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Q&A

The SARS-CoV-2 Outbreak: Diagnosis, Infection Prevention, and Public Perception

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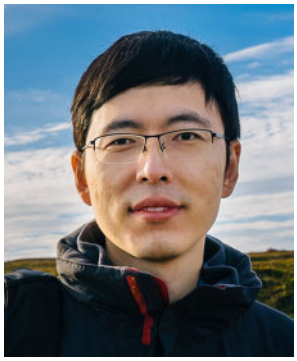
At the end of 2019 and early 2020, an outbreak of pneumonia of unknown etiology emerged in the city of Wuhan in China. The cases were found to be caused by a novel beta coronavirus, which was subsequently named SARS-CoV-2 by the World Health Organization (WHO). The virus has since spread further in China and to other regions of the world, having infected more than 88 K people, and causing close to 3000 deaths as of March 1, 2020. More than 50 million people remain in quarantine at this time. Scientists and clinicians globally are working swiftly to combat COVID-19, the respiratory disease caused by the virus. Notably, diagnostic assays have been developed rapidly in many countries, and have played significant roles in diagnosis, monitoring, surveillance, and infection control. Starting February 29, 2020, the development and performance of molecular testing for SARS-CoV-2 in high complexity Clinical Laboratory Improvement Amendments (CLIA) laboratories prior to emergency use authorization was allowed by the US FDA. Although the epidemic is evolving rapidly, many valuable lessons have been learned and many questions remain to be answered. Here we invited multiple experts across the globe from clinical laboratories, public health laboratories, infection control, and diagnostic industry to share their views on the diagnosis, infection control, and public perception of SARS-CoV-2.

What should healthcare providers know about the assays available for the detection of SARS-CoV-2? What is known about assay performance? Can the assays detect virus in incubation or recovery periods?

Yang Pan: Two kinds of traditional methods for pathogen detection are nucleic acid testing (NAT) and



serological testing. SARS-CoV-2 is no exception. Among all available testing methods, NAT plays a pivotal role in the public health response to SARS-CoV-2. It is the most sensitive method combined with high specificity and high efficiency. For available tests, the limit of detection reaches 10^2 copies/mL, and the nonspecific amplification caused by low specificity is rare in current settings. However, stringent performance assessment of NAT in SARS-CoV-2 detection is still an urgent need, and depends on the availability of a proper testing panel containing clinical samples with different viral loads. In addition, traditional serological testing for specific IgM, IgG, or viral antigens, such as ELISA, CLIA, and rapid serological testing should not be neglected. To some degree, they could help clinically discriminate among infections when the NAT result is negative. However, sensitive and specific serological assays are not as easily established as NAT assays. More evaluator efforts should be spent on these assays.

Leo Poon: My concern is whether assays are properly evaluated. There currently are assays that have not been properly evaluated, resulting in false negative results. When considering an approach for testing, I recommend reviewing the multiple assays described by the WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance), which were extensively used early in the outbreak.

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Considering viral dynamics, growing studies indicate that viral load peaks in the first week of disease onset. Viral RNA can be detected in patients in the 2nd week of disease onset, but the viral load is low. There are asymptomatic cases and recovering cases with documented RT-PCR positivity.

Carmen Charlton and Nathan Zelyas: The assays used in many laboratories across Canada and internationally are real-time PCR assays targeting two different amplification regions, the E (envelope protein) and RdRp (RNA-dependent RNA polymerase) genes. In the beginning of the outbreak, both positive and negative samples were being sent to the National Microbiology Laboratory for confirmation by all provinces. However, as testing volume increased and all parallel testing was concordant with National Microbiology Laboratory results, sending negative samples was discontinued for those provinces with high enough test volumes. This is similar to what has been done in the European Union where positive specimens can be sent for confirmation to any of the European Expert Laboratories.

An additional assay has been designed by the United States Centers for Disease Control (CDC), which is also a real-time PCR assay, using three different amplification regions. The NS3 is designed for universal detection of SARS-like coronaviruses, and the N1 and N2 regions are specific for SARS-CoV-2.

Assays have been validated for all performance characteristics (including sensitivity and specificity); however, some validations have been done using synthetic sequences that have been spiked into respiratory samples. This seed and recovery style testing is common for validations when true positive control material is rare (e.g., North America) or not commercially available. The analytical sensitivity and analytical specificity have been calculated for each assay, but due to the relatively low number of positive human cases that have been tested in North America, there are few data in North America for diagnostic sensitivity and specificity.

