

COVID-19 Report

Finding the evidence for you

A weekly report to answer clinically relevant questions by summarizing the most recent evidence.

This information is intended for health care professionals.

Clinical Description & Epidemiology

What proportion of adults infected with SARS-CoV-2 are co-infected with other respiratory pathogens? Is there any difference in clinical presentation in co-infected patients?

- There is limited data regarding co-infection of patients with COVID-19. One study from China indicated that 6.5% of adults with COVID-19 were possibly co-infected with another respiratory tract virus.¹ Another, also from China, indicated that up to 4.35% of adults with COVID-19 were co-infected with Influenza²
- Co-infection rate among the pediatric population is potentially higher (see the pediatric section below for details).³
- There is insufficient data to conclude the clinical relevance of co-infection with multiple respiratory pathogens. Rates of concurrent bacterial pneumonia are also unclear. It is important to be mindful that a patient could still be positive for COVID-19 even if they have tested positive for another respiratory tract virus.

What proportion of patients that have a positive test for SARS-CoV-2 only develop mild symptoms (e.g. upper respiratory tract symptoms without significant dyspnea)?

- Among 44,415 cases (hospitalized and non-hospitalized, 62% lab-confirmed) in China, 81% were classified as mild (non-pneumonia or mild pneumonia). 14% were classified as severe (dyspnea, RR \geq 30, SpO₂ \leq 93%, P_aO₂/F_iO₂ <300, and/or lung infiltrates >50% within 24-48 hours). Critical cases (respiratory failure, septic shock,

and/or multiple organ dysfunction/failure) comprised 5% of cases. All recorded deaths occurred in the critical category.¹

- In another study of 1,099 hospitalized patients in China with lab-confirmed COVID-19, 84.3% met IDSA/ATS criteria for non-severe community-acquired pneumonia.² 17.9% of non-severe patients had no radiographic or CT abnormality, and only 2.6% eventually developed disease severe enough to result in ICU admission, invasive mechanical ventilation, or death.³

Is there any data to suggest whether people can become reinfected?

- There have been news/government reports of some recently discharged patients apparently relapsing and requiring re-admission,¹ these reports are anecdotal. Thus far, no proven cases of reinfection have been published in the scientific literature.
- Two papers have documented cases of patients who recovered and were discharged after negative nasopharyngeal RT-PCR tests, but later tested positive on follow-up swab. These patients remained well with no clinical recurrence of disease, no new chest CT findings, and no new exposures.^{2,3} The significance of these findings is unclear.
- In a small preprint trial involving rhesus macaques, two monkeys who recovered from COVID-19 did not become reinfected when re-exposed to the virus 28 days after the initial infection.⁴

What is the risk of infection for healthcare workers?

- A descriptive article from China reported 1,716 healthcare workers (HCWs) diagnosed with COVID-19 as of February 11, 2020. Of the infected HCWs, 14.8% had severe or critical disease (vs. 14% in the general population) and 5 died (0.3% vs. 2.3% of confirmed cases in the general population).^{1,2} The WHO-China Joint Mission on COVID-19 on February 24, 2020 announced the infection of 2,055 HCWs and 22 deaths (1.1%).³
- One case report from Singapore assessed 41 HCWs with exposure (aerosol-generating procedures for >10 minutes, distance <2m from patient) to a patient who ultimately was found to be infected with SARS-CoV-2, but at the time of care was not suspected to have COVID-19. Routine infection control procedures were followed (85% used surgical masks, 15% N95 masks). None of the HCWs became infected based on 14 days of surveillance.⁴
- A preprint commentary from Chinese researchers suggests many infections of healthcare workers resulted from identifiable and potentially preventable deficits including lack of communication, lack of general preparedness, lack of infection control and prevention training, inappropriate or lack of appropriate PPE, lack of

point of care testing and RT-PCR testing supplies, and patient misinformation related to exposure risk.³

Diagnostics & Surveillance

Can saliva be used as a specimen to detect SARS-CoV-2?

