



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Short Communication

## Human coronavirus data from four clinical trials of masks and respirators

C. Raina MacIntyre<sup>a,\*</sup>, Abrar A. Chughtai<sup>b</sup>, Holly Seale<sup>b</sup>, Dominic E. Dwyer<sup>d</sup>, Wang Quanyi<sup>c</sup><sup>a</sup> The Biosecurity Program, The Kirby Institute, UNSW Medicine, University of New South Wales, Australia<sup>b</sup> The School of Public Health and Community Medicine, UNSW Medicine, University of New South Wales, Australia<sup>c</sup> Institute for Infectious Disease and Endemic Disease Control, Beijing CDC, China<sup>d</sup> The Institute for Clinical Pathology and Medical Research, Westmead Hospital, Sydney, Australia

## ARTICLE INFO

## Article history:

Received 7 May 2020

Received in revised form 22 May 2020

Accepted 26 May 2020

## 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.

© 2020 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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; Simmerman 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.

\* Corresponding author at: The Biosecurity Program, The Kirby Institute, UNSW Medicine, University of New South Wales, Sydney, NSW 2052, Australia  
E-mail address: [rainam@protonmail.com](mailto:rainam@protonmail.com) (C. R. MacIntyre).

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), CoVOC43 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 arms 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  $R_0$  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.

## Funding

There was no external funding involved in this research.

## 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.

## References

- Aiello AE, Murray GF, Perez V, Coulborn RM, Davis BM, Uddin M, et al. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. *J Infect Dis* 2010;201(4):491–8.
- Aiello AE, Perez V, Coulborn RM, Davis BM, Uddin M, Monto AS. Facemasks, hand hygiene, and influenza among young adults: a randomized intervention trial. *PLoS one* 2012;7(1):e29744.
- Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intens Care Med* 2020;46(5):854–87.
- Cowling BJ, Chan K-H, Fang VJ, Cheng CKY, Fung ROP, Wai W, et al. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. *Ann Intern Med* 2009;151(7):437–46.
- Jacobs JL, Ohde S, Takahashi O, Tokuda Y, Omata F, Fukui T. Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: a randomized controlled trial. *Am J Infect Control* 2009;37(5):417–9.
- Johnson DF, Druce JD, Birch C, Grayson ML. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. *Clin Infect Dis* 2009;49(2):275–7.
- Larson EL, Ferng Y-h, Wong-McLoughlin J, Wang S, Haber M, Morse SS. Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households. *Public Health Rep* 2010;125(2):178–91.
- Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med* 2020;. doi:http://dx.doi.org/10.1038/s41591-020-0843-2 Online first.
- Loeb M, Dafeo N, Mahony J, John M, Sarabia A, Glavin V, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA* 2009;302(17):1865–71.
- MacIntyre CR, Cauchemez S, Dwyer DE, Seale H, Cheung P, Browne G, et al. Face mask use and control of respiratory virus transmission in households. *Emerg Infect Dis* 2009;15(2):233–41.
- MacIntyre CR, Wang Q, Cauchemez S, Seale H, Dwyer DE, Yang P, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir Viruses* 2011a;5(3):170–9.
- MacIntyre C, Wang Q, Cauchemez S, Seale H, Dwyer D, Yang P, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir Viruses* 2011b;5(3):170–9.
- MacIntyre CR, Wang Q, Seale H, Yang P, Shi W, Gao Z, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med* 2013;187(9):960–6.
- MacIntyre CR, Zhang Y, Chughtai AA, Seale H, Zhang D, Chu Y, et al. Cluster randomised controlled trial to examine medical mask use as source control for people with respiratory illness. *BMJ Open* 2016;6(12):e012330–e.
- MacIntyre CR, Chughtai AA, Rahman B, Peng Y, Zhang Y, Seale H, et al. The efficacy of medical masks and respirators against respiratory infection in healthcare workers. *Influenza Other Respir Viruses* 2017;11(6):511–7.
- Radonovich Jr. LJ, Simberloff MS, Bessesen MT, Brown AC, Cummings DAT, Gaydos CA, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. *JAMA* 2019;322(9):824–33.
- Simmernan JM, Suntrattiwong P, Levy J, Jarman RG, Kaewchana S, Gibbons RV, et al. Findings from a household randomized controlled trial of hand washing and face masks to reduce influenza transmission in Bangkok, Thailand. *Influenza Other Respir Viruses* 2011;5(4):256–67.
- Suess T, Remschmidt C, Schink SB, Schweiger B, Nitsche A, Schroeder K, et al. The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009–2011. *BMC Infect Dis* 2012;12:26–.
- US Centers for Disease Control. Interim Infection Prevention and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 (COVID-19) or Persons Under Investigation for COVID-19 in Healthcare Settings. 2020.
- US Centers for Disease Control. Guidance for wearing and removing personal protective equipment in healthcare settings for the care of patients with suspected or confirmed COVID-19. 2020.

- Van der Hoek L. Human Coronaviruses: What Do They Cause?. *Antivir Ther* 2007;12:651–8.
- Wang XP, Cheng Z. Association between 2019-nCoV transmission and N95 respirator use. *MedRxiv* 2020;. doi:<http://dx.doi.org/10.1101/2020.02.18.20021881> [Pre-publication manuscript]. In press.
- W.H.O. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19). Interim guidance 2020;.
- Wu ZM, J. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China. *JAMA* 2020;.