Generally, respiratory viral loads peak 2 days after symptom onset, and therefore collection of specimens as close to symptom onset as possible is recommended. For example, for human metapneumovirus, nearly 60% of cases are detected by NAT within the first 2 days, while only 19% are detected greater than 4 days after symptom onset. Delays in specimen collection can result in false negative results for respiratory viruses in general, and mean viral peak time varies by virus, the severity of symptoms, and the immune status of the individual. This suggests more work will be needed to determine the exact mean viral peak time for the SARS-CoV-2 virus.

Similar to other respiratory viruses, the ability of the assay to detect coronavirus will largely be dependent on the collection of the sample. If a nasopharyngeal (NP) swab is not inserted properly to the nasopharyngeal space, and only to the nares, it is likely that this will result in a false negative result, even if the patient is infected with SARS-CoV-2. we would recommend emphasizing to healthcare workers the importance of proper specimen collection, because if the specimen has not been collected from an area the virus is likely to be, the virus will not be detected regardless of how good the assay is.

The optimal specimen type for SARS-CoV-2 detection is yet to be determined. One non-peer reviewed study indicated that sputa may be the best noninvasive specimen type when compared to nasal and throat swabs, although additional studies are needed to confirm the best specimen type in the context of clinical symptomatology (lower versus upper respiratory tract symptoms) and timing of collection.

Daniel Rhoads: The methods by which to detect SARS-CoV-2 have been developed only after the recent emergence of the infection, so this short time frame has afforded little to be studied and reported to date that confidently describes the accuracy of the methods in clinical specimens. What is remarkable is the rapidity with which the virus' genome was sequenced and

released to the public. This rapid sequence reporting enabled manufacturers of FDA-cleared coronavirus assays to quickly recognize and report that their assays appeared to fail to detect SARS-CoV-2 according to in silico testing.

David Persing: There are very few published data on clinical performance characteristics. No diagnostic modality is likely to be perfect. Radiologic findings, even if characteristic, are likely to be confined to later stages of disease, and NAT's could be false negative early on, especially if applied to the wrong sample type. Public health testing capacity is likely to become overwhelmed in areas of widespread disease activity, and turn-around-times are likely to be prolonged. Decentralized testing will likely need to be made available at the hospital level.

Should nucleic acid testing results be required for diagnosing SARS-CoV-2 infection in endemic regions, in addition to clinical presentations and computed tomography findings? How should false negative results be managed?

Yang Pan: In some regions of China where the virus is epidemic in the community and the needs of clinical diagnosis exceed the capacity of NAT, a definition of "clinically diagnosed cases" based on clinical assessment and radiological presentations has been applied. This definition is particularly useful in outpatient clinics, where timely diagnosis reduces patient gathering, shortens the length of stay, and promotes effective infection control management. For those clinically diagnosed cases, empiric antiviral treatment and supportive management can be implemented immediately. Necessary epidemic investigation will also be triggered at the same time.

An essential point is that healthcare personnel must be educated on result interpretation of NAT. Despite high sensitivity, a negative NAT is insufficient to exclude SARS-CoV-2 infection in patients with high clinical suspicion. The time of sample collection, the quality of the sample (preferably lower respiratory tract samples), the performance of testing methods, the quality controls, and the training of testing professionals all contribute to the accuracy of the testing. Especially, for those patients with typical clinical presentations or clear epidemic indications, clinical treatment and case management is necessary, even if a negative NAT is observed at one or two time points. In this instance, other approaches for testing should be considered, including specific IgM and IgG assays.

Leo Poon: The initial clinical presentation is nonspecific. This becomes problematic in a flu season. Thus, a virological laboratory test is still recommended. However, we are still not sure about the best type of clinical samples for the test for highly suspected cases; multiple samples should be taken.

Carmen Charlton and Nathan Zelyas: In endemic areas, the case definitions for probable and confirmed cases will likely be different than areas with very low prevalence. In an endemic region, if a patient presented with SARS-CoV-2-like symptoms, and neither treatment nor management of the patient would be changed by performing a laboratory test (i.e., a positive or negative result would not impact patient management), then NAT testing would not be required. However, if a positive or negative NAT result would impact infection prevention and control procedures (i.e., isolation of the patient to a particular ward) or patient management (i.e., different therapy), then testing would be warranted. This decision will likely be handled separately by each institution based on their current level of SARS-CoV-2 circulation, and available clinical intervention.

