

Early Guidelines and Protocols About COVID-19

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In just six months, the coronavirus changed the world very quickly. The protocols and guidelines to face and to manage the pandemic of COVID-19 is as fast as the changes in people's lives during this period. However, some policies, protocols and guidelines are established. This article compiled the global management strategies for COVID-19 infection pandemic preparedness, the issues about peaking of the outbreak, and "flattening the curve", and the guidelines and protocols by World Health Organization (WHO), Center for Disease Control (CDC), Brazil Ministry of Health, European Union guidelines, Panamerican Health Organization (PAHO), the protocols of China, Belgium, Italy, Netherlands, and Infectious Diseases Society of America (IDSA). We searched the data in the main database (PubMed/Medline, Elsevier Science Direct, Scopus, Isi Web of Science, Embase, Excerpta Medica, UptoDate, Lilacs, Novel Coronavirus Resource Directory from Elsevier), and in the health Organizations around the world, such as World Health Organization, Panamerican Health Organization (PAHO), Center for Disease Control, National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID). We prior selected meta-analysis, systematic reviews, article reviews and original articles in this order. We reviewed 41 articles and sites and used 20 from March to June 2020, adopting the terms coronavirus, SARS-CoV-2, novel coronavirus, Wuhan coronavirus, severe acute respiratory syndrome, 2019-nCoV, 2019 novel coronavirus, n-CoV-2, covid, n-Sars-2, COVID-19, corona virus, coronaviruses, protocols, guidelines, CDC, WHO, European Union, PAHO, China, Italy, IDSA, with the tools MeSH (Medical Subject Headings), AND, OR, and characters [,“; /, to ensure the best review topics. We concluded that all guidelines and protocols tend to use WHO as a reference with particular differences between countries. Also, the more the COVID-19 is known, the more the protocols and guidelines change. **Keywords:** COVID-19. SARS-CoV-2. Guidelines. Protocols.

Introduction

The current knowledge about epidemiology, pathogenesis, treatments, protocols and guidelines of COVID-19 disease is updating quickly so that as we are writing this paper a novel information is being publishing. Nevertheless, there is some establishing knowledge and management about the disease that we could present here, however regarding protocols and guidelines, which are the aim of this review, the reports change all the time. The objective of this manuscript was to summarize the updating protocols and guidelines against COVID-19 adopted from the main centers in the world (World Health Organization (WHO),

Center for Disease and Preventing Control (USA), the European protocols, and Infectious Diseases Society of America) in order to present an overview about systematic procedures and actions established against the COVID-19 by full reproduce.

Pandemic Preparedness

WHO and other leading epidemiology organizations universally recognize the indispensable task of pandemic preparedness and a project at global and national levels to mitigate the public health emergency of COVID-19 or any future outbreaks. Pandemic preparation is an effort of the government and the society requiring inputs from each person susceptible to the infection agente as well as policy makers at national and international levels, frontline healthcare providers, infrastructure developers and maintenance personnel, pharmaceutical industry and researcher community, and so forth. Moreover, the pandemic

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preparedness project needs constant reviewing and improvisation [1, 2].

The magnitude of the COVID-19 pandemic requires worldwide action plans. The United States quickly created the United Nations' Strategic Preparedness and Response Plan (SPRS) to control the transmission of the virus in order to delaying the spread of COVID-19, provide optimal care for all patients, and minimize the impact on healthcare systems and socioeconomic activities. Several nations are well placed to implement this action plan with minimal support. However, each country has its own issues that the place authority has to adjust the guidelines and protocols for the reality of each country or district. Thus, all nation has to prepare a COVID-19 Country Preparedness and Response Plan (CPRP) against the COVID-19 [1]. These CPRPs need constant monitoring and reviewing using indicators shared by WHO and CDC, for example, updating as the situation evolves. Part of these plans is the protocols and guidelines adopted in each country [3].

