, was observed for the N95 arm. One might think that to assess the performance of a treatment it would be essential to comply with all of the elements of the standard protocols under study, which is not the case in the Loeb et al study.

Although N95s are disposable PPE, workers were forced to accept extended wear or re-use when required because of shortage. The authors stated, "Participants were asked to discard the medical masks or N95 respirator if it became soiled or damaged or if breathing through the device became difficult. If the institutional policy was for extended use, and masks were not typically removed after a patient encounter, the extended use period was to be followed". This may have resulted in some confusion among participants.

In addition, as previously noted, the key to the effectiveness of respirators is an effective seal (or proper face fit). Using an unadjusted (poorly fitted respirator) is like using gloves with holes and hoping to be protected. Even though the study states that the N95's were fit-tested, the fit-testing methodology used wasn't provided nor described.

Further confounding this study are the facts that in the Canadian cohort, those in the surgical mask arm had the choice of using N95's based on a point of care risk assessment, while those in the N95 arm did not always wear them at work when they may have been exposed to infectious aerosols. Therefore, participants in both arms used N95's some of the time and did not use them at other times while at work, blurring the comparison between the groups. In addition, the study did not account for possible exposures outside of work when participants were unmasked.

The effectiveness of other exposure controls was not assessed across different workplaces (filters on general ventilation, non-recirculated systems, etc.) The ventilation for the Egypt and Pakistan HCW was noted as "minimum total air exchanges per hour - varies between units". According to CSA Z94.4 ¹⁹, where ventilation is suboptimal (≤ 4 air changes per hour) and where the risk of transmission is higher – then

powered air-purifying respirators (PAPR) are required. As noted, no reference to CSA Z94.4¹⁹ was provided, nor was discussion that alluded to more efficacious respiratory protection in situations where there is sub-optimal ventilation.

When considering compliance of healthcare workers to the proper use of personal protective equipment, including respiratory protection in Egypt, non-compliant HCWs represented 53.2% of participants for use of PPE generally²⁶. Further, Loeb et al acknowledge that Egyptian subjects were over 80% seropositive at the beginning of the study, inferring that most had acquired natural immunity from previous infections, making it illogical to lump outcome data together with Canadian subjects who had no such immunity.

To perform a real control, trial authors should have made sure to maintain optimal use conditions for both treatments, as well as excluding subjects with differing immune statuses at the start of observation period. This study revealed deficiencies in respiratory protection programs, knowledge, and competency, rather than non-inferiority of the medical masks when compared to deficient utilisation of N95 FFRs.

The design only addresses transmission from patients. Transmission between health care workers (e.g., in office or lunchroom settings) and “community spread” (the latter which varied substantially between sites and over time) is not considered. In addition, there was no attempt, as part of the study design, to carry out stratified analysis to look at how the “N95 effect” differs based on community rates. When community rates are high, and community transmission is more likely, we would expect the impact of N95s to decrease in their design, because people transmission is occurring in a myriad of situations, not primarily care for COVID positive patients.

Factoring in community and staff to staff transmission is important. This was demonstrated in one study of Ontario health care workers²⁷, where overall, 31% of COVID-19 cases were deemed occupationally acquired. Incidence of HCW infections closely followed community incidence where 45% of infections resulted from staff-to-staff contact.

Results

The authors summarized the overall and country findings in Figure 2., expressed as a Hazard Ratio with 95% CI. For Canada, the HR was 2.83, almost a tripling of risk with extremely wide CI (0.75-10.72). For Israel and Pakistan, the HR represented approximately a 50% excess in risk, both with relatively wide CI. For Pakistan the HR was 1.50, a 50% excess in risk with an extremely wide CI (0.25-8.98). For Egypt, the HR was approximately unity (0.95, CI (0.60-1.50)).

Despite high excess of HR with wide CI in Canada, Israel, and Pakistan, the authors use the average for all sites (HR of 1.14, CI (0.77-1.69)) to conclude that the effect of surgical masks and N95 filtering face-piece respirators achieve non-inferiority (relative parity) in protecting nurses. Based on the authors' own results we come to a contrary conclusion. Averaging the data to an HR of 1.14 with a relatively narrow CI compounds the flaws in the study design. The excesses observed in Canada, Israel, and Pakistan should have driven the authors to concede the probability that surgical masks are inferior to N95 in protecting nurses exposed to SARS-CoV-2 confirmed positive patients.

The real finding of this study is that surgical masks and respirators were both ineffective - but for different reasons. Surgical masks were not effective at preventing disease transmission because they are not designed for personal protection. Respirators were not effective at preventing transmission because they were not worn during all possible exposures and may have not been used correctly. Even with

these deficiencies, however, the study results show that FFRs were in fact, more effective than surgical masks – they just did not meet the study’s aim of demonstrating that they were twice as effective.

Dangers of Misinterpreting Results

The errors, conclusions, and subsequent misinterpretation of the findings from this study put the health and safety of workers worldwide at risk. If the findings from this study are misinterpreted to communicate that there is “no difference”, how would the findings translate to the control expectations for other inhalable ²². aerosol transmissible diseases ²⁸?

We agree with CIDRAP ²⁹. that misinterpretation of results from this study has real world implications for the health and safety of Health Care Workers. Misrepresentation and communication of these findings pose a serious risk to HCW globally, including their families and communities.

Finally, on March 23, 2021, Justice Philippe Bouvier has noted the significant risk of airborne transmission in a court decision. Quebec’s court decision ensures that all health-care professionals are provided an N95 respirator immediately when a resident or patient is suspected to be infected with COVID-19. “Justice Philippe Bouvier recognized that one of the modes of transmission of COVID-19 is via aerosols and that medical masks are not a sufficient protection for health care workers in hot or warm zones” ³⁰.

In view of the deficiencies in this study and the dangers of misinterpretation, with resulting grave consequences for worker protection, we request that the Journal rescind this study.

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