The possibility of a false-negative result exists with any laboratory test. In the case where a patient presents with SARS-CoV-2-like symptoms and is NAT-negative, but other sources of infection are not found, a physician would have to use their best clinical judgement in treatment of the patient. According the interim guidance from the WHO, a single negative test result does not exclude infection with SARS-CoV-2 (https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117). Additionally, "repeat testing using a lower respiratory sample is strongly recommended in severe or progressive disease" (https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117). However, repeat testing all negatives would essentially double all testing requests, and that capacity may not be available in view of otherwise increasing test requests. Some jurisdictions are requesting two samples for testing be sent on every patient (a combination of an NP and throat or lower respiratory sample) to overcome the possibility of a false negative. One case in Ontario, for example, was identified on a throat sample, but not by the NP sample, while all other cases have been identified by an NP in Canada.

Daniel Rhoads: NAT should be an integral part of the routine diagnostic work up of SARS-CoV-2, especially in nonendemic areas. However, if the pretest probability

is very high due to high disease prevalence and if many cases of the disease have already been confirmed by NAT in an endemic area, then there is little utility to requiring laboratory or radiological confirmation of the disease. This proposed approach is similar to the CDC recommendations for influenza testing in the US (https://www.cdc.gov/flu/professionals/diagnosis/consider-influenza-testing.htm). If NAT or computed tomography are not employed to confirm the diagnosis, then internationally harmonized diagnostic criteria based on the clinical syndrome (signs, symptoms, exposure) should be employed and used.

Who should be offering SARS-CoV-2 testing and in what settings should it be performed?

Yang Pan: The virological, epidemiologic, and clinical settings determine the preferred flow of SARS-CoV-2 testing. In the first stage of the outbreak in China, all tests were completed by the China CDC and public health laboratories. Over time, sustained cross-regional transmission was observed. In this situation, a rapid diagnostic test becomes an essential component of patient management during the outbreak. Limited testing in centralized laboratories becomes no longer ideal, as this requires specimen transport, extends turnaround time, and increases biosafety concerns. Given the high rate of circulation in China at this time, all qualified laboratories, including CDC laboratories, public health laboratories, hospital clinical laboratories, and independent laboratories should provide in vitro diagnostic services for this outbreak. At this moment, what we know is the faster we confirm an infection, the fewer people may be infected.

Carmen Charlton and Nathan Zelyas: At the current stage of the outbreak, it makes sense for public health laboratories in North America to perform SARS-CoV-2 testing. Testing is restricted to individuals with specific travel locations or exposure histories, commercial tests are only starting to become available, and testing numbers overall are relatively low, making this assay perfectly suited to public health laboratories to perform. However, given the speed with which the virus is spreading, and the inability of countries to adequately contain the virus, testing volumes will likely increase substantially. Additionally, the current test gate-keeping (i.e., testing only those with compatible symptoms and travel/exposure history) that public health is providing will quickly outstrip capacity, and this gate-keeping system will no longer be sustainable. We have already seen this occur in both Ontario and British Columbia (who have higher testing volumes) where the Medical Officer of Health triaging has been stopped.

If the viral infection is sustained in the North American population, this will impact where testing is needed. At that time, a re-assessment of resources may be required to test all suspect cases. Some jurisdictions are currently examining how to incorporate SARS-CoV-2 testing into routine respiratory viral testing workflows. As the virus becomes more common-place in North America, SARS-CoV-2 testing may need to be disseminated to acute care laboratories to accommodate testing volumes. This has already started to occur in certain areas of Canada.

Daniel Rhoads: The location of NAT for SARS-CoV-2 detection should be congruent with the prevalence of the virus in balance with the clinical and public health needs. If the prevalence of disease becomes high in the US, and the virus become endemic, then it would be appropriate to distribute the testing to all labs that currently are competent to perform NAT respiratory virus testing. If the cases in the US continue to be limited to mostly those acquired from foreign exposure, then it would be reasonable to continue to limit testing to public health laboratories where the laboratories can work closely with public health epidemiologists to help to identify and track cases. If a widely available medication is identified as an important measure in the management of patients with SARS-CoV-2 infection, then the turnaround time for NAT becomes of heightened importance in order to more rapidly achieve optimal medical management, and if this were to occur, then it could help to justify more distributed laboratory testing even if disease prevalence is relatively low.