- Non-invasive and does not require healthcare worker to collect.¹
- So far the data available shows sensitivity may be as high as 91.7% to detect SARS-CoV-2 in saliva, but this was based on a series of only 12 patients.¹
- Throat wash and saliva specimens have previously been shown to outperform nasopharyngeal aspirate (NPA) in detection of respiratory viruses in general.³
- Currently no widespread clinical use and requires further studies to determine suitability for SARS-CoV-2 detection compared to other methods.

What is the ideal sample type based on clinical syndrome?

- Respiratory samples are the most sensitive for SARS-CoV-2 detection, with lower tract specimens BAL and sputum having highest positivity rates, 80-93% and 75-89%, respectively.^{1,2,3}
- For upper tract specimens, nasopharyngeal swabs showed higher positivity rates (63-73%) over oropharyngeal swabs (32-60%).^{2,3}
- Anal swabs (25-39% positivity) appear to remain PCR-positive ~2 days longer than oral swabs.^{2,4} SARS-CoV-2 has also been detected (29-35% positivity)^{2,3} in stool up to 3 weeks after the onset of symptoms⁵, suggesting possibility of transmission by fecal-oral route. However, note virus did not grow in cell culture.⁵
- Other specimens including blood, urine, amniotic fluid and breast milk have little to no detectable viral RNA.^{1,2,6}

How are specimens stored before testing?

- With a national shortage of universal transport media (UTM), labs across the country have adopted to in-house made viral transport media (VTM).
- Other suitable alternatives, including saline,¹ alcohol^{2,3} and even dry flocced swabs,^{1,2} have been used in the past for many respiratory viruses with similar viral RNA recovery rates to UTM.

How useful is a chest CT scan in detecting COVID-19?

- In a study of 1,014 COVID-19 cases from China, CT scans had a sensitivity of 97%, specificity of 25%, positive predictive value of 65%, and negative predictive value of

83%.¹

- When serial RT-PCRs were obtained, initial positive chest CTs were consistent with COVID-19 (60-93%) 6-8 days after symptom onset.¹
- CT scans from 0-2 days less sensitive (44%) than 3-12 days (91-96%) after symptom onset.²

Therapeutics

What is the evidence regarding (hydroxy)chloroquine as treatment for COVID-19?

- Chloroquine and hydroxychloroquine are antimalarial and anti-inflammatory agents with *in vitro* activity against SARS-CoV-2.^{1,2}
- Attention to these agents recently increased after Donald Trump tweeted about their potential use in treating COVID-19. His tweet referred to an open-label, non-randomized French study of 20 patients treated with hydroxychloroquine (6 patients also received azithromycin). The primary outcome was viral clearance as opposed to clinical outcome. While hydroxychloroquine was associated with improved viral clearance, this study was limited by the post-hoc exclusion of 6 treated patients with poor outcomes and the small sample size.³
- Multiple large RCTs are currently ongoing worldwide and results are pending.
- This week, a Canadian RCT was launched in Manitoba, Quebec and Alberta looking at the use of hydroxychloroquine for post-exposure prophylaxis (<https://www.covid-19research.ca/hydroxychloroquine-study>), and a Canadian pre-exposure prophylaxis and treatment RCT are also underway.

Which high-yield critical care interventions are recommended in severe COVID-19 and associated acute respiratory distress syndrome (ARDS)?

- Only a few retrospective studies with small sample sizes describe critical care and ventilation strategies in COVID-19.^{1,2}
- In the absence of more robust data, the Surviving Sepsis Campaign (SSC) and WHO COVID-19 guidelines support the use of ventilation with low tidal volumes (4-8 mL/kg predicted body weight), higher PEEP and plateau pressures below 30 cm H₂O for COVID-19 related ARDS.^{3,4}
- Other SSC recommendations include: video-guided over direct laryngoscopy, conservative fluid strategy, norepinephrine as first-line vasopressor and target SPO₂ 92 to 96%.⁵

What is the evidence for interleukin-6 (IL-6) monoclonal antibodies for treating COVID-19?

