KFAS covid-19 weekly brief
(31/05/2020)
Introduction

As the COVID-19 continues to impact the wealth and welfare of our society, much remains to be understood about the pandemic and its impact. Hence, the importance of using scientific research, facts and data for a better understanding of the nature of the pandemic, as well as its associated public health issues, to drive policy making in addressing challenges related to healthcare and wellbeing of the population. This newsletter is intended to provide a weekly overview on the latest information on health-related topics surrounding the COVID-19 pandemic, covering five main themes: infection control and prevention, diagnosis and testing, treatment and therapy, training for healthcare professionals and exit strategies. Each edition of the newsletter will cover a specific sub-theme under the five main themes, providing up to date information on available resources, research, data and studies, along with policy recommendations and implications, based on scientific evidence and facts, for decision makers to utilize in developing polices and measures to address the challenges associated with COVID-19 within the healthcare sector.
News Highlights (up to May 12th, 2020)

• Beijing uses smart bracelets to monitors students’ temperatures: CNN
• Doctors continue to discover new ways the coronavirus attacks the body: Washington Post
• Trump administration announces plan to distribute Covid-19 drug amid concerns over allocation: STAT
• AI-centric health companies landed crucial funding in early 2020: STAT
• Telehealth rules have shifted rapidly during the pandemic. Are the changes here to stay?: STAT
• Study Finds Nearly Everyone Who Recovers From COVID-19Makes Coronavirus Antibodies: NIH
• Renewed outbreaks in South Korea, Germany and China show continued risk as more countries seek to reopen: CNN
• Coronavirus can attack your gut as well as your lungs. This is what we know so far: World Economic Forum
Infection Control and Prevention

It is crucial during the COVID-19 pandemic to ensure the safety of healthcare workers and patients. Providing unified guidelines on infection control in all healthcare sectors is essential to maintain a consistent standard of safety for HCWs and patients. This section will outline the main guidelines related to the use of personal protective equipment recommended by the US Center for Disease Control (CDC), the World Health Organization (WHO) and the recommendations by the Ministry of Health of New Zealand.

Diagnosis and Testing

This report provides a technical overview of current diagnostic methods, including recent US FDA approval of three new testing techniques: an antibody assay from pharmaceutical company Roche, an antigen assay from diagnostic company Quidel Corporation, and CRISPR-based technology SHERLOCK.

Treatment and Therapy

During COVID-19 pandemic, when there are no clinically proven treatments, the treatment guidelines were based on evidence from best available clinical studies with patient-important endpoints. The safety of drugs used, especially in patients who are critically ill has not been fully studied. There are multiple promising ongoing trials e.g. Remdesivir, some with adaptive designs, which potentially can quickly answer pressing questions on efficacy and safety of drugs in the treatment of patients with COVID-19.

Training Healthcare Professionals

The rapid transmission of COVID-19 poses a serious threat to healthcare workers (HCW). It also requires HCW to assume roles they do not usually hold. This has led to the urgent need to train HCW on processes and procedures related to infection control, testing, and critical care. The following report will outline key accredited training programs available to HCW and administrators in the following areas: The use of personal protective equipment (PPE), COVID-19 testing procedures, and critical care training for the non-ICU clinician.

Exit Strategy

As more and more countries and government are confronted with the challenge on devising measures to remove the imposed lockdown restrictions to mitigate the impact of COVID-19, the nature of these exit strategies will be based on the three Ts: treatment, testing and tracing.
US Center for Disease Control (USA) guidelines:

**Respirator or Facemask:** (Cloth face coverings are NOT PPE and should not be worn for the care of patients with known or suspected COVID-19 or other situations where a respirator or facemask is warranted)

- Put on an N95 respirator (or higher level respirator) or facemask (if a respirator is not available) before entry into the patient room or care area, if not already wearing one as part of extended use or reuse strategies to optimize PPE supply. Higher level respirators include other disposable filtering facepiece respirators, powered air-purifying respirators (PAPRs), or elastomeric respirators.
- N95 respirators or respirators that offer a higher level of protection should be used instead of a facemask when performing or present for an aerosol generating procedure. Disposable respirators and facemasks should be removed and discarded after exiting the patient’s room or care area and closing the door unless implementing extended use or reuse. Perform hand hygiene after removing the respirator or facemask.
- If reusable respirators (e.g., powered air-purifying respirators PAPRs) are used, they must be cleaned and disinfected according to manufacturer’s reprocessing instructions prior to re-use.
- When the supply chain is restored, facilities with a respiratory protection program should return to use of respirators for patients with known or suspected COVID-19. Those that do not currently have a respiratory protection program, but care for patients with pathogens for which a respirator is recommended, should implement a respiratory protection program.
Eye Protection:
- Put on eye protection (i.e., goggles or a disposable face shield that covers the front and sides of the face) upon entry to the patient room or care area, if not already wearing as part of extended use or reuse strategies to optimize PPE supply. Personal eyeglasses and contact lenses are NOT considered adequate eye protection.
- Remove eye protection before leaving the patient room or care area.
- Reusable eye protection (e.g., goggles) must be cleaned and disinfected according to manufacturer’s reprocessing instructions prior to reuse. Disposable eye protection should be discarded after use unless following protocols for extended use or reuse.

Gloves:
- Put on clean, non-sterile gloves upon entry into the patient room or care area.
  - Change gloves if they become torn or heavily contaminated.
- Remove and discard gloves when leaving the patient room or care area, and immediately perform hand hygiene.
Gowns:

- Put on a clean isolation gown upon entry into the patient room or area. Change the gown if it becomes soiled. Remove and discard the gown in a dedicated container for waste or linen before leaving the patient room or care area. Disposable gowns should be discarded after use. Cloth gowns should be laundered after each use.

- If there are shortages of gowns, they should be prioritized for:
  - Aerosol generating procedures.
  - Care activities where splashes and sprays are anticipated.
  - High-contact patient care activities that provide opportunities for transfer of pathogens to the hands and clothing of healthcare workers. Examples include:
    - dressing
    - bathing/showering
    - transferring
    - providing hygiene
    - changing linens
    - changing briefs or assisting with toileting
    - device care or use
    - wound care

Donning (putting on the gear):

1. Identify and gather the proper PPE to don. Ensure choice of gown size is correct (based on training).
2. Perform hand hygiene using hand sanitizer.
3. Put on isolation gown. Tie all of the ties on the gown. Assistance may be needed by another HCP.
4. Put on NIOSH-approved N95 filtering facepiece respirator or higher (use a facemask if a respirator is not available).
   - If the respirator has a nosepiece, it should be fitted to the nose with both hands, not bent or tented. Do not pinch the nosepiece with one hand.
   - Respirator/facemask should be extended under chin. Both your mouth and nose should be protected. Do not wear respirator/facemask under your chin or store in scrubs pocket between patients.*
   - Respirator: Respirator straps should be placed on crown of head (top strap) and base of neck (bottom strap). Perform a user seal check each time you put on the respirator.
   - Facemask: Mask ties should be secured on crown of head (top tie) and base of neck (bottom tie). If mask has loops, hook them appropriately around your ears.
5. Put on face shield or goggles. Face shields provide full face coverage.
6. Perform hand hygiene before putting on gloves. Gloves should cover the cuff (wrist) of gown.
7. HCP may now enter patient room.

