Cloth Masks May Prevent Transmission of COVID-19

TO THE EDITOR: We appreciate Clase and colleagues’ (1) efforts to show the potential efficacy of cloth masks in filtering virus-containing aerosols. The effect of wearing masks in the community to prevent coronavirus disease 2019 (COVID-19) is worth investigating. However, we have several concerns.

Clase and colleagues cite an unpublished review (2) on the effects of face masks and state that integrated odds ratios were between 0.81 and 0.95. Three of the 4 cited odds ratios were derived in home environments where a member of the household was infected with influenza-like illness. Only 1 odd ratio integrated from 3 studies done in a university residence and during the hajj pilgrimage was 0.94 (95% CI, 0.75 to 1.19).

Even if wearing masks reduces the risk for transmission by 6%, extrapolating how this measure will benefit the general community is difficult. Public health interventions requiring that populations wear masks may reduce transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) without harm. If authorities can spend sufficient funds, advocacy and distribution of materials are feasible. However, implementation of physical distancing, hand hygiene, and sanitation is not perfect. How should authorities allocate resources? The cost-effectiveness of cloth masks should be evaluated in comparison to that of other options.

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1. Clase CM, Fu EL, Joseph M, et al. Cloth masks may prevent transmission of COVID-19: an evidence-based, risk-based approach [Editorial]. Ann Intern Med. 2020;173:489-91. [PMID: 32441991]. doi: 10.7326/M20-2567
2. Bae S, Kim MC, Kim JY, et al. Effectiveness of surgical and cotton masks in blocking SARS-CoV-2: a controlled comparison in 4 patients [Letter]. Ann Intern Med. 2020;173:W22-3. [PMID: 32251511]. doi: 10.7326/M20-1342

TO THE EDITOR: In a comment on Clase and colleagues’ commentary (1), FitzGerald cites Bae and associates’ conclusion that “both surgical and cotton masks seem to be ineffective in preventing the dissemination of SARS-CoV-2 from the coughs of patients with COVID-19 to the environment and external mask surface” (2). Of note, Bae and associates’ brief research report was retracted on 2 June 2020. Further, my analysis of Bae and associates’ published data indicates that filtration efficiency with patients coughing into their masks averaged approximately 76% or possibly slightly lower because of their limits of detection. Surgical masks are often found to have 98% to 99% virus filtration efficiency under ideal conditions and approximately 80% in actual practice, with variation among brands, models, and wearers. As such, Bae and associates’ data were within normal expectations in that regard. Unfortunately, more than 80 news outlets repeated Bae and associates’ claim that masks were “ineffective.”

Clase and colleagues encourage mask wearing while stating, “There is absence of evidence that public mask wearing protects either the wearer or others” (3). However, Leffler and coworkers’ analysis (4) published on 23 April 2020 is evidence that public mask wearing reduced COVID-19 by an order of magnitude.

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IN RESPONSE: We found a body of evidence on a first, mechanistic question that showed that some cloth masks substantially reduce the passage of particles. The second question was whether this makes a difference in clinical outcomes. We characterized this answer as “unknown,” citing Brainard and colleagues’ evidence synthesis.

Drs. Harada and Harada Sassa describe Brainard and colleagues’ review in more detail than we were able to because of space limitations. Brainard and colleagues classified the evidence that they summarized as low certainty and very low certainty. The evidence is also highly indirect, containing no data on COVID-19 transmission. Furthermore, Brainard and colleagues do not mention whether any of their included studies in Figure 1 of their review were conducted during a pandemic. Like Greenhalgh and associates (1), who summarized many other meta-analyses and publications that discussed this second question, we regarded this as absence of evidence.

Consistent, convincing evidence showed that most (but not all) cloth masks reduce droplet and aerosol transmission. Evidence that public mask wearing protects either the wearer or others was lacking. Applying the ideas of uncertainty and risk to this question, we thought that during a pandemic that at that point had claimed more than 300 000 lives, community wearing of cloth masks was likely to be a useful adjunct to the public health interventions of physical distancing and hand hygiene.

Good evidence that cloth and cloth masks have useful properties, no evidence on whether wearing a cloth mask in the community makes a difference in transmission, and the presence of an unprecedented pandemic led to our decision to recommend using cloth masks first and conduct necessary further research second.