What safety measures are needed for health care providers involved with lab testing or caring for patients with SARS-CoV-2 and patients suspected of having SARS-CoV-2?

Hilary Babcock: Testing for SARS-CoV-2, and testing samples from potential COVID19 patients, does not appear to require different safety measures than are routinely used for other respiratory viral pathogens. The samples can be safely managed in the lab using standard safety techniques. In clinical settings, protection recommendations are guided by transmission routes. It appears that this new coronavirus is transmitted through large respiratory droplets, similar to most other respiratory viruses. These droplets are expelled when infected people cough or sneeze and either land in the nose, mouth, or eyes of another person, or land on a

surface that someone can touch, thereby potentially carrying the virus to their nose, mouth, or eyes. CDC recommendations for personal protective equipment while providing care for infected patients include gown, gloves, eye protection, and a respirator.

Yang Pan: Numerous infections of healthcare providers were reported during the outbreak of SARS. For SARS-CoV-2, healthcare providers are also at high risk of infection, and health-care-associated nosocomial infection is another key concern. Once the health-care-associated nosocomial infection is located, enhanced infection control measures should be implemented in the hospitals, which require extensive resources. Up until now, the transmission route of SARS-CoV-2 has not been fully elucidated. Besides spreading via respiratory droplets and via contact, which have been confirmed, the potential spreading via aerosol and fecal route cannot be ignored. Based on these pieces of evidence and the pathogenicity of SARS-CoV-2, biosafety level 3 laboratory is needed to perform viral isolation and related testing, while clinical samples can be handled in biosafety level 2 laboratory by specialists with appropriate personal protective equipment. Specimen processing after inactivation procedures is also practiced in some laboratories. Although its impact on analytical sensitivity is unknown, the possibility of false-negative results caused by inactivation procedures requires attention.

Carmen Charlton and Nathan Zelyas: In a laboratory setting, universal precautions (gown, gloves, working inside a biosafety cabinet) are sufficient to protect health care workers manipulating primary samples. If aerosol generating procedures are performed outside of a biosafety cabinet, then enhanced level 2 precautions should be used (such as wearing an N95 mask in addition to those listed above).

Healthcare workers looking after the patient should adhere to contact and droplet precautions when caring for a suspect/confirmed case. Nasopharyngeal swabs can be safely collected using contact and droplet precautions, which includes wearing a surgical mask and eye protection; an N95 respirator is not required. If any procedures are being performed where aerosols are being generated (intubation, suctioning the respiratory tract), then airborne precautions should also be implemented, including an N95 respirator and eye protection.

The use of nebulizers could be sources of infection when patients are tightly packed (<1 m apart; https://www.ncbi.nlm.nih.gov/pubmed/20923611). In the SARS outbreak there were a number of factors that led to nosocomially acquired infections in hospital wards, including use of supplemental oxygen, close distance between beds, the availability of hand washing stations, and whether resuscitation was ever performed on the ward (https://www.ncbi.nlm.nih.gov/pubmed/17366443). Given the speculation that SARS-CoV-2 may be transmitted fecal-orally, the availability, and the use of, hand washing stations may be significant in preventing spread within hospital wards.

Daniel Rhoads: The CDC is maintaining up to date laboratory biosafety recommendations based on the current understanding of the virus and the disease. Currently, routine biosafety level 2 laboratory practices are adequate for specimens from patients that may have SARS-CoV-2 infection with the exception that potentially infectious specimens from these patients should be manipulated only in a biological safety cabinet (https://www.cdc.gov/coronavirus/2019-ncov/lab/lab-biosafety-guidelines.html). The CDC explicitly recommends against viral culture from specimens that may contain SARS-CoV-2.

How has the current SARS-CoV-2 outbreak compared to past respiratory virus outbreaks?

Leo Poon: SARS-CoV-2 seems to have high infectivity, with an R_0 of about 2.5. Unlike SARS and MERS, it can spread between humans in early disease onset. In addition, there are asymptomatic cases in this outbreak, a presentation that was not seen in the SARS outbreak. This makes it very challenging to stop the transmission chain. Even worse, most of the world population are immunologically naïve, except for those who have recovered from SARS-CoV-2 infection.