Doffing (taking off the gear):

1. Remove gloves. Ensure glove removal does not cause additional contamination of hands. Gloves can be removed using more than one technique (e.g., glove in glove or bird beak).
2. Remove gown. Untie all ties (or unsnap all buttons). Some gown ties can be broken rather than untied. Do so in gentle manner, avoiding a forceful movement. Reach up to the shoulders and carefully pull gown down and away from the body. Rolling the gown down is an acceptable approach. Dispose in trash receptacle.*
3. HCP may now exit patient room.
4. Perform hand hygiene.
5. Remove face shield or goggles. Carefully remove face shield or goggles by grabbing the strap and pulling upwards and away from head. Do not touch the front of face shield or goggles.
6. Remove and discard respirator (or facemask if used instead of respirator).*
   - Respirator: Remove the bottom strap by touching only the strap and bring it carefully over the head. Grasp the top strap and bring it carefully over the head, and then pull the respirator away from the face without touching the front of the respirator.
   - Facemask: Carefully untie (or unhook from the ears) and pull away from face without touching the front.
7. Perform hand hygiene after removing the respirator/facemask and before putting it on again if your workplace is practicing reuse.

*Facilities implementing reuse or extended use of PPE will need to adjust their donning and doffing procedures to accommodate these practices.

www.cdc.gov/coronavirus
The WHO published a position paper titled: “Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19)”. This document summarizes WHO’s recommendations for the rational use of personal protective equipment (PPE) in health care and community settings, as well as during the handling of cargo. In this context, PPE includes gloves, medical masks, goggles or a face shield, and gowns, as well as for specific procedures, respirators (i.e. N95 or FFP2 standard or equivalent) and aprons. It is intended for those involved in distributing and managing PPE, as well as public health authorities and individuals in health care and community settings. It provides information about when PPE use is most appropriate. The publication outlines the recommended personal PPE needed during the outbreak of COVID-19, according to the setting, personnel, and type of activity. The full publication may be accessed through:

The Ministry of Health (MOH)-New Zealand Government:

The MOH in New Zealand created guidelines for PPE use in health care settings including care provided in homes. The guidelines were developed as a high level reference document. For more details:


<table>
<thead>
<tr>
<th>PPE TYPE</th>
<th>FRONTLINE HEALTH CARE WORKERS</th>
<th>FRONTLINE HEALTH CARE WORKERS</th>
<th>PATIENTS</th>
<th>VISITORS</th>
<th>FAMILY CARERS</th>
<th>CLEANERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGICAL MASKS</td>
<td>Caring for or contact with clients/patients of unknown COVID-19 status</td>
<td>Caring for or contact with patients who meet the case definition for COVID-19</td>
<td>Caring for or contact with patients who meet the case definition for COVID-19</td>
<td>Visiting clients/patients who meet the case definition for COVID-19</td>
<td>Caring for clients/patients who meet the case definition for COVID-19</td>
<td>Current COVID-19 positive case in room or after exit from room</td>
</tr>
<tr>
<td>N95/LE Particulate respirators</td>
<td></td>
<td></td>
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<tr>
<td>GOWNS/ APRONS</td>
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<td>GLOVES</td>
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<tr>
<td>EYE PROTECTION</td>
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<tr>
<td>OTHER MEASURES</td>
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**GOOD HAND HYGIENE PRACTICES AND COUGH/SNEEZE ETIQUETTE.**
Is RT-PCR really the best method for testing?

The rapid global spread of the novel acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and resulting COVID-19 pandemic have led to significant diagnostic evaluation challenges\(^1\). Currently, no therapeutics or vaccines exist as treatments for or prophylactics against COVID-19, making diagnostics essential for controlling the spread of the infection. Testing enables identification, isolation, and contact tracing for quick suppression of disease spread\(^2\). Additionally, results from widespread community testing would play a major role in informing any governmental plans to lift lockdown restrictions before an effective vaccine or treatment is made available where the infection rate is expected to rebound rapidly\(^3\).

Diagnostic tests can be divided into three categories based on the technique: molecular diagnostic methods, serological methods (more commonly known as antibody tests or rapid tests), and computer tomography and imaging methods. The molecular diagnostic method RT-PCR remains the primary choice for diagnostics among healthcare providers worldwide. This brief will describe the different testing tools that are currently available or in development, their advantages and disadvantages, as well as how testing strategies can be used to achieve the goals of suppressing the resurgence of local outbreaks, gaining intelligence on the epidemic, and identifying people who have developed some form of immunity and can safely return to work\(^2,3\).

**Molecular Diagnostic Methods**

RT-PCR is only 66-80% sensitive most likely due to inefficiencies in patient sampling.

Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) tests involve obtaining viral RNA samples from the upper and lower respiratory tracts of subjects, reverse transcribing the genetic material into DNA, increasing the copies of that converted DNA, and checking for the presence of the virus\(^2\). While RT-PCR remains the primary means for diagnosing COVID-19, it’s not without limitations and is only 66-80% accurate. This means that 20-34% of patients with COVID-19 out of 100 would test negative despite being infected, the wide range of sensitivity due to variation in testing time and sample preparation. A single test, therefore, is not sufficient to rule out infection and repeat testing should be performed\(^4\).

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While it is possible to obtain a false negative due to wrong patient sampling or sample processing, a positive result is less likely to be incorrect\(^5\). The United States Center for Disease Control uses a one-step real time RT-PCR assay and there are different implementation workflows for RT-PCR tests in clinical settings\(^2\).

**RT-PCR only identifies those infected at the time of testing and not those previously infected.**

Another disadvantage to PCR is its reliance on the virus being present in the sample taken, since the detectable viral load depends on the number of days between virus onset and testing. In the initial 14 days of illness SARS-CoV-2 was most reliably detected in Sputum followed by nasal swabs. Throat swabs have been found unreliable eight days after symptom onset. Upper respiratory samples are generally recommended, however lower respiratory samples are recommended for patients exhibiting a productive cough. Upper tract samples include nasopharyngeal swabs, oropharyngeal swabs, nasopharyngeal washes, and nasal aspirates. Lower respiratory tract samples include sputum, Bronchoalveolar lavage (BAL) fluid and tracheal aspirates, however BAL fluid and tracheal aspirates are at high risk for aerosol generation\(^5\). The CDC recommends collecting samples from the upper respiratory tract for initial testing\(^6\). A recent study comparing nasal swabs to sputum samples found a significant statistical difference in diagnosing positive results. In a study assessing 52 subjects, sputum analysis identified 40 positive cases (76%) while the throat swabs method identified 23 positive cases (44.2%), suggesting a higher efficiency. Another recent study indicates that viral loads were found to be higher in nasal swabs in comparison to throat swabs. Finally, a third study found the highest positive rates in BAL fluid specimens (93%), followed by sputum (72%), and nasal swabs (63%)\(^7\).

