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Editorial

Respirators versus medical masks: evidence accumulates but the jury remains out

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This edition of *Influenza and other Respiratory Viruses* sees the publication of a cluster randomised trial performed by Raina McIntyre and colleagues, which compares the relative effectiveness of medical (or surgical) masks and respirators to prevent respiratory infection in healthcare workers.[1] The use of medical masks (MM) and respirators as methods of protection against influenza is complex and hotly debated; central to this is a lack of robust evidence for their effectiveness and a lack of clarity about the potential superiority of respirators. MMs present a barrier to droplet transmission and by virtue of covering the mouth and nose can also reduce hand to face contact transmission. Respirators have the added potential benefit of reducing airborne transmission, that is, transmission mediated by small aerosolised particles (hereafter referred to as aerosols).

For some infections, the choice of mask would appear to be relatively straightforward. For example, it is accepted that tuberculosis is transmitted via aerosols and that wearing a properly fitted respirator as part of a hierarchy of infection control measures can reduce a healthcare worker's (HCW) exposure; as such, respirators are widely recommended.[2] Influenza is more complicated. First, the relative contributions made by the different routes of transmission are uncertain.[3,4] It is likely that specific circumstances related to the environment (e.g. humidity, ventilation) and individuals (e.g. viral shedding, aerosol production) will dictate which route(s) predominate; for example several reports suggest that aerosol transmission can occur if conditions are favourable.[5–7] This ongoing uncertainty was reflected in the diverse approaches adopted by different countries in relation to the recommendations for the use of MMs and respirators by HCWs during the 2009 pandemic.[8–10] It is not surprising that the U.S. Institute of Medicine, the European Centre for Disease Control and the World Health Organization have all prioritised understanding the modes of influenza transmission as a critical requirement for pandemic planning.[11–13] Second, the pressures brought to bear on healthcare systems during a pandemic may be enormous, magnifying the need to prevent nosocomial infection and to reassure and protect staff. Third, there may be instances during a pandemic when the general public are advised to wear masks; and finally, protection from vaccination can be deficient because of poor uptake, unavailability or sub-optimal immunogenicity in certain age groups.[14]

Two systematic reviews that included studies on mask (MM and/or respirator) use have been conducted. One looked at the potential of masks to reduce the spread of respiratory infections and concluded (primarily on the basis of data from SARS outbreaks) that masks could be useful.[15] The other looked specifically at reducing influenza transmission and concluded that there are few data to endorse the wearing of a mask to prevent the wearer from becoming infected.[16] Some evidence from prospective community intervention studies indicates that masks may be beneficial,[17–19] but no studies have shown positive results with regard to their primary intention-to-treat objectives.[17–20] Of particular relevance to the issue of mask use by HCWs is the RCT conducted by Loeb *et al.* that compared MMs with respirators to protect HCWs from influenza; no significant differences in rates of laboratory-confirmed (mainly by serology) influenza were found. However, as influenza-like illness was reported by only 11 nurses (nine in the MM group and two in the respirator group; a non-significant difference), the study was probably underpowered for clinical- and PCR-based endpoints.[21]

MacIntyre *et al.* report the findings of a large cluster randomised trial comparing the relative effectiveness of MM and N95 respirators to prevent respiratory infection in HCWs. It should be noted that findings from this study were first reported at ICAAC (September 2009); however, the data have since been re-analysed. Participants from 15 hospitals in Beijing were recruited and wore a mask for four weeks from 1 December 2008. Randomisation into three groups took place by hospital: MMs, non-fit-tested N95 respirators and fit-tested N95 respirators. A fourth, non-randomised convenience group of HCWs who did not wear any masks was also recruited; local ethical constraints

prohibited the use of a randomised no-mask control arm. However, because of its non-random nature, any comparisons with this group should be interpreted extremely cautiously. HCWs were asked to wear the assigned mask throughout each shift, regardless of whether they were providing direct patient care; this is an important feature as it is difficult to identify every transmission risk. Although respirator wearers were split into fit-tested and non-fit-tested groups, fit-testing success was remarkably high (>98%) so differences between the groups may have been negligible. A number of clinical- and laboratory-based end-points were used, and the study was powered to detect an absolute difference in attack rates between masks of 7%.

Despite randomised allocation, there was some maldistribution of demographic variables between groups (e.g. lower vaccination rates and fewer exposures to high-risk procedures in the fit-tested respirator arm compared to the MM arm), and it is important to note that hospitals in China are graded (1–3 where 3 is highest) based on a number of 'quality' indicators, some of which may impact on infection control standards. In this study, all HCWs using MMs worked in level 3 hospitals, whilst 69% of fit-tested respirator users worked in level 2 hospitals.

For each infection outcome, respirators were associated with an approximate halving of risk compared to MMs, but after adjustment for clustering, the only significant finding was that non-fit-tested respirators were more protective against clinical respiratory infection (CRI) compared to MMs (OR 0·48; 95%CI 0·24–0·98, $P = 0·045$). In a further analysis to adjust for confounders, wearing a respirator and hospital level were both associated with significantly lower rates of CRI and any laboratory-confirmed virus infection. Overall event rates were low; in the randomised arms, CRI was reported by fewer than 7%, ILI by <1% and laboratory testing confirmed influenza in ≤1%. This compromises the power of the study, and the authors rightly draw attention to the fact that there was a 46% chance of finding at least one falsely significant difference. Conversely, all point estimate individual comparisons favoured respirators, and post hoc bootstrapping suggests this would be an unlikely chance finding. The study is therefore inconclusive.

This is a laudable and ambitious study, but it has faced difficulties common to other intervention studies, the primary issue being low event rates. Omitting serologic assessment of influenza infection has not helped, especially given the high asymptomatic infection rates sometimes seen,[22] but it was presumably avoided because of the difficulty in interpretation for those vaccinated. Studies based on a mixture of CRIs are able to generate more power, but have to assume that the contributions of different modes of transmission are the same for all respiratory viruses. Given the available data on influenza, RSV and rhinovirus, this is probably a false assumption.[23] Conducting the study in China, where mask acceptance is high, helped to overcome the hurdle of low compliance with mask wearing, but this does make it difficult to generalise the findings to settings where compliance is less.

The debate about whether respirators are more effective than MMs at preventing respiratory infections, in particular influenza, will continue. There is a growing body of evidence to suggest that the aerosol route of infection could be significant;[24] if we could identify the circumstances in which this becomes likely, then a respirator should have a place. However, until we are able to do this reliably or conduct a trial large enough to capture a high event rate, a proportion of which are generated by aerosol-mediated transmissions, we are unlikely to be able to conclude from RCTs that respirators are superior for all situations.

Despite the interest generated by the debate on the effectiveness of masks, it is imperative that this does not divert attention and resources from other interventions to interrupt influenza transmission. Use of isolation rooms, administrative and engineering controls, and seeking to improve stubbornly low rates of HCW vaccination have to feature more prominently on influenza infection control agendas.

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