Saxena [1] reported that the success against a pandemic is grounded in the following actions, which have to be included in the protocols and guidelines:

- Surveillance of the pathogen: characterization of the pathogen, epidemiology, transmission, symptoms, pathogenesis, diagnosis and detection, testings, infection, contact tracing, data from confirmed cases, predicting mass infection outbreak, keeping a count, and estimation of mortality.
- Response management: production and supply of protective/preventive pharmaceutical interventions or non-pharmaceutical interventions; extensive test the community, education of the Community about the disease and how it spreads, transmit and all information about the disease.
- Medical help: access to hospitals/healthcare providers, personal and public hygiene, disinfection, and quarantine services.
- Lesson from the present outbreak to facilitate future action strategies and preparedness.

Global Management Strategies for COVID-19 Infection

The authorities of worldwide and Health Organizations created strategies, which including protocols and guidelines, due to the exponential transmission of SARS-CoV-2 and social-economic impact of the pandemic [4-6], such as:

- Social distancing;
- Travel restrictions;
- Implementation of personal and public hygiene (non-pharmaceutical interventions);
- Implementation of diagnosis (clinical with symptoms and laboratorial);
- Extensive testing for community;
- Medicines interventions.

All these practices (Figure 1) delay the peaking of the outbreak, avoid burden on the healthcare infrastructure, "flattening the curve" of the infected patients (Figure 2) [7].

In the sections below, we presented the guidelines and some protocols from WHO and CDC in the combat against COVID-19.

World Health Organization (WHO) Guidelines

Individual protections against the transmission of COVID-19 between the the people is following [9]:

- Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash them with soap and water. Why? Washing your hands with soap and water or using alcohol-based hand rub kills viruses that may be on your hands.
- Maintain at least 1 metre (3 feet) distance between yourself and others. Why? When someone coughs, sneezes, or speaks they spray small liquid droplets from their nose or mouth which may contain virus. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person has the disease.
- Avoid going to crowded places. Why? Where people come together in crowds, you are more

Figure 1. Tips to prevent coronavirus transmission and alert about symptoms.

COVID-19

Coronavirus Disease 2019

BE AWARE.

COVID-19 is a new respiratory illness that was first discovered in Wuhan, China. It is transmitted from person to person.

SYMPTOMS*

RUNNY NOSE

COUGH

SORE THROAT

HIGH FEVER

PNEUMONIA

SEVERE RESPIRATORY DISEASE

COMMON SYMPTOMS

SEVERE CASES

*Symptoms may appear 1 to 12 days following exposure to the virus

Who is most at risk of becoming seriously ill?

- People over age 60
- People with pre-existing conditions such as diabetes and heart disease

How is it transmitted?

- Through close contact with an infected person
- By an infected person coughing or sneezing
- By touching contaminated objects or surfaces and then touching your mouth, nose or eyes

Currently there is no vaccine or specific treatment. We can only treat the symptoms. Serious cases may require oxygen and ventilatory support.

PREPARE.

- Make sure you get your information from a reliable source.
- Wash your hands regularly with soap and water or use an alcohol-based gel.
- Cover your mouth with the inside of your elbow when you cough or sneeze or use a tissue and dispose of used tissue immediately and wash your hands.