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6. CDC.gov “Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Person for Coronavirus Disease 2019 (COVID-19)” May 5th, 2020

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*Figure 1. Distribution of RT-PCR results on throat swabs and sputum specimens in patients with suspected COVID-19*  
Clinical Chemistry and Laboratory Medicine (CCLM) 2020; 10.1515/cclm-2020-0187
The main disadvantages of RT-PCR are related to logistics

Whether it’s the intense workload of processing procedures or the limited supply of needed materials such as reagents and swabs, the main drawbacks of using RT-PCR testing to diagnose COVID-19 are related to logistics. Samples take a couple hours to process, but logistics surrounding transporting the samples and communicating the results substantially increase the time it takes for the patient to get their results. Furthermore, obtaining samples depends on the availability of swabs and reagents in short supply due to increased global demand. Point of care tests and automated extraction RT-PCR techniques that would enable testing on site at hospitals and testing locations outside of centralized facilities have been developed. This would reduce the burden on clinical laboratories, but the techniques are proprietary to the companies that have optimized them and are a limited by specialized equipment and required reagents.8,9

Isothermal Amplification is a molecular diagnostic technique currently in development to enable point-of-care testing.

Test Name: Isothermal Amplification techniques

How it works

The technique is performed at a single temperature unlike RT-PCR and therefore does not need the same specialized laboratory instruments to provide accurate results. One example of these techniques is Loop-mediated Isothermal Amplification (LAMP). LAMP uses DNA polymerase and 4-6 primers to target the viral genome and is highly specific due to the higher number of primers in comparison to RT-PCR techniques. A sample from a patient is added to a tube and a positive result is easily detected by a change in the turbidity, color, or fluorescence of the solution within an hour.9

Advantages

LAMP exhibits increased sensitivity and specificity due to increased primers, is significantly rapid (less than one hour for results) and does not require expensive reagents or devices. Furthermore, LAMP enables point-of-care qualitative confirmation of positive results by a change in turbidity, color or fluorescence.

Disadvantages

The disadvantage of LAMP is that the primers and reaction times need to be optimized which can be significantly challenging. Similar to RT-PCR, a positive LAMP result identifies who is currently infected at the time of the test and cannot detect if the patient has had the virus and recovered. The test is also dependent on the virus being present at the site the sample was taken from. Other isothermal amplification techniques are still in development as well.

CRISPR technologies create new solutions to testing problems and technique has been granted emergency approval by the United States Food and Drug Administration (US FDA).

Besides thermal amplification, CRISPR technology can be utilized to test for SARS-CoV-2\textsuperscript{11}. CRISPR/Cas9 is a powerful gene editing technology harnessed from a bacterial immune system with the potential to treat human disease. More recently, Cas13, another protein naturally found in bacteria, has been found to allow for the detection of diseases in humans\textsuperscript{12}. Two testing techniques are suggested by MIT and Harvard University’s Broad Institute and are detailed in the section below. A third technique from Mammoth Biosciences called DNA endonuclease targeted CRISPR trans reporter (DETECTR) is also in development. DETECTR is currently being evaluated as per guidelines from the FDA but has not been approved yet for use as a clinical diagnostic. DETECTR is also found to be less sensitive than PCR-based testing and is therefore not discussed in the section below\textsuperscript{13}.

**Test Name:** Specific High-Sensitivity Enzymatic Reporter Unlocking (SHERLOCK)

**How it works**

This detection technique uses a Cas13a ribonuclease and CRISPR-based detection system to detect viral RNA. Similar to RT-PCR a nasal, throat, or BAL swab is used to obtain a sample. The RNA target is reverse transcribed into cDNA and amplified using the RT-PCR system, next the samples are transcribed back into RNA. If viral target RNA is present in the sample, the Cas13a ribonuclease will bind to the target, activate and produce a fluorescent signal.

**Advantages**

Studies demonstrate SHERLOCK was able to detect ZIKA virus presence at low viral concentrations in samples, as low as 1 copy per microliter\textsuperscript{14}. The test is as sensitive and specific as RT-PCR techniques in addition to being rapidly field deployable. SHERLOCK techniques have been optimized for rapid detection during viral outbreaks. Optimizations of this technique have enabled it to detect viruses directly in bodily fluids such as saliva or blood, using minimal lab equipment, reducing the costs associated with testing\textsuperscript{14}. A protocol for detecting SARS-COV-2 has been released\textsuperscript{15}. On May 7\textsuperscript{th}, 2020 the US FDA granted emergency use authorization to the diagnostics company, Sherlock Biosciences for the production of SHERLOCK test kits which delivers results within one hour\textsuperscript{16}.

**Disadvantages**

CRISPR detection techniques like SHERLOCK, still rely on an RNA extraction step that is time consuming and dependent on reagents and equipment being available. Despite recent optimization, this disadvantage remains.

\textsuperscript{10} CEBM.net Center for Evidence-Based Medicine develops, promotes, and disseminates better evidence for healthcare “What tests could potentially be used for the screening, diagnosis, and monitoring of COVID-19 and what are their advantages and disadvantages?” April 20, 2020
\textsuperscript{12} MIT McGovern Institute (mcgovern.mit.edu) “Researchers advance CRISPR-based tool for diagnosing disease” February 15, 2018
\textsuperscript{16} Sherlock.bio Press Release May 7, 2020
**Test Name:** Combinatorial Arrayed Reactions for Multiplexed Evaluation of Nucleic Acids (CARMEN)

**How it works**

Recently developed by researchers at MIT, CARMEN combines CRISPR-based detection technology and microfluidics to produce a rubber diagnostic chip, slightly larger than an iPhone, able to perform thousands of tests simultaneously to detect viruses\(^1\). The rubber chip is designed to hold thousands of micro-compartments or wells, each developed to hold a pair of nanoliter-sized droplets, one containing the sample and the other containing detection reagents. The sample is obtained and processed in the same way as RT-PCR and SHERLOCK but the CARMEN technique differs in the detection mixture which contains the CRISPR protein Cas13, a guide RNA to target the viral sequence, and a reporter molecule to detect results. In the presence of a target virus the Cas13 protein will bind and activate the reporter molecule to produce a fluorescent signal visible under a fluorescence microscope.

**Advantages**

Adapted from SHERLOCK technology, the advantage of CARMEN is the ability to test many samples at once while simultaneously testing for multiple pathogens to enable routine surveillance and epidemiological insight\(^1\). The technology has been validated in patient samples and provides same day results. CARMEN can perform more than 4,500 samples in a single chip\(^1\). CARMEN-Cas13 matches the sensitivity of SHERLOCK and PCR-based assays and reduces concerns of off-target amplification common in other nucleic acid detection methods. This in addition to successful testing data published in Nature on April 29\(^{th}\) 2020 indicates that ‘this approach could readily be translatable in the clinic’ according to the MIT research team\(^1\).

