HiREB
Hamilton Integrated Research Ethics Board

May 10,2021

Kimberly Mason
Academic Integrity Officer
Office of Academic Integrity

Dear Dr Mason,

We are writing in in response to the concerns raised by the group of "Canadian and International Scientists and Medical Professionals" and signed by Dr Kevin Hedges, CIH, COH, Workplace Health Without Borders (International). In that letter, Dr Hedges raises concerns about the research study headed by Dr Mark Loeb, "Medical Masks versus N95 Respirators to Prevent 2019 Novel Coronavirus Disease (COVID-19) in Healthcare Workers: A Randomized Trial". We are writing as the co-chairs of the Hamilton Integrated Research Ethics Board. This is the board that provided ethical approval for this research study to take place at multiple clinical settings in Ontario under the collective agreement encompassed within Clinical Trials Ontario.

This group expressed concerns that this study "unnecessarily puts the safety of front-line healthcare workers at significant risk of contracting COVID-19". Their fundamental concern is with the ethics of the study, in 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". They feel that "In light of what we know now in the context of the urgent need for "airborne precautions" and in line with the TCPS article 11.6 and perhaps other articles that may be relevant, we feel compelled to bring this to your attention." Article 11.6 is included here:

Article 11.6

Researchers shall provide the REB with an acceptable plan for monitoring safety, efficacy/effectiveness (where feasible) and validity. This plan shall describe:

a. how participant safety will be monitored and what actions will be taken in the event of a threat to participant safety;
b. how intervention efficacy will be monitored (where feasible) and what actions will be taken if efficacy is found to be greater than expected;
c. the criteria by which participants may be removed from a study for safety reasons;
d. the study-wide stopping rules (if any) by which studies may be stopped or amended due to evidence of inferior safety, superior efficacy or futility; and
e. the reporting procedure that will be followed to ensure any information relevant to participant welfare or consent is reported clearly and in a timely fashion to the REB.

A data and safety monitoring plan may (but need not) include the establishment of an independent DSMB (Article 11.7).

To address these concerns, we are confirming that:

1. Article 11.6 and indeed all articles within the TCPS2 were considered when reviewing and approving this study. This is the case with all HiREB approved research studies

2. There is no new evidence that has been provided since the approval of this research project that would change HiREB's stance on the safety or ethical nature of this research. Of particular relevance here is that the state of equipoise between the two arms of the study still exists.
3. In light of the above, HiREB continues to stand behind and support our original decision of approving this study.

Importantly, we would like to commend this group of concerned individuals. The question of the ethics associated with this study has been questioned previously by the union representing local nurses (CUPE) and by the Ontario Nursing Association. Concerns were also raised and presented to HiREB by Dr Hedges and the group for which he is the spokesperson on two previous occasions. In each of these cases, detailed responses were prepared by HiREB, addressing all of the concerns raised. Concerns have also been raised by these Unions and presented to the University and participating hospitals (HHS and St Joseph's Health care). HiREB assisted in preparing responses to those concerns. HiREB has also been contacted on two occasions by the Government of Canada, Responsible Conduct of Research, Tri-council Federal Office Panel in relation to concerns raised either by CUPE or by Dr Hedges. On both of those occasions we met directly with senior members of this panel and satisfied their concerns as to whether this study was ethically sound and that there was equipoise in relation to the primary question.

It is our experience that concerns raised with this study have arisen from a lack of understanding of the study design. To address this, the researchers have prepared a version of the protocol that can be shared (only funding information has been removed) and given permission to share the complete consent form used with the study. These documents have been sent to all groups who have raised concerns with the research, including the group of individuals who have raised the current concern.