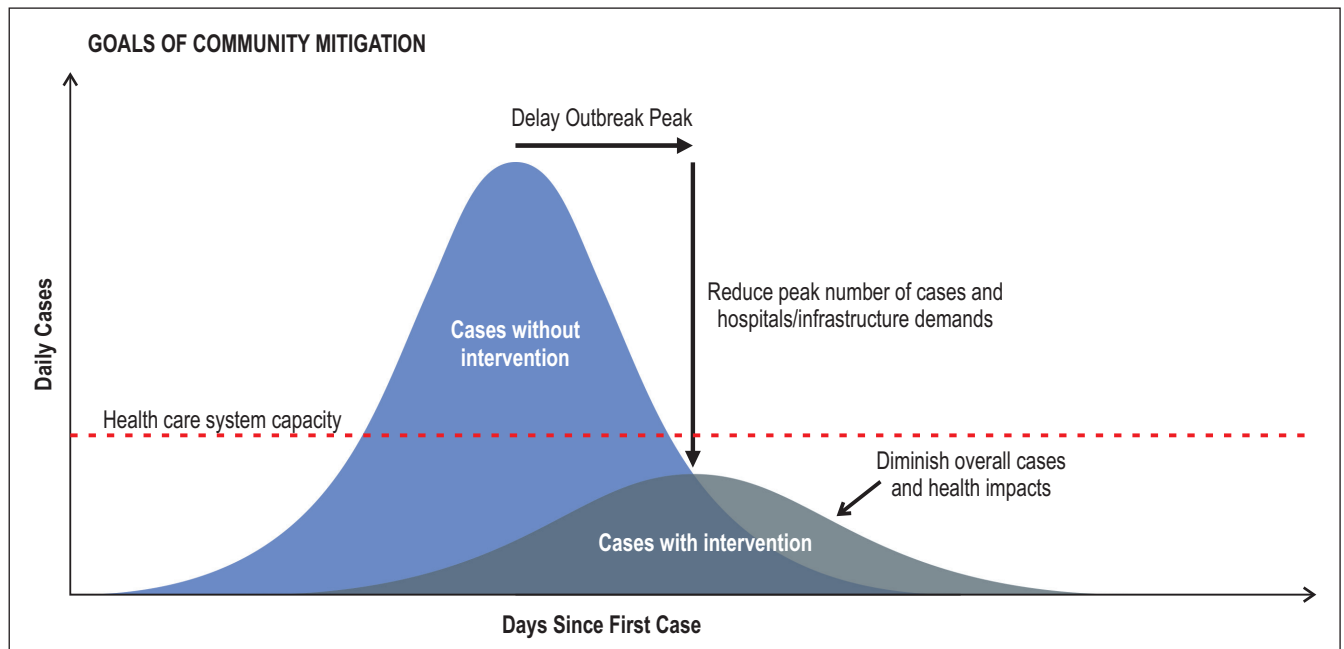
ACT.

- Avoid close contact with people who have flu-like symptoms.
- Avoid touching your eyes, nose or mouth with unwashed hands.
- Avoid sharing cups, plates or other personal items and disinfect all surfaces that are touched frequently.
- If you have traveled to areas where COVID-19 is circulating or have been in contact with someone who has it and you experience fever, cough or difficulty breathing, seek medical attention immediately. Do not self-medicate.

Note: Information may change when more is known about the disease. February 2020.

BE AWARE. PREPARE. ACT.
www.paho.org/coronavirus

source: PAHO [8].

Figure 2. Flattering the curve.

likely to come into close contact with someone that has COVID-19 and it is more difficult to maintain physical distance of 1 metre (3 feet).

- Avoid touching eyes, nose and mouth. Why? Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose or mouth. From there, the virus can enter your body and infect you.
- Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately and wash your hands. Why? Droplets spread virus. By following good respiratory hygiene, you protect the people around you from viruses such as cold, flu and COVID-19.
- Stay home and self-isolate even with minor symptoms such as cough, headache, mild fever, until you recover. Have someone bring you supplies. If you need to leave your house, wear a mask to avoid infecting others. Why? Avoiding contact with others will protect them from possible COVID-19 and other viruses.

- If you have a fever, cough and difficulty breathing, seek medical attention, but call by telephone in advance if possible and follow the directions of your local health authority. Why? National and local authorities will have the most up to date information on the situation in your area. Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also protect you and help prevent spread of viruses and other infections.
- Keep up to date on the latest information from trusted sources, such as WHO or your local and national health authorities. Why? Local and national authorities are best placed to advise on what people in your area should be doing to protect themselves.