**Disadvantages**

CARMEN still relies on the same extraction techniques as RT-PCR which are time consuming and dependent on reagents and equipment being available. The test is also dependent on the virus being present at the site the sample was taken from\(^2\).

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18. CEBM.net Center for Evidence-Based Medicine develops, promotes, and disseminates better evidence for healthcare “What tests could potentially be used for the screening, diagnosis, and monitoring
## Molecular Diagnostics

<table>
<thead>
<tr>
<th></th>
<th>RT - PCR</th>
<th>LAMP</th>
<th>CRISPR (SHERLOCK)</th>
<th>CRISPR (CARMEN)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How it works</strong></td>
<td>Detects the presence of viral genetic material in a sample</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tests for current infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Tests for previous infection</strong></td>
<td></td>
<td>No</td>
<td>A Positive result means viral RNA is currently present in the patient</td>
<td></td>
</tr>
<tr>
<td><strong>Time to receive results</strong></td>
<td>2-4 hours to process the samples but due to the logistics results are typical received days after testing</td>
<td>1 hour to deliver results</td>
<td>1 hour to deliver results</td>
<td>Same day results for thousands of samples at once</td>
</tr>
<tr>
<td><strong>Most common use for this test</strong></td>
<td>Currently the standard to detect current cases of infection</td>
<td>Point-of-care qualitative assessment of current infection</td>
<td>High sensitivity rapid identification of current cases could be optimized for front line workers</td>
<td>To scale capabilities or from community surveillance and to test for multiple viral infections at once.</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Accepted by medical staff as robust and well documented</td>
<td>Positive results cause the reaction mix to turn cloudy allowing for easy identification</td>
<td>Viral detection at low concentrations for more accurate testing</td>
<td>Can test more than 4,500 samples in a single chip.</td>
</tr>
<tr>
<td></td>
<td>The technology is already available</td>
<td></td>
<td>Optimized for rapid detection using saliva or blood</td>
<td>Matches the sensitivity of SHERLOCK</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Relies on the virus being present in the sample taken. Previous infections are not detected</td>
<td>Newer and less established than RT - PCR</td>
<td>Like RT - PCR this test relies on a time-consuming RNA extraction step</td>
<td>Like RT- PCR this test relies on a time-consuming RNA extractions step</td>
</tr>
<tr>
<td></td>
<td>Limited by the availability of swabs and reagents in high demand globally</td>
<td>Previous infections are not detected</td>
<td>Making it dependent on reagents and equipment being available that are currently in short supply</td>
<td>Making it dependent on reagents and equipment being available that are currently in short supply</td>
</tr>
<tr>
<td><strong>FDA Approval?</strong></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

*Figure 2. Summary of Molecular Diagnostic Methods*
Serological testing or Antibody testing reveals who has had the infection in the past and might be safe to return to work and has recently been approved for use by the FDA.

**Test Name:** Antibody based Immunoassay (Serological Tests)

**How it works**

Serological tests measure the body’s immune response to the infection rather than the infection itself. The assay identifies the presence of anti-viral antibodies, IgG and IgM present in the blood when the body responds specifically to COVID-19. These tests are most often used to assess overall infection and immunity rates in a community.

**Advantages**

The technique allows healthcare professionals to identify those who have been infected in the past and therefore might be immune and potentially able to safely return to work. They can be laboratory based or used for point-of-care assessment depending on the design of the test. The FDA recently granted emergency use authorization to the company Roche for the production of rapid detection antibody tests, which allegedly have a specificity greater than 99.8% and a sensitivity of 100% fourteen days after an RT-PCR test confirms infection and can be used to assess patients’ immune response. The pharmaceutical company, Roche also claims to be able to deliver millions of tests per month currently to the US and Europe. Healthcare company Abbott Laboratories was also granted emergency approval for an antibody test kit on May 11, 2020 with similar sensitivity and specificity to the Roche test and can deliver results in as little as 5 minutes.

**Disadvantages**

Since the immune system can take a few days to respond to infection, antibodies may not be detected in early days of infection. Because of this antibody tests are not recommended for diagnosing active cases of COVID-19, and molecular diagnostic tests such as RT-PCR would be necessary to confirm patients who currently have the virus and patients who have recovered from the virus but still test positive using the antibody tests.

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19. Foundation for Innovative New Diagnostics (Finddx.org) “COVID-19 Diagnostics are tests used to detect infection with the SARS-COV-2 Virus” March 24, 2020
20. Diagnostics.roche “Roche’s COVID-19 antibody test receives FDA Emergency Use Authorization and is available in markets accepting the CE mark” May 03, 2020
22. FDA.gov “FDA Statement COVID-19 Update Serological Tests” April 07, 2020
Antigen Testing has recently been granted emergency use authorization by the FDA to enable rapid point-of-care detection of COVID-19.

The most urgent priority for COVID-19 diagnostics research, based on the WHO, is the development of techniques that would allow point-of-care testing. Lateral Flow Antigen detecting tests are currently being developed to detect the presence of viral material. One such test has been authorized emergency use approval by the US FDA.

**Test Name:** Antigen Based Immunoassay Test

**How it Works**

The test uses antibodies specific to the antigens of the COVID-19 virus and detects the presence of these viral antigens or proteins in the sample. The test is also adaptable to nucleic acid testing.

**Advantages**

The tests are cheap, easy to produce, and results can be obtained within minutes. On May 9th, 2020 the FDA authorized the use of the first antigen test to ‘help in the rapid detection of the virus’ from the manufacturer Quidel Corporation. The test, dubbed the Sofia 2 SARS Antigen FIA, was authorized for use in high and moderate complexity laboratories and for point-of-care testing in approved facilities.

**Disadvantages**

While the test is very specific to the virus it is less sensitive than RT-PCR techniques, meaning while positive results are likely to be accurate there is a higher chance of false negatives, thus the FDA concludes that negative results from an antigen test would need to be confirmed with a RT-PCR test to avoid spreading the virus due to false negatives. A test that detects IgM and IgG has been found to possess a sensitivity of 82%.

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24. FDA.gov “FDA Authorizes First Antigen Test to Help in the Rapid Detection of the Virus that Causes COVID-19 in Patients” May 09, 2020
Computer Tomography (CT) exams have a high sensitivity in making an early diagnosis of COVID-19 while X-rays have a poor sensitivity.

Computer Tomography (CT) scans are a useful diagnostic tool for the diagnosis of COVID-19. The largest CT diagnostic study found a 95% sensitivity in early diagnosis of the virus using the characteristic identification of ground glass opacities, meaning five out of 100 tests will be falsely negative. Another significant study found CT sensitivity was 98% compared to 71% for RT-PCR for patients tested within three days of admission into a hospital. The use of CT scans is suggested to prevent infected patients visiting the hospital from being discharged back into the community. The drawback for testing using CT scans is the substantial cost and economic burden it could place on healthcare resources as well as the potential contamination of CT scanners. Chest X-rays alternatively, have been found to have a poor sensitivity, however if the presence of ground glass opacities is noted then it is recommended the patient be isolated.