This study involves healthcare workers who volunteer. No participants are "persuaded" to take part, as has been suggested by Dr Hedges in his correspondence. Once volunteered, healthcare workers are randomized to the usual protection group, or the N95 group. A crucial point that we feel is being missed by concerned individuals is that the usual protection group will receive the same level of protection as all the healthcare workers who do not volunteer for this research project. Currently, that protection, consistent with recommendations at all participating hospitals across Canada, involves the use of surgical/medical masks for the routine care of all patients, including COVID-19 positive patients. Healthcare workers in the usual care group will use N95 masks for all procedures where N95 masks are currently recommended. In fact, they may also use an N95 mask for any procedure or in any setting in which they feel that this is appropriate. Procedures where they will be required to use an N95 mask include settings where there is known or suspected risk of aerosolization of patient fluid. To be clear, this group receives exactly the same level of protection as all the healthcare workers at the participating centers who have not volunteered to be in the study. No study participants are asked to use a lesser form of protection than all of their colleagues who are not taking part in the research study. The healthcare workers randomized to the N95 mask group will wear the N95 mask at all times when caring for COVID-19 infected patients, even in settings where there is no suspected risk of aerosolization. That level of protection is not suggested at any care institution taking part in this study or any other institution in Canada that we are aware of. Agreeing to take part in this study does not result in any nurses "opting for a lesser level of personal protection than they could obtain pursuant to Directive 5" as

has been stated to us by Dr Hedges. Healthcare workers are also free to opt out of this research study at any time with no fear of repercussions from their employer. The chiefs of staff of the healthcare workers are not involved in the research study and no pressure has been placed on any healthcare workers to volunteer to take part. If a healthcare worker felt that he/she would like to wear an N95 mask at any time, they would be free to make that decision.

The objective of the study is to demonstrate non-inferiority of medical/surgical masks use in routine care of COVID-19 infected patients in comparison with N95 masks. The primary outcome is the scientifically confirmed COVID-19 infection rate. What that means is that if the group of healthcare worker receiving the current recommended approach of routinely using medical/surgical masks develop more infections than the group of healthcare workers who have been asked to routinely use the N95 masks, then that will be uncovered by this study. This is a crucial point that we have attempted to make when responding to the groups who are opposed to this study. If, as these groups claim, routine use of N95 masks is needed in the care of COVID-19 patients, then this study will show that. If that were to happen, then the findings of this study would be profoundly important. The current recommendation that healthcare workers should be routinely protected using medical/surgical masks would need to be changed and as a result all healthcare workers may be required to wear N95 during the routine care of COVID-19 infected patients. Without this research, that crucial piece of knowledge would not be uncovered.

As with many clinical trials, this study is subject to oversight by an independent safety board. What that means is that a group of experts, who are not the researchers, regularly look at all of the data that has been collected to see if there are any differences in the rate of infection between the regular care and the N95 mask groups. The latest report from this board was received in the past month and there is no indication that either of the treatment groups is subject to a greater number of infections. That means that equipoise still exists. Based on this continual oversight of this research project, HiREB remains assured that the participants in this research study – and all of the healthcare workers across Canada who are not participating in this study - are to the best of our knowledge receiving the appropriate level of protection.

In his correspondence with you, Dr Hedges included a letter that he received from Howard Njoo, MD, MHSc, FRCPC, Deputy Chief Public Health Officer and Interim Vice-President, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada. In that letter, Dr Njoo directly addressed Mr Hedges concerns with the following statement:

"The guidance recommends that a minimum of Droplet and Contact Precautions be implemented for patients, residents or clients considered exposed to, or suspected, or confirmed to have COVID-19, and that substitution of an N95 or equivalent respirator in place of a medical mask may occur based on a healthcare staff point-of-care risk assessment. This includes use of an N95 or equivalent respirator during planned or anticipated exposure to aerosol-generating medical procedures, and consideration in other circumstances under which risk of exposure to aerosolized virus may occur. The guidance states that aerosols are generated during other activities such as coughing, sneezing, or shouting. N95 or equivalent

respirator fit-testing is recommended for staff in acute, long-term, outpatient and ambulatory care settings, as well as for home care staff."

That advice precisely describes the standard of care that is in practice at most medical institutions across Canada – the use of N95 masks is required in aerosol generating settings and may be considered in other settings where the risk of exposure to aerosolized virus may occur. When that occurs, then all healthcare workers (whether they participate in this study or not), will be required to use an N95 mask.

We would be more than happy to discuss this project further if you feel that is needed.

Sincerely,

Mark Inman, MD PhD
Professor, Dept of Medicine, McMaster University
Co-Chair, Hamilton Integrated Research Ethics Board

For:

Frederick Spencer, MD
Professor, Dept of Medicine, McMaster University
Co-Chair, Hamilton Integrated Research Ethics Board

Cc, B Davis, University Legal

K Mossman, Vice President , Research