- Elevation of IL-6 correlates with COVID-19 severity and predicts clinical deterioration.¹
- Tocilizumab is an example of a recombinant humanized monoclonal antibody that binds to IL-6 receptors and inhibits IL-6 signalling.² It is approved for rheumatoid arthritis and cytokine release syndrome.
- In a recent case series of 21 patients with severe COVID-19, tocilizumab was associated with more rapid defervescence, decreased CRP, decreased oxygen requirements, and resolution of lung opacities.³
- There are currently 4 clinical trials investigating anti-IL-6 monoclonal antibodies for treatment in COVID-19. No results are available yet.

Infection Prevention & Control

What respirator should be used to care for patients with COVID-19?

- Procedure masks ("surgical face masks"), are effective for preventing diseases spread via droplets.¹ Procedure masks are used for non-aerosol generating activities pertaining to the assessment and care of those affected by COVID-19. N95 respirators should be used ONLY during activities where aerosols are generated (click this link for list: [AGMPs](#)).
- NOTE: Current Manitoba infection control guidelines suggest using enhanced droplet and contact precautions when caring for a patient with confirmed or suspected COVID-19; which includes gloves, a gown, and eye protection in addition to a face mask.

In the setting of a shortage of N95 respirators, can respiratory protection be used over extended periods of time? Can they be re-used and/or sterilized?

- Viral particles can persist on the surface of used procedure masks and N95 respirators. **Removing a mask or respirator is a particularly high risk time for contaminating your hands.**¹ However, the risk of re-aerosolizing particles from a mask to subsequent patients is low.
- With repeated removal and reapplication, the fit and protection provided by an N95 respirator decreases. Masks and respirators that are obviously soiled are likely no longer effective.
- At present, there is no well-studied and reliable method available to decontaminate standard surgical masks or respirators.

Key Points:

1. Extending the use of a mask or respirator is preferred over repeated reuse.
2. If a mask is visibly soiled it should be discarded.
3. Review proper technique for donning and doffing PPE - there is a high risk for health care workers to become exposed during this process.

Review: <https://professionals.wrha.mb.ca/old/extranet/ipc/ppe-videos.php>

4. If you inadvertently touch your mask or need to adjust it - properly clean your hands before and afterwards.

Are cloth masks safe to use? Are they as effective as medical masks in preventing infection?

- Cloth masks have minimal to no protective benefits and only marginally prevent outward aerosol transmission. Compared to medical face masks, their use is associated with significantly higher rates of infection.¹
- Cloth masks should only be considered as a last resort, when no medical masks are available.

Public Health Interventions

A few terms:

R_0 = basic reproduction number (the average number of people that one person will infect). An outbreak is expected to end if $R_0 < 1$

R_t = R_0 over time

What are the transmission dynamics in congregated settings such as personal care homes and cruise ships?

- SARS-CoV-2 has the potential to spread extremely quickly in congregated settings such as cruise ships, personal care homes, places of worship and health care sites.

Princess Diamond cruise ship:

- 712 of 3,700 passengers and crews (19.2%) ended up testing positive for SARS-CoV-2.^{1,2}
- One study calculated 11.2 as the maximum value of R_t , which was much higher than the R_0 for the virus in the community.³
- Once the outbreak was recognized and quarantine measures put into place, the R_t was reduced to less than 1, meaning that the measures were effective.³

Personal care homes (PCHs):

- Currently, there is limited data on the transmission dynamics in PCHs setting.
- One outbreak occurred in a long-term care facility in King County, Washington, resulting in the infection of 81 residents, 34 staff members, and 14 visitors. There were 23 deaths.⁴
- As of March 24th, British Columbia has seen outbreaks in 8 long-term care facilities with 12 deaths associated with COVID-19.⁵
- Many provinces have implemented reduced visitor access to personal care homes and set strict guidelines for staff. Manitoba, for example, has banned visitors and discontinued communal meal programs.⁶
- It should be noted that social disconnectedness and isolation puts older adults at a higher risk of depression and anxiety, which may worsen other health conditions.⁷ Technology may be one solution to this problem.