<table>
<thead>
<tr>
<th>Serological Tests</th>
<th>Antibody Tests</th>
<th>Antigen Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How it works</strong></td>
<td>Detects the presence of antibodies in a sample</td>
<td>Detects the presence of viral proteins or antigens in a sample</td>
</tr>
<tr>
<td><strong>Test for current infection</strong></td>
<td>A Positive result could mean you are recovering from the virus or have had it in the past. Follow up RT – PCR is recommended to confirm present or previous infection</td>
<td>No</td>
</tr>
<tr>
<td><strong>Tests for previous infection</strong></td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td><strong>Time to receive results</strong></td>
<td>Roche Antibody test Elecsys provides results in 18 minutes or 300 tests/hour</td>
<td>Quidel test Sofia 2 SARS Antigen FIA delivers results in 15 minutes.</td>
</tr>
<tr>
<td><strong>Most common use for this test</strong></td>
<td>To assess the overall infection and immunity rates in a community. Could be used to screen for current infection.</td>
<td>Screening for suspected COVID-19 cases. Positive results are followed up with RT-PCR to confirm current infection.</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Rapid detection, easy to use, low cost, can be supplied globally and used at point-of-care facilities 99.8% specificity reported 100% sensitivity reported</td>
<td>Rapid detection, easy to use, low cost, can be supplied globally and used at point-of-care facilities</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Test dependent on patient immune response which takes a few days to respond to infection</td>
<td>Higher rate of false negatives than PCR tests and should also be followed up with RT-PCR testing</td>
</tr>
<tr>
<td><strong>Antibodies may not detect in early days of infection and RT-PCR is recommended to confirm Negative Results</strong></td>
<td>Typically, false negatives are less desirable than false positives</td>
<td></td>
</tr>
<tr>
<td><strong>US FDA Approval</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Figure 3. Summary of Serological Testing Methods

**THE COVID-19 TESTING PROCESS**

1. **SPECIMEN COLLECTION**
   - Nasopharyngeal swab
   - Oropharyngeal swab

2. **SPECIMEN TRANSPORT**
   - Viral Transport Medium in Biohazard Bag

3. **VIRUS INACTIVATION**
   - in a Bio Safety Level 2 Cabinet

4. **VIRAL RNA EXTRACTION**
   - with specialized RNA Extraction Kit

5. **COVID-19 DETECTION via RT-PCR TESTING**
   - GenAmpify COVID-19 Detection Kit by MTek, Fortitude Kit 2.0 by A*Star, Coronavirus Detection Kit by Sansure Biotech

6. **RESULTS GENERATION**

7. **REPORT**
   - after 48 hrs
Treatment and Therapy: Current Guidelines

With few definitive studies published but volumes of information being circulated, Infectious Diseases Society of America (IDSA), National Institute of Health (NIH), and many other international entities have formulated interim guidance for managing patients with COVID-19 infections.

These Treatment Guidelines have been developed to inform clinicians how to care for patients with COVID-19, the Guidelines will be updated frequently as published data and other authoritative information becomes available.

Therapeutic options under investigation:

At present, no drug has been proven to be safe and effective for treating COVID-19. There is no Food and Drug Administration (FDA) approved drugs specifically to treat patients with COVID-19, definitive clinical trial data are needed to identify optimal treatments for this disease. However, there have been some specific guidelines developed on treatments that have and have not shown progress, as well as issuing an Emergency Use Authorization (EUA) for promising investigational drugs for the treatment of suspected or laboratory confirmed COVID-19. Guidelines provide guidance to manufacturers and advising developers on how to handle clinical trial issues and keep the public informed.

1. Antivirals:

- **Hydroxychloroquine** is an antimalarial drug also used in treating autoimmune diseases. It also inhibits replication of different viruses by interfering with viral protein maturation. Hydroxychloroquine and chloroquine have shown antagonism against COVID-19 in vitro and was at some point considered as potential treatment, however, they have not been shown to be safe and effective for treating or preventing COVID-19 in patients. They are being studied in clinical trials for COVID-19, and FDA authorized their temporary use during the pandemic for treatment of hospitalised patients through EUA.

According to IDSA COVID-19 Treatment Guidelines and NIH guidelines there are insufficient clinical data to recommend either for or against using chloroquine or hydroxychloroquine for the treatment of COVID-19.

The IDSA COVID-19 Treatment Guidelines Panel recommends against the use of the Hydroxychloroquine and chloroquine when they are combined with the antibiotic **azithromycin**. Hydroxychloroquine and chloroquine can cause abnormal heart rhythms such as QT interval prolongation and rapid heart rate called ventricular tachycardia. These risks may increase with **azithromycin**.
• **Remdesivir** is a broad spectrum antiviral with in-vitro activity against a range of RNA viruses including SARS-CoV. Its use improved disease outcomes and reduced viral loads in SARS-CoV infected mice. Hospitalised patients with advanced COVID-19 and lung involvement who received remdesivir had a 31% faster recovery time than patients who received placebo, and a mortality rate of 8% versus 11.6% for the placebo group.¹

The FDA is discussing making remdesivir available for patients as quickly as possible, and on May, 1st 2020 the EUA by FDA was granted allowing the drug to be given to patients with COVID-19 only if they are severely ill - with blood oxygen levels at least at 94% or lower or otherwise requiring supplemental oxygen². However, this authorization is not permanent. Remdesivir is still an investigational drug that needs to get authorization from FDA. Therefore, there are insufficient clinical data to recommend either for or against using the investigational antiviral drug remdesivir for the treatment of COVID-19. (IDSA COVID-19 Treatment Guidelines and NIH guidelines)

• **Lopinavir-ritonavir** is a combination of protease inhibitors for the treatment of HIV infection. It inhibits viral growth, infectivity and replication. **Lopinavir-ritonavir** has been shown to have in-vitro antiviral activity against SARS-CoV, and MERS-CoV, but except in the context of a clinical trial the IDSA COVID-19 Treatment Guidelines Panel recommends against the use of the Lopinavir-ritonavir or other HIV protease inhibitors for the treatment of COVID-19, because of unfavourable pharmacodynamics and negative clinical trial data³.

2. Immune Based Therapy

• **COVID-19 Convalescent Plasma for prophylaxis**

There is a long history of using convalescent plasma as treatment for infectious diseases, including several viral lower respiratory tract infections. Individuals who have recovered from SARS-CoV-2 infection may generate neutralizing antibodies. A trial from patients recovered from SARS-CoV-2 infection for use as prophylaxis in adults with high-risk exposure is expected to begin recruiting shortly. On May 1st 2020, FDA has issued guidance to provide recommendations on the administration and study of investigational convalescent plasma collected from COVID-19 recovered individuals during the public health emergency⁴.