Carmen Charlton and Nathan Zelyas: The transmission for MERS is quite different than what we are currently experiencing with the SARS-CoV-2 outbreak. MERS does not have sustained transmission between humans and is thought to have been re-introduced from multiple zoonotic sources to the human population. This is one reason relatively few cases have been identified (~2500) and the outbreak has not had global spread. The R_0 of MERS is generally considered to be <1, however in nosocomial outbreaks of the disease, mathematical modelling studies have estimated the R_0 to be between 2 and 5.7.

SARS, on the other hand, did have sustained transmission between humans, and led to over 8000 cases. The R_0 of SARS is between 2 and 5, and transmitted through airborne droplets. Transmission was most often seen between close contacts (members in the same household) through direct mucus membrane contact, fomites, and infectious droplet particles. Transmission of SARS was rarely seen in casual contacts, and only in

high exposure settings (on an airplane, aerosolization procedures for healthcare workers, etc.). This is unlike the current outbreak with SARS-CoV-2. Transmission to close and casual contacts has been widespread, with an estimated R_0 value of 1.4-3.9. However, as more information is gathered on the virus, this number may change.

Hilary Babcock: So far, the COVID19 outbreak has spread more widely and affected more people than our last two coronavirus outbreaks, SARS and MERS. While current estimates are that 80% of cases are mild, and the case fatality rate is estimated to be around 2%. However, we still do not really know the extent of asymptomatic or very mild illness. Those patients are unlikely to get diagnosed, so the case fatality rate out of all infected people, not just out of those who are presenting to a healthcare setting for evaluation, may be much lower.

Daniel Rhoads: Recently emerged respiratory viruses include 2009 H1N1 influenza, SARS, and MERS. SARS and MERS were more virulent than SARS-CoV-2, but the outbreaks were smaller in size, either because the person-to-person transmission of SARS and MERS was less likely to occur or because containment was able to be achieved more readily. Of the three viruses mentioned, H1N1 is probably most similar to SARS-CoV-2 in morbidity and mortality. Although many people have died of SARS-CoV-2 worldwide, the fatality rate is much lower than SARS (est. 15% https://www.who.int/csr/sars/en/WHOconsensus.pdf) and MERS (est. 34% https://www.who.int/emergencies/mers-cov/en/). The fatality rates of both H1N1 and SARS-CoV-2 are substantially lower than the SARS and MERS fatality rates (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4528954/pdf/kwv054.pdf; https://smw.ch/article/doi/smw.2020.20203).

How has public perception affected the management of the SARS-CoV-2 outbreak?

Yang Pan: SARS raised public awareness in preparing for an infectious disease outbreak, particularly in China. With wide social acceptance, some strict containment measures were implemented to control the outbreak, including shutting down cross-regional migrations, cancelling public gatherings, school closure, and home isolation. Considering possible presymptomatic transmission and asymptomatic transmission, the containment alone may not be enough to control the outbreak of SARS-CoV-2 in a short period. At least some short-term positive effects, such as reducing the number of cases and delaying the spread of the virus, have been observed. The long-term effectiveness and cost of such measures remain to be determined.

Carmen Charlton and Nathan Zelyas: In Canada (and we imagine in many other areas), the media coverage has prompted a noteworthy level of fear of the virus. Many requests have been received for SARS-CoV-2 testing based on perceived, but not actual, risk of exposure. This has led some jurisdictions to require triage and assessment for all cases, while in other areas, although they have accepted that some requests will be inappropriate, the volume of testing is too much to vet and all requests are tested.

The management of cases from the public health perspective in Canada has been largely rational. In Alberta, for example, any suspect cases are triaged through the Medical Officers of Health, and if the patient is not sick enough to warrant a hospital stay, they are advised to self-isolate until SARS-CoV-2 has been ruled out. Other provinces are using the same strategy to discharge patients who are well enough to return home and to self-isolate so as not to unnecessarily occupy hospital beds, and to mitigate spread of the virus to vulnerable populations (hospitalized individuals).

In rare instances, public perception of the virus originating in China has led to racial prejudice and fear. Some of our Asian staff members, one with a cough, have been targeted over fears for SARS-CoV-2 infection, and many test requests have come in for individuals not meeting requirements for testing. Making voices of public health and clinical experts heard in the media to educate regarding origin and transmission routes of the virus may help promote more rational responses.