Like Drs. FitzGerald and Anderson, we, too, had converted the log numbers in Bae and associates’ brief research report to natural numbers and calculated filtration efficiency using standard methods. When we did so, the results and our conclusions differed from those of Bae and associates and supported use of cloth masks. At approximately the same time, others noted that many of the numbers used in Bae and associates’ calculations might be lower than the limit of detection of the assay. At the time of publication, we chose to be silent rather than disseminate uncertain information. Bae and associates’ brief research report has since been retracted (2).

Ueki and coworkers (3) have subsequently used mannequins with and without masks to study aerosolized SARS-CoV-2. They found consistent reductions in transmission when cloth masks, medical masks, and respirators were worn by the index mannequin and protection of the wearer when medical masks and respirators were worn by the receiving mannequin. The filtration efficiency of the cloth masks used in the experiment is not known.

Our evidence summary of the filtration efficiency of cloth and cloth masks has since been peer-reviewed and published (4). We created a parallel plain-language website (clothmasks.ca) (5). The between-country comparisons of Lefler and coworkers have also been peer-reviewed and published, finding that per capita coronavirus mortality increased on average each week by 16% in countries that supported masks compared with 62% in those that did not (6).

In summary, subsequent evidence suggests that community use of cloth masks is effective in reducing transmission of SARS-CoV-2. However, we believe that the important philosophical point is the recognition that decision making under uncertainty is not counter to evidence-based medicine but at its heart. Had masks not been proved effective, authorities who recommended them in April 2020 still would have been right to have done so.

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Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy

TO THE EDITOR: We read with interest del Amo and colleagues’ article (1) on the incidence and severity of coronavirus

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disease 2019 (COVID-19) in a large cohort of persons living with HIV (PLWH) in Spain. The authors examined COVID-19 outcomes stratified by antiretroviral therapy (ART) regimen. They concluded that PLWH receiving tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) had better outcomes than those receiving either tenofovir alafenamide (TAF)/FTC or abacavir (ABC)/lamivudine (3TC).

Although these findings are interesting, the authors did not control for comorbidities—key confounders that may have substantially affected these results. Non-AIDS-related comorbidities, including cardiovascular disease, chronic kidney disease, and diabetes, have all been associated with both increased risk for severe acute respiratory syndrome coronavirus 2 infection and worse clinical outcomes from COVID-19 (2).

In addition, non-AIDS-related comorbidities are highly prevalent among PLWH (3). The results presented do not account for whether persons in the “protected” TDF/FTC group simply had fewer comorbidities than those in the TAF/FTC and ABC/3TC groups. The relationship between comorbidities and ART is bidirectional.

Several ART regimens are most appropriate for patients with few comorbidities. For example, TDF is not recommended for patients with chronic kidney disease. Furthermore, the choice of ART may directly affect the incidence of non-AIDS-related comorbidities. Recent studies have reported significant metabolic abnormalities and weight increases in patients receiving TAF-containing regimens compared with those receiving TDF-containing regimens (4), and ABC has been independently associated with increased risk for cardiovascular events (5).

As such, patients in the TDF/FTC group in this study were likely to have had a lower prevalence of non-AIDS-related comorbidities that confer high risk for COVID-19 and related adverse outcomes. We would be interested in seeing the prevalence of non-AIDS-related comorbidities stratified by ART group in this cohort, as well as a multivariable analysis that controlled for these comorbidities. These factors would elucidate whether patients receiving TDF/FTC were protected because of their ART regimen or because they had fewer non-AIDS-related comorbidities.

In light of recent experiences with hydroxychloroquine for treatment of COVID-19, caution is warranted when extrapolating the data presented in this study to support the hypothesis that TDF/FTC may be useful for preexposure prophylaxis and treatment of COVID-19. Such assertions may fuel off-label use of antiretroviral drugs for COVID-19 and have serious implications for drug resistance in undiagnosed HIV infection and drug shortages for PLWH.

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IN RESPONSE: We thank Dr. Titanji and colleagues for their thoughtful comments about our article. We did not have individual data on comorbidities and thus could not adjust for them. In a recent publication (1), we reported 3 sensitivity analyses exploring the possible effect of confounding by comorbidities. Those findings suggest that confounding by individual clinical characteristics cannot completely explain the lower risk for COVID-19 diagnosis and hospitalization among HIV-positive persons receiving TDF/FTC. A recent analysis from South Africa (2) also found a lower risk for COVID-19 death among HIV-positive persons receiving TDF/FTC after adjustment for kidney disease and HIV viral suppression.