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1. www.covid19treatmentguideline.nih.gov
2. www.cnn.com
3. www.idsociety.org
4. www.fda.gov
The IDSA due to insufficient clinical data does not recommend either for or against the use of convalescent plasma or hyperimmune immunoglobulin for the treatment of COVID-19. However, the FDA has limited the administration to severe or immediately life-threatening COVID-19, for example, blood oxygen saturation ≤ 93%, respiratory frequency ≥ 30/min.

- Interleukins inhibitors are immunosuppressive agents which are used to manage inflammatory conditions. Interleukin-6 (IL-6) inhibitors may ameliorate severe damage to lung tissue caused by a cytokine storm along with other inflammatory mediators release in patients with serious COVID-19 infections. There are still insufficient clinical data to recommend either for or against the use of the following agents for the treatment of COVID-19:
  - Interleukin-6 inhibitors (e.g., sarilumab, siltuximab, tocilizumab)
  - Interleukin-1 inhibitors (e.g., anakinra)

- Interferons a group of signalling proteins which have the ability to interfere with viral replication, however, because of lack of efficacy in treatment of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and toxicity. IDSA panel recommends against its use.

- The IDSA Panel recommends against the use of other immunomodulators, such as: Janus kinase inhibitors (e.g., baricitinib), because of their broad immunosuppressive effect.

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Pharmaceutical company</th>
<th>Stage</th>
<th>Notes and updates</th>
<th>Concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>Antimalarial drug sold under the brand</td>
<td>Sanofi</td>
<td>Phase 3</td>
<td>April 20: The company started phase III trial</td>
<td>• Risk of cardiac arrhythmias.</td>
</tr>
<tr>
<td>HCQ and chloroquine CQ</td>
<td>Name Plauenil which is FDA approved for lupus and rheumatoid arthritis.</td>
<td>Clinical trial</td>
<td></td>
<td>Assessing hydroxychloroquine. FDA agreed to launch a study of 440 patients sponsored by Norvartis 5.</td>
<td>• Risk of retinal damage.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Caution in G6PD deficiency patients.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Caution in diabetics.</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Remdesivir, is an intravenous treatment prevents viral replication. It was developed as an all-purpose antiviral.</td>
<td>Gilead sciences</td>
<td>Phase 3</td>
<td>May 1: The FDA issues an emergency use authorization EUA for remdesivir, allowing the drug to be used in limited cases. May 7: Japan›s health ministry approves remdesivir to treat Covid-19 6.</td>
<td></td>
</tr>
</tbody>
</table>
### Remdesivir and Baricitinib

Baricitinib is an anti-inflammatory Janus kinase inhibitor used as treatment for adults with rheumatoid arthritis.

NIAID* conducts and supports the study at NIH. Baricitinib is licensed to Eli Lilly and Company by Incyte and marketed under the brand name Olumiant.

Clinical trial

May 8: Controlled clinical trial evaluating the safety and efficacy of a treatment regimen of the investigational antiviral remdesivir plus the anti-inflammatory drug baricitinib for COVID-19 has begun. The trial is now enrolling hospitalized adults with COVID-19 in the United States1.

### Lopinavir-Ritonavir

It inhibits viral growth, infectivity and replication.

AbbVie

Pre-clinical

May 7: In hospitalised adults with severe COVID-19, no benefit was observed with Lopinavir-Ritonavir treatment beyond standard care. 7

- Risk of cardiac arrhythmias.
- Caution in patients with hepatic disease.
- Significant drug interactions.

### Convalescent plasma

Individuals who have recovered from SARS-CoV-2 infection may generate neutralizing antibodies.

Grifols

Pre-clinical

May 1st: FDA has issued guidance to provide recommendations on the administration and study of investigational convalescent plasma collected from COVID-19 recovered individuals during the public health emergency 4.

Risk of transfusion related acute lung injury or a theoretical risk of Antibody-dependent enhancement of infection ADE.

### IL-6 inhibitor Tocilizumab (Actemra)

Immunosuppressive agent.

Genentech

Phase 2/3 trial

April: working with FDA to initiate phase 3 clinical trial 5.

- IL-6 inhibitor can be immunosuppressive and potentially increase risk of secondary infections.
- Risk of hepatotoxicity.
- Caution in patients with thrombocytopenia and neutropenia.
Training Opportunities for Health Care Providers on Personal Protective Equipment

The rapid transmission of COVID-19 poses a serious threat to healthcare workers (HCW). According to the WHO, over 22,000 HCW have been infected by COVID-19 globally. The protection of first responders and HCW should be one of the top priorities of the healthcare system. It is crucial to keep them safe and healthy during the COVID-19 pandemic. One essential way of ensuring the safety of HCW, first responders, and patients is providing training programs for the proper use of personal protective equipment (PPE). To ensure that PPE is properly utilized and to ease the demand for PPE, it is recommended that all HCW are adequately trained in the use of PPE. Training should include:

• When to use PPE
• What type of PPE is necessary
• How to properly don (put on), and doff (take off) PPE
• How to properly dispose of or disinfect, inspect for damage, and maintain PPE
• The limitations of PPE
• Minimizing self-contamination.
• Guidance on extended use or limited re-use of PPE (in the case of any shortage)

Formal training of HCWs on infection control protocols and the use of PPE has been shown to improve clinical outcomes. A recently accepted study by Wenhui et al. evaluated an emergency training program developed for the use of PPE for general HCWs dealing with COVID-19 in China. They found that the training program significantly improved the performances of participants when comparing pre- and post-test scores. The study also found that most staff in the pre-test scores were deficient in the use of N95 respirators. Additionally, the staff’s post-test “proficiency level” was low. The course addressed these issues by adding flow charts and “mutual checks” where people work in dyads to help each other with PPE and infection control. The study utilized a high-fidelity simulation center to conduct the training. Simulation-based approaches have been widely used in protective skill training against infectious diseases. Simulation enables medical staff to become familiar with the actual environment and workflow. It can also help to identify potential deficiencies. A recent Cochrane review on the effects of PPE on preventing self-contamination in HCW found that face-to-face training in PPE use may reduce errors more than “folder-based” training.
However, with the current restriction of social distancing, training may have to be delivered online. Ideally, online training should be supplemented with live simulation and assessment for competency. Only trained and competent staff should then be allowed to work with COVID-19 patients or patients under investigation.

It must be noted that PPE should be part of a more extensive infection control protocol and should be implemented as part of a multimodal strategy for the management of COVID-19 patients. Again, only clinical staff who are trained and competent in the use of PPE should be allowed to enter the patient’s room. Refresher courses should also be conducted to maintain the quality of the procedures.