What public health interventions (PHIs) were taken in countries that have so far been successful in containing the COVID-19 outbreak? (PART 1)

Singapore

- As of March 25, Singapore had 564 documented cases of COVID-19 with a mortality rate of 0.35%.¹
- PHIs implemented after the first documented case of COVID-19 included: aggressive testing for COVID-19 (individuals that meet case definition, close contacts with positive cases, ill patients with pneumonia and based on physician's clinical suspicion), isolating positive cases in hospitals, contact tracing, and active quarantine of close contacts.^{2,3}
- The quarantine process in Singapore is unique. To ensure compliance during quarantine, public health officials video-call close contacts thrice daily to verify their location. Quarantine violators are tagged with continuous tracking devices and are subject to prosecution.^{2,4}
- Additional measures taken since March 18-26 include: restricting social gatherings to less than 10 people, closing non-essential public venues and restricting travel abroad (all returning travelers must self-isolate for 14 days).^{5,6}

South Korea

- As of March 25, South Korea had 9,137 documented cases of COVID-19 with a mortality rate of 1.38%.¹
- PHIs implemented after the surge in COVID-19 cases at the end of February included: wide scale aggressive testing for COVID-19 (35,7896 tests have been performed as of March 25th; up to 15,000 tests can be performed daily), isolating

positive cases, contact tracing and quarantine of close contacts (violators are subject to prosecution) and transparent communication from the government.^{2,4}

- Contact tracing method is unique. The Korean government thoroughly identifies the location of confirmed cases and their close contacts by using credit card transaction logs and GPS to track cell phone location, as well as using closed circuit TVs to identify the route taken by the patient and to evaluate the exposure risk to contacts.³
- One unique aspect of the Korean government's communication strategy is to send messages to the public regarding the location where a person tests positive for COVID-19 and the places they recently visited in order to reduce movement in those locations.⁴



Pediatric Corner

What proportion of children with COVID-19 are co-infected with other respiratory pathogens?

- A few small studies have shown that children can be co-infected with SARS-CoV-2 and other respiratory pathogens.^{1,2,3,4} Co-infection rates ranged from 0 - 47%.
- The studies varied in which respiratory pathogens were tested, but most included Influenza A or B, and Mycoplasma.
- None of the studies specifically looked at clinical features that help differentiate between children with or without co-infections.

Our takeaway message:

- In children, co-infection with SARS-CoV-2 is possible and should be considered even when another respiratory pathogen has been found.

What is the evidence on vertical transmission of SARS-CoV-2?

- In a review¹ of published case series,^{2,3,4,5,6} samples were obtained including placenta, amniotic fluid and umbilical cord blood from a combined total of 37 women with confirmed COVID-19 infection. Samples were also taken from a total of 29 neonates including oropharyngeal swabs, gastric secretions, urine, and feces. All the samples tested negative for SARS-CoV-2 by RT-PCR.
- Breastmilk samples from 6 mothers with SARS-CoV-2 tested negative.²

- To date, there is no laboratory evidence of vertical transmission of SARS-CoV-2 among pregnant women infected in the third trimester. This correlates with previous studies that demonstrated no evidence of vertical transmission of SARS-CoV and MERS-CoV.^{7,8,9}
- In one case series, 3 of 33 neonates born to mothers with COVID-19 became symptomatic and had nasopharyngeal and anal swabs positive for SARS-CoV-2 RT-PCR on days two and four of life.¹⁰ The three neonates were all born by C-section. The authors postulate the possibility of vertical transmission, but there is not enough data to draw this conclusion.
- Further studies are needed to investigate the possibility of vertical transmission. Of all the neonates reported with SARS-CoV-2 so far, none have been critically ill.

The information presented reflects the data that is currently available to us. In the context of a pandemic where rapid dissemination of information is essential, we have included information from evolving medical literature which may be awaiting peer-review.

This report was produced by a collaboration of fellows, residents, medical students, faculty leads, and librarians from the University of Manitoba and the Medical Microbiology and Infectious Diseases community.

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