We share Dr. Titanji and colleagues’ concerns that overinterpretation of research findings may lead to inappropriate off-label use of drugs. To exclude the possibility of confounding, we are currently conducting a randomized, placebo-controlled, clinical trial (EPICOS [Randomized Clinical Trial for the Prevention of SARS-CoV-2 Infection in Healthcare Personnel]) (3) to estimate the efficacy of TDF/FTC and hydroxychloroquine as preexposure prophylaxis for COVID-19 among health care workers.

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TO THE EDITOR: We read Bastos’ and colleagues’ timely review (1) with interest. However, we have noted a few discrepancies between the data in their Figure and the original data in some of the articles that they cite (specifically, references 41 and 50 to 58 of their review). We suspect that the rows of this forest plot became misaligned, because some of the incorrect data seem to pertain to a different article that the authors cite.

Although it seems unlikely that these errors will change the authors’ conclusions, they warrant correction. Of note, we have verified data only from published articles, not those posted on preprint servers.

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Acute Cardiovascular Events Associated With Influenza in Hospitalized Adults

TO THE EDITOR: Chow and colleagues’ article (1) strongly supports the known association between influenza infection and acute cardiovascular events. It then goes 1 step further by detailing the spectrum and prevalence of such events, with acute heart failure (aHF) and acute ischemic heart disease (IHD) being the most common. Of note, nearly half of the 9046 patients who had an acute cardiovascular event were diagnosed with acute IHD. Because heart disease remains the leading cause of death in the United States, identifying these types of associations is imperative.

The article’s Methods section describes how acute cardiovascular events were identified using the International Classification of Diseases (ICD), Ninth Revision, Clinical Modification, and ICD, 10th Revision. Appendix Table 1 reveals the ICD codes that encompass acute IHD, including acute myocardial infarction (MI), ST-segment elevation MI, unstable angina, subendocardial infarction, non-ST-segment elevation MI, and “other acute and subacute forms of IHD.” The article does not reveal the percentage of cases attributed to each ICD code. The prognostic and therapeutic implications of ST-segment elevation MI are undoubtedly different from those of unstable angina. A large-scale study showed greater 30-day mortality among patients with ST-segment elevation MI (2). In addition, the ICD codes do not distinguish between different types of MI or reveal whether myocardial injury is considered a form of IHD.

A common taxonomy for acute myocardial injury is provided in the fourth universal definition of MI, which defines 5 subtypes of MI and nonischemic myocardial injury. Type I MI refers to acute coronary syndrome due to coronary atherothrombosis. Type II MI is caused by a mismatch of oxygen supply and demand through a pathophysiologic cause other than type I MI. Type II MI is becoming exceedingly common with the development of high-sensitivity troponin assays and is associated with worse short-term outcomes than type I MI (3). Elucidating these factors would help reveal the projection of acute IHD associated with influenza virus.

Chow and colleagues’ article is a convincing reminder of the need for greater uptake of seasonal influenza vaccination, highlighting that only 47.2% of the study population received an influenza vaccine in the current season (1). Several large meta-analyses show that influenza vaccination has been associated with a reduction in mortality and other adverse outcomes in adults hospitalized with laboratory-confirmed influenza infection (4, 5). This further emphasizes the importance of promoting vaccination to reduce cardiovascular events by means of primary prevention.

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TO THE EDITOR: Chow and colleagues’ study (1) evaluated the spectrum of 9046 acute cardiovascular events identified among 80 261 adults hospitalized with confirmed influenza (11.5%) and their effect (23.7% of all in-hospital deaths had an associated acute cardiovascular event). It was fascinating to read and a substantial addition to the literature. However, a few noteworthy points were missing from the discussion.

First, the risk for acute ischemic stroke is also significantly increased during infection with influenza (2) and may share pathogenetic mechanisms with acute IHD noted in 4412 of Chow and colleagues’ patients. Moreover, a substantial proportion of ischemic strokes in influenza may be cardioembolic; thus, influenza and ischemic stroke are closely linked and the association should have been discussed, even if these data were reserved for a separate study.