The following chart is a list of accredited free online resources that may be utilized to train individuals that require to use PPE during the COVID-19 pandemic

<table>
<thead>
<tr>
<th>Source</th>
<th>Description of training materials</th>
<th>Recommended for</th>
<th>Link to PPE training</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nation Institute of Health (NIH)-National Institute of Environmental Health Sciences</strong></td>
<td>In-depth webinars and training on a variety of issues related to PPE: 1. The use of PPE in relation to modes of transmission. 2. Best practices in protecting HCW from exposure to COVID-29 3. Train the trainer on worker safety and infection control. In-depth evidence-based training material in the form of PDF documents and slides related to protecting HCW through PPE and infection control</td>
<td>MOH leadership Hospital administrators Heads of departments Preventative medicine officers</td>
<td><a href="https://tools.niehs.nih.gov/wetp/index.cfm?id=2592">https://tools.niehs.nih.gov/wetp/index.cfm?id=2592</a></td>
</tr>
</tbody>
</table>
## Source: World Health Organization (WHO)

<table>
<thead>
<tr>
<th>Recommended courses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How to put on and remove personal protective equipment (PPE): Two modules that detail donning and doffing of PPE according to droplet and airborne precautions for COVID-19</td>
</tr>
<tr>
<td>2. Standard precautions: Hand hygiene course</td>
</tr>
<tr>
<td>3. Infection Prevention and Control (IPC) for Novel Coronavirus (COVID-19): The course is a more comprehensive course that provides information on what facilities should be doing to be prepared to respond to a novel coronavirus, how to identify a case once it occurs, and how to properly implement IPC measures to ensure there is no further transmission to HCW or to other patients and others in the healthcare facility. <strong>The course is also offered in Arabic</strong></td>
</tr>
<tr>
<td>4. ePROTECT Respiratory Infections: This course provides a general introduction to acute respiratory infections and basic hygiene measures to protect against infection. The course consists of 4 modules that introduce the learner to the basic principles of acute respiratory infections, how to assess the risk of infection and basic hygiene measures to protect against infection.</td>
</tr>
</tbody>
</table>

WHO online course participants receive a certificate of achievement if they score at least 70% on a post-test

<table>
<thead>
<tr>
<th>Recommended for</th>
</tr>
</thead>
<tbody>
<tr>
<td>All healthcare workers and administrators</td>
</tr>
<tr>
<td>Healthcare workers</td>
</tr>
<tr>
<td>Hospital administrators</td>
</tr>
<tr>
<td>Heads of departments</td>
</tr>
<tr>
<td>Preventative medicine officers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Link to PPE training</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="https://openwho.org/courses/IPC-PPE-EN">https://openwho.org/courses/IPC-PPE-EN</a></td>
</tr>
<tr>
<td><a href="https://openwho.org/courses/IPC-HH-en">https://openwho.org/courses/IPC-HH-en</a></td>
</tr>
<tr>
<td><a href="https://openwho.org/courses/COVID-19-IPC-EN">https://openwho.org/courses/COVID-19-IPC-EN</a></td>
</tr>
<tr>
<td><a href="https://openwho.org/courses/eprotect-acute-respiratory-infections">https://openwho.org/courses/eprotect-acute-respiratory-infections</a></td>
</tr>
</tbody>
</table>

## Source: High Speed Training

<table>
<thead>
<tr>
<th>High speed training offers an online training course used by the NHS. The course provides trainees with the knowledge and techniques needed to safely use (PPE) within a healthcare setting. The course has 4 modules:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How to Use Healthcare PPE: Part 1</td>
</tr>
<tr>
<td>2. How to Use Healthcare PPE: Part 2</td>
</tr>
<tr>
<td>3. Changing, Disposal, Storage, and Maintenance of PPE</td>
</tr>
<tr>
<td>4. PPE Training for Healthcare Workers Assessment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare workers and front liners</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Link to PPE training</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="https://www.highspeedtraining.co.uk/health-and-safety/ppe-training-for-healthcare.aspx">https://www.highspeedtraining.co.uk/health-and-safety/ppe-training-for-healthcare.aspx</a></td>
</tr>
</tbody>
</table>
Training Opportunities for Health Care Providers on Essential Skills

COVID-19 Testing:

Testing for COVID-19 is an essential part of dealing with the pandemic. New testing centers will have to be set up for widespread testing. With the pandemic putting extreme pressure on the health care system, students and volunteers from the healthcare system are stepping up to assist with the testing process. Testers will require training to ensure safe and correct testing of patients and the safety of those professionals who will be administering the tests.

The following chart is a list of free accredited online resources that may be utilized to train individuals that will be required to conduct testing during the COVID-19 pandemic.

<table>
<thead>
<tr>
<th>Source</th>
<th>Description of training materials</th>
<th>Recommended for</th>
<th>Link to PPE training</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAIN</td>
<td>TRAIN is a learning network that provides quality training opportunities for professionals who protect and improve the public’s health. Many COVID-19 specific courses are offered. The platform provides training material from multiple reputable organization under one roof. The courses offered are form multiple source: CDC, WHO, VHA...etc.</td>
<td>Healthcare workers and front liners</td>
<td><a href="https://www.train.org/main/welcome">https://www.train.org/main/welcome</a></td>
</tr>
<tr>
<td>Penn Foster in collaboration with Southern New Hampshire University</td>
<td>30-minute complete course on: • Content of the testing kit • Proper patient and specimen identification • Correct medical procedures for nasal and throat swabs • Guidelines for storing specimens • PPE</td>
<td>Healthcare workers and front liners</td>
<td><a href="https://www.pennfoster.edu/covid19-testing-training">https://www.pennfoster.edu/covid19-testing-training</a></td>
</tr>
</tbody>
</table>
Critical Care Training for the non-ICU clinician during COVID-19 pandemic

Critically ill patients have increased significantly in the COVID-19 pandemic surge. Consequently, healthcare systems have quickly become overwhelmed with patients. To cope with high volume of patients that require critical care, healthcare workers from other clinical areas will be required to work in the ICU. This pattern has been seen in different parts of the world. Physicians, trainee doctors, nurses, and other health care providers from specialties areas other than critical care medicine may be required to practice in a critical care environment. In preparation for this scenario, training for the above groups must be provided. Ideally, training should be under the direct supervision of a critical care physician or nurse. However, the following chart is a list of free accredited online resources that may be utilized to train licensed healthcare providers to work in the ICU.