Daniel Rhoads: The public's attention on SARS-CoV-2 has increased the number of worried-well presenting to emergency departments with fear that they have been exposed to the virus or have COVID-19 disease. Common diseases are still common, and patients presenting during flu season with influenza-like illness probably have the flu and not the new coronavirus. About 1 in 15 individuals in the US have had flu this season, whereas the incidence of SARS-CoV-2 to date is much lower.

What can be learned so far to improve response strategy and better prepare for future outbreaks? In what ways can professional societies, public health agencies, and regulatory agencies aid in the response to outbreaks similar to SARS-CoV-2?

Yang Pan: SARS-CoV-2 showed some unique characteristics compared with the past respiratory pathogens. Compared with SARS-CoV and MERS-CoV, it showed

a low mortality rate with high transmissibility. Compared with other human coronavirus or seasonal influenza, SARS-CoV-2 caused high morbidity and mortality in older patients and patients with underlying conditions. The first lesson that we learned from SARS-CoV-2 is that pathogens are always changing, and the initial assessment and prediction based on previous knowledge should be revised in a timely manner. Second, improved awareness of early identification of infection caused by novel pathogens is essential for both healthcare providers and public health specialists. Case management and protection for healthcare providers should be implemented as soon as possible. Third, the capability to develop rapid diagnostic testing needs to be constantly maintained for emerging and reemerging infectious diseases. In this outbreak of COVID-19, numerous molecular testing methods and serological methods were developed in a very short amount of time. The full genome of SARS-CoV-2 was sequenced using NGS, which greatly facilitated the outbreak control. The future will likely see the development of even more sensitive, more specific, timely and flexible tests for emerging pathogen detection.

David Persing: We need to rethink the response strategy of simply reacting to "Disease X." Rather, we need to be proactive by building more efficient and accessible pipelines towards better diagnostics and therapeutics to be better prepared for the next outbreak.

Carmen Charlton and Nathan Zelyas: One of the main challenges we are dealing with at the public health laboratory is maintaining supplies for testing. We are experiencing global shortages of many reagents, specimen collection kits, and N95 respirators. Even maintenance of supplies for routine respiratory testing has been challenging, and we have needed to work with multiple different suppliers to maintain normal testing capacity. Following the emergence of the H1N1 pandemic strain, emergency stockpiles of reagents were created, however, the wrong supplies were stocked. Millions of surgical masks are available for use, but N95 respirators were not included in the stockpile, for example. Hospital administrators should be encouraged to talk to their microbiology laboratories in the creation of these emergency stockpiles to ensure they will actually be useful in the event of an emerging issue.

Hilary Babcock: The public health response needs to be both nimble and forward thinking. Guidance that is appropriate for a small number of cases may not be feasible with widespread community transmission. Early access to reliable testing is a key feature of the response that allows better assessment of actual case numbers, geographic and community spread, and appropriateness of control measures.

Daniel Rhoads: Rapid dissemination of information has been beneficial to public health, clinical teams, and the public. There is opportunity to better organize and curate this information and to potentially create template plans for future outbreaks. For example, in our hospital system, we have living documents for different groups of care givers, such as primary care providers, emergency medicine providers, hospitalists, infection control practitioners, laboratory personnel, and environmental services. Each group involved in clinical and public health care plays a different but essential role, and they will each be important in future outbreaks, too. We have the opportunity to work together to create a place online to share guidance documents and checklists tailored toward each patient care role.

Challenges remain at the interface of these different care groups. For example, the CDC prefers NP/oropharyngeal swabs for testing, but we never collect this specimen type as part of routine clinical care. Our institutions have had to decide how to approach this discrepancy. Similarly, primary care providers do not have negative pressure rooms, so if a provider realizes that a patient in the office potentially has this novel infection, there is no way to meet the infection control recommendations due to engineering limitations. These issues are not unique to one institution, and there is opportunity to provide and disseminate practical information more quickly and with a single voice.

Leo Poon: We learned a lot from SARS and MERS incidents. WHO set up a R&D blueprint in 2015 and coronavirus has been always listed as one of the prioritized diseases (https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts). So we have already shown we can learn from the past to prepare for the next big outbreak. COVID-19 emerged only recently. A lot of work has been done in the past few weeks, some of which has led to very successful outcomes. Based on the lessons that we are learning each day about this virus, I am sure there are things that we will improve on for the sake of the future.

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