Second, because acute viral perimyocarditis was seldom encountered (116 patients [0.2%]), the high incidence of influenza-associated acute congestive heart failure (CHF) (6.2% of patients) remains a surprising and novel observation. Acute CHF affected more patients than did acute IHD; we hope that these conditions did not overlap, considering that the authors never mention the likely co-occurrence of acute IHD and CHF. This finding is especially noteworthy because 4457 of 9046 patients with CHF (49.2%) had no prior diagnosis of CHF or cardiomyopathy (see the Appendix and Table 2 of Chow and colleagues’ article). Previously, only a temporal association between influenza-like illness activity and CHF hospitalizations had been shown (3), and the cause of prevalent CHF in influenza remains an intriguing target of research.

Finally, prior seasonal influenza vaccination was associated with 14% to 20% absolute risk reduction for both acute IHD and CHF (even in patients who contracted influenza). This important finding prompted the authors to suggest, “Practitioners may play an essential role ... by maintaining high rates of annual influenza vaccination.” This well-meaning recommendation hardly suffices; vaccine hesitancy remains prevalent worldwide, and set goals of influenza vaccine uptake fail to be reached even among the most vulnerable populations (4).

Our recent study (5) suggests that the protective effect of influenza vaccination against the increased risk for influenza-associated acute IHD and ischemic stroke (up to 50%) can be used to increase vaccine uptake among the elderly population. Informing patients that influenza increases their risk for “heart attack and stroke” (a vivid risk, unknown to most) and that many of these dreaded events can be prevented by vaccination may often help overcome patients’ vaccine hesitancy. When explained by a physician in a short, focused encounter, the hope of mitigated risk was sufficient to motivate at least 27 of 53 patients who had previously declined vaccination (51%) to be vaccinated (5). Pending confirmation, this simple, frugal intervention may significantly increase vaccine uptake and potentially affect morbidity, mortality, and costs.

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IN RESPONSE: We thank Drs. Newton and Yeh and Dr. Schattner for emphasizing the need to further understand the relationship between influenza virus infection and acute cardiovascular events. In our analysis based on ICD codes, 4412 patients hospitalized with laboratory-confirmed influenza had acute IHD. Among these, 4.6% had ST-segment elevation MI. 43.6% had non–ST-segment elevation MI, 12% had acute MI without specification of the presence of ST-segment elevation, and 38.4% had other acute IHD not otherwise specified; only 1.4% of patients had unstable angina as the only evidence of acute IHD. For patients with MI, we were unable to further differentiate between type I or II, because of limitations of the ICD coding system. As for in-hospital outcomes among those with MI, patients in all 3 categories had a similar length of stay (median of 5 days). However, those with ST-segment elevation predictably had the highest percentage of intensive care unit admissions (59.7%), mechanical ventilatory support (32.6%), and in-hospital mortality (26.7%).

In our analysis, acute IHD and aHF were the most common acute cardiovascular events and included 4.9% with aHF only, 4.5% with acute IHD only, and 1.2% with both aHF and acute IHD. Those with both aHF and acute IHD had a median length of stay of 6 days, and 40.3% required admission to the ICU; 16.7% required mechanical ventilatory support, and 8.4% experienced in-hospital mortality. We agree that acute ischemic stroke overlaps mechanistically with acute IHD, as discussed in our article. However, consistent with proposed changes to ICD, 11th Revision, we classified cerebrovascular events as neurologic diagnoses rather than acute cardiovascular events.

Among all adults hospitalized with influenza and included in our analysis, 0.6% experienced an acute cerebrovascular event, including cerebral infarction, cerebral ischemia, or acute cerebrovascular insufficiency. Adults with both an acute cerebrovascular event and acute IHD made up only 0.1% of the patient population, whereas 0.5% had only a cerebrovascular event and 5.6% had only acute IHD. Among patients with any acute cerebrovascular event, the median length of stay was 7 days, 38.8% required ICU admission, 24.4% required mechanical ventilatory support, and 15.3% died in the hospital.

Our analysis was not designed to assess vaccine effectiveness but does highlight the need to improve influenza vaccine uptake. Schattner’s article (1) offers a novel approach to vaccine messaging among patients most at risk for influenza-related
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disease. Vaccination is our primary defense against influenza and its associated complications, and additional studies are needed to better understand the role influenza vaccination has in preventing acute cardiovascular events.

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