<table>
<thead>
<tr>
<th>Source</th>
<th>Description of training materials</th>
<th>Recommended for</th>
<th>Link to PPE training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Care Education Pandemic Preparedness University of Toronto Toronto Academic Health Sciences Network (TAHSN)</td>
<td>Quick, accessible learning resources and reference materials for those who are upskilling, renewing, or reviewing their knowledge and skill for redeployment to critical care during the COVID-19 global pandemic. • Short lectures • Procedural videos • Pocket cards • Additional resources</td>
<td>Physicians, Nurses, Respiratory therapists, Other Clinicians</td>
<td><a href="https://www.quickicutraining.com">https://www.quickicutraining.com</a></td>
</tr>
<tr>
<td>OSLER ICU skills for the non-intensivist</td>
<td>A collection of modules designed to support the upskilling of doctors who do not usually practice in the intensive care unit who are asked to work in the critical care setting during the COVID-19 outbreak. Modules cover theory, resuscitation, airway management, basic procedures, advanced procedures, and multiple simulation scenarios.</td>
<td>General practitioners, Junior doctors, Family medicine, Internists, Surgeons</td>
<td><a href="https://osler.force.com/covid/s/ward-to-icu">https://osler.force.com/covid/s/ward-to-icu</a></td>
</tr>
<tr>
<td>edX Harvard University</td>
<td>Mechanical Ventilation for COVID-19 A comprehensive course that provides licensed medical professionals with an understanding of mechanical ventilation so they can support the critical care team caring for patients receiving mechanical ventilation during the COVID-19 pandemic.</td>
<td>Non-ICU hospital clinicians</td>
<td><a href="https://www.edx.org/course/mechanical-ventilation-for-covid-1">https://www.edx.org/course/mechanical-ventilation-for-covid-1</a></td>
</tr>
<tr>
<td>World Health Organization (WHO)</td>
<td>Clinical Care of Severe Acute Respiratory Infection: A hands-on practical guide to be used by health care professionals involved in clinical care management during the COVID-19 pandemic. By the end of the course participants should possess some of the necessary tools that can be used to care for the critically ill patient from hospital entry to hospital discharge. The course consists of 14 modules and a total of 10 hours of training.</td>
<td>Clinicians who are working in the ICUs in low and middle-income countries and managing adult and pediatric patients with severe forms of acute respiratory infection</td>
<td><a href="https://openwho.org/courses/severe-acute-respiratory-infection">https://openwho.org/courses/severe-acute-respiratory-infection</a></td>
</tr>
</tbody>
</table>
Exit/Recovery Strategies

Exit Strategies

The “New Normal” and the Triple Ts

For past five months, countries have been dealing with the dire repercussions of the COVID-19 pandemic, each with their own national response to mitigate the impact of the disease. As the economic and social pressures of the restrictions start to burden societies, several countries have started to reflect on the lessons learned, and devise exit strategies from the ongoing restrictions that have been imposed to mitigate and prevent the onset of infections. While exit strategies may vary depending on the nature of the pandemic in a particular country and its relation to the “peak” of infection, as well as the availability of particular resources, there are several common characteristics amongst most of the national strategies for lifting restrictions and exiting from the current situation (herein referred to as exit strategy). Most of these plans focus on the 3T’s: Treatment, Testing, and Tracing1,2.

Treatment is safest exit strategy

Without a doubt, the safest exit strategy is having an effective vaccine or treatment in place and available in mass quantities for distribution. Scientific cooperation is leading to accelerated progress towards developing an effective treatment and vaccine, or both, with several ongoing clinical trials some showing progress and potential, such as Remdesivir3. While there is much effort on this front, the lack of both, at this time, make exit strategies more complicated, and require considerations for the other 2 Ts: testing and tracing.

2. Peto et al. Lancet_2020
Testing and Tracing are essential to successful exit strategies

As countries start to devise what their strategies would look like and entail without an approved treatment or vaccine, most are turning to the success of other countries that have started to open economies and try to remove some of lockdown restrictions to regain a sense of “normalcy”, such as such as South Korea, Singapore, Taiwan, Germany and Sweden in mitigating and preventing the onset of COVID-19\textsuperscript{4}. The lessons learned from their experiences, as well as those from other countries and region, along with the critical support of scientific data and evidence, have provided general frameworks for a progressive exit strategies, which include\textsuperscript{5,6,7}:

1. **Mass Testing:** The diagnostic capacity and capability of each country would need to be drastically scaled up to implement mass testing. This is essential to reopening the economy, without the worry about a second, more severe, surge. Both RNA and serology testing should be used to support the greater population as a whole, providing information on the potential transmission in hot spots and the risk profile of individuals.

2. **Contact Tracing:** Along with testing, using technology to implement an effective disease surveillance and control mechanism for monitoring and tracking and spread of the virus, is the most effective strategy for mitigating and preventing the onset of second surge. Countries, such as South Korea, Singapore and Taiwan, imposed these measures almost immediately, curbing the impact of the virus and spread of infection drastically.

3. **Social Distancing Measures:** Elements of social distancing measures to reduce overall transmission should continue so that healthcare systems are not overburdened. This also allows for strained healthcare facilities and personnel time to recover and address logistical and strategic shifts needed to prevent the onset of a greater surge in the anticipated second wave. This also involves ensuring that there is an effort to restock or purchase appropriate medical and laboratory equipment, including personal protective equipment for all healthcare professionals and first responders.

4. **Continuous Monitoring of the Infection Status:** Both testing and tracing need to be complemented by quantitative mathematical modeling that provides projections and forecasts that can be used by policymakers to drive new actions or policies. The incidence rate\textsuperscript{8}, doubling rate\textsuperscript{9}, case contacts\textsuperscript{10}, and testing positivity rate\textsuperscript{11} should all be monitored and uses as thresholds and techniques for analyzing the infection profile of the country.

\textsuperscript{5} Joint European Roadmap towards lifting COVID-19 containment measures; European Council
\textsuperscript{6} Mitigating COVID-19 With Lockdowns: A Possible Exit Strategy Rakesh Sarwal, MBBS, DrPH (Johns Hopkins) and Tanvi Sarwal,MBBS Intern (MAMC); Date written: 29.3.2020;
\textsuperscript{7} TESTING FOR COVID-19: A WAY TO LIFT CONFINEMENT RESTRICTIONS © OECD 2020
\textsuperscript{8} Incidence Rate it defined as the number of new cases within a time period, as a proportion of the number of people at risk.
\textsuperscript{9} Number of days needed to double the number of infected people
\textsuperscript{10} Number of contacts generated per case (assuming to be one or less)
\textsuperscript{11} Proportion of all people testing positive
5. Considerations for workforce: There are several questions regarding how workplaces should reopen and what future workplace would look like. In an article in Nature Medicine, the Gilbert et al. recommend that people of working age but that are considered high risk for COVID-19 should be exempt from returning to work encouraged to work remotely\textsuperscript{12}. This will require a tailored approach for each country, to maximize the social acceptance, which will be key in implementation. In order of priority, those that are immunized should be the first to return to work, followed younger, lower risk individuals, who are virus free but not immunized, slowly building “herd immunity”, and potentially reducing the intensity of a second surge of infections. The goal is to shift from comprehensive lockdown and social distancing measures, to a more targeted, systematic approach: testing, tracing and targeted confinement measures.

6. Importance of Public Awareness: It is vital that governments are transparent and consider community acceptance as a part of any plan moving forward for the “new normal”. Adequate, transparent and timely public information, in all languages applicable to the population should be consistently provided and updated.

\textsuperscript{12} Gilbert et al. Nature Medicine; April 14, 2020