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Short Communication

Human coronavirus data from four clinical trials of masks and respirators

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\section*{Abstract}

There are few published data on the efficacy of masks or respirators against coronavirus infections. This is an important research question to inform the response to the COVID-19 epidemic. The transmission modes of human coronaviruses are similar, thought to be by droplet, contact, and sometimes airborne routes. There are several randomized clinical trials of masks and respirators, but most used clinical endpoints or tested only for influenza. In four trials that we conducted, we tested for human coronaviruses, but only composite viral endpoints were reported in the trials. We reviewed and analyzed the coronavirus data from four of our trials. Laboratory-confirmed coronavirus infections were identified in our community household trial (one case), health worker trials (eight cases), and trial of mask use by sick patients (19 cases). No coronavirus infections were transmitted in households to parents who wore P2 or surgical masks, but one child with coronavirus infection transmitted infection to a parent in the control arm. No transmissions to close contacts occurred when worn by sick patients with coronavirus infections. There was a higher risk of coronavirus infection in HCWs who wore a mask compared to a respirator, but the difference was not statistically significant. These are the only available clinical trial data on coronavirus infections associated with mask or respirator use. More clinical trials are needed to assess the efficacy of respiratory protection against coronavirus infections.

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COVID-19 is caused by SARS-CoV-2, a beta-coronavirus which is genetically similar to SARS-CoV. Seasonal alpha- (NL63, 229E) and beta- (OC43, HKU1) coronaviruses cause common colds, croup, and bronchiolitis. The transmission modes of human coronaviruses are similar, thought to be by droplet, contact, and sometimes airborne routes. (Van der Hoek, 2007; Wu and J., 2020) Currently, the WHO recommends surgical masks for healthcare workers (HCW) providing routine care to a COVID-19 patient, (W.H.O., 2020) while the US CDC (US CDC, 2020a) and ECDC (US CDC, 2020b) recommend respirators. There are several randomized controlled trials (RCT) of community mask use in healthy people (Aiello et al., 2010; Aiello et al., 2012; Cowling et al., 2009; Larson et al., 2010; MacIntyre et al., 2009; Sumnerman et al., 2011; Suess et al., 2012). Masks used in the community may provide some protection, especially if users are compliant, it is used early, and it is combined with hand hygiene (Aiello et al., 2010; Aiello et al., 2012; MacIntyre et al., 2009). The use of masks as source control (i.e., preventing transmission by the symptomatic patient) is probably protective (Johnson et al., 2009; MacIntyre et al., 2016), but larger trials are needed. There are five HCW trials comparing masks and respirators (Jacobs et al., 2009; Loeb et al., 2009; MacIntyre et al., 2011a; MacIntyre et al., 2013; Radonovich et al., 2019), with only two showing a difference in efficacy. (MacIntyre et al., 2011a; MacIntyre et al., 2013)

Across all available trials, many tested only for influenza (Aiello et al., 2012; Larson et al., 2010), while others did not undertake laboratory testing at all, using clinical influenza-like illness as an outcome. (Aiello et al., 2010; Jacobs et al., 2009) Our trials tested for a range of viruses by multiplex PCR, including human coronaviruses. (MacIntyre et al., 2009; MacIntyre et al., 2016; MacIntyre et al., 2013; MacIntyre et al., 2011b) Only influenza and composite viral endpoints were presented in these trials. We reviewed the data on respiratory protection and human seasonal coronavirus infections from these four trials.

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In the community household trial in Australia, (MacIntyre et al., 2009) we recruited children with influenza-like illness and studied the use of medical masks and P2 masks against controls by healthy parents. Parents and children were tested by RT-PCR following the collection of a nose and throat swab. One index child was positive for coronavirus OC43. One parent of this child, who was in the control (no mask) arm, developed an infection with the same coronavirus. No parents in the medical mask or P2 mask arm developed coronavirus infection.

In the two HCW trials in China (MacIntyre et al., 2017), well HCWs wore a medical mask (n = 1064), an N95 respirator (n = 2046), or were controls (481) for four weeks while working in a hospital ward and were followed for symptom development. Symptomatic HCWs were tested by RT-PCR. There were eight coronavirus infections identified over four weeks, one in the first trial and seven in the second trial. Across both trials, three cases (3/2043, 0.1%) were reported in the N95 respirator arm, 4/1060 (0.4%) in the medical mask arm, and 1/480 (0.2%) in the control arm. CoV229E or NL63 was identified in six cases (three in the N95 respirator arm, two in the medical mask arm and one in the control arm), CoV43C or HKU1 was identified in one case (mask arm), and PIV1/229E/NL63 was also detected in one case (mask arm). Although the rate of infection was lower in the N95 arm, the difference was not significant (Odds ratio 0.4, 95% confidence intervals 0.07–1.9).

Since most coronavirus cases (7/8) were reported in the second trial, we did a separate analysis of the second trial. There were 4/572 subjects (0.7%) in the medical mask arm and 3/1097 (0.3%) in the N95 respirator arm who developed coronavirus infection, with a risk ratio of 2.57 for medical masks (95% CI 0.5743, 11.39) but the difference was not significant (OR 0.39 (CI 0.08 to 1.75).

In the source control trial, (MacIntyre et al., 2016) 245 sick (index) patients recruited at a fever clinic in China wore a mask for one week while in the same room as their 597 household contacts. They stopped wearing the mask when symptoms ceased. There were 20 coronavirus NL63, C229E or OC43 infections in 19 index cases - 11 NL63, seven C229E, and one OC43/NL63 co-infection. There were ten index cases positive for coronavirus in the mask group and nine positive for coronavirus in the control group, including one person in the mask group who was co-infected with OC43 and NL63. No coronavirus cases were identified among the household contacts in either mask or control groups after seven days follow-up. There was some degree of mask use reported in the control group – 5/9 infected index cases reported wearing a mask during the study period.

Despite small numbers of laboratory-confirmed coronavirus infections identified in our community, HCW and source control trials, and lack of statistical significance, no coronavirus infections were transmitted in households to parents who wore P2 or surgical masks. No transmissions to close contacts occurred when worn by sick patients with coronavirus infections. A recent study from Hong Kong showed that seasonal coronaviruses can be exhaled in tidal breathing and that they are blocked effectively by a mask (Leung et al., 2020). For well health workers, we found there was a higher risk of coronavirus infection in HCWs who wore a mask compared to a respirator, but the difference was not statistically significant. A pre-publication report from China showed protection by N95 respirators for HCW treating COVID-19 patients. (Wang and Cheng, 2020) It is essential to gather more data specific to coronaviruses, as the R0 of COVID-19 is estimated to be 2.3 compared to 1.28 for influenza (Alhazzani et al., 2020). So studies on influenza may not be generalizable. More clinical trials are needed to assess the efficacy of respiratory protection against coronavirus infections.

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Ethical approval

Ethics approval was obtained for each of the trials as outlined in the original publications (MacIntyre et al., 2009; MacIntyre et al., 2016; MacIntyre et al., 2011a; MacIntyre et al., 2013).

Conflicts of Interest

The authors have no conflicts of interest to declare.

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