Center for Disease Control (CDC)

Protecting Yourself and Others Against COVID-19 and Related Informations [10]

Knowing How It Spreads

- There is currently no vaccine to prevent coronavirus disease 2019 (COVID-19).

- The best way to prevent illness is to avoid being exposed to this virus.
- The virus is thought to spread mainly from person-to-person.
 - o Between people who are in close contact with one another (within about 6 feet).
 - o Through respiratory droplets produced when an infected person coughs, sneezes or talks.
 - o These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs.
 - o Some recent studies have suggested that COVID-19 may be spread by people who are not showing symptoms.
- o Cover your mouth and nose with a cloth face cover when around others.
- You could spread COVID-19 to others even if you do not feel sick.
- Everyone should wear a cloth face cover when they have to go out in public, for example to the grocery store or to pick up other necessities.
 - o Cloth face coverings should not be placed on young children under age 2, anyone who has trouble breathing, or is unconscious, incapacitated or otherwise unable to remove the mask without assistance.
- The cloth face cover is meant to protect other people in case you are infected.
- Do NOT use a facemask meant for a healthcare worker.
- Continue to keep about 6 feet between yourself and others. The cloth face cover is not a substitute for social distancing.

Wash Your Hands Often

- Wash your hands often with soap and water for at least 20 seconds especially after you have been in a public place, or after blowing your nose, coughing, or sneezing.
- If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of your hands and rub them together until they feel dry.
- Avoid touching your eyes, nose, and mouth with unwashed hands.

Avoid Close Contact

- Avoid close contact with people who are sick, even inside your home. If possible, maintain 6 feet (1.5 meters) between the person who is sick and other household members.
- Put distance between yourself and other people outside of your home.
 - o Remember that some people without symptoms may be able to spread virus.
 - o Stay at least 6 feet (about 2 arms' length) from other people.
 - o Do not gather in groups.
 - o Stay out of crowded places and avoid mass gatherings.
 - o Keeping distance from others is especially important for people who are at higher risk of getting very sick.

Cover Coughs and Sneezes

- If you are in a private setting and do not have on your cloth face covering, remember to always cover your mouth and nose with a tissue when you cough or sneeze or use the inside of your elbow.
- Throw used tissues in the trash.
- Immediately wash your hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.

Clean and Disinfect

- Clean AND disinfect frequently touched surfaces daily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.
- If surfaces are dirty, clean them. Use detergent or soap and water prior to disinfection.
- Then, use a household disinfectant. Most common EPA-registered household disinfectants external icon will work.

Monitor Your Health

- Be alert for symptoms. Watch for fever, cough,

shortness of breath, or other symptoms of COVID-19.

- o Especially important if you are running essential errands, going into the office or workplace, and in settings where it may be difficult to keep a physical distance of 6 feet.
- Take your temperature if symptoms develop.
 - o Don't take your temperature within 30 minutes of exercising or after taking medications that could lower your temperature, like acetaminophen.
- Follow CDC guidance if symptoms develop.

Steps to Help Prevent the Spread of COVID-19 If You Are Sick

If you are sick with COVID-19 or think you might have COVID-19, follow the steps below to care for yourself and to help protect other people in your home and community.

Stay Home Except to Get Medical Care

- Stay home. Most people with COVID-19 have mild illness and can recover at home without medical care. Do not leave your home, except to get medical care. Do not visit public areas.
- Take care of yourself. Get rest and stay hydrated. Take over-the-counter medicines, such as acetaminophen, to help you feel better.
- Stay in touch with your doctor. Call before you get medical care. Be sure to get care if you have trouble breathing, or have any other emergency warning signs, or if you think it is an emergency.
- Avoid public transportation, ride-sharing, or taxis.
- Separate yourself from other people. As much as possible, stay in a specific room and away from other people and pets in your home. If possible, you should use a separate bathroom. If you need to be around other people or animals in or outside of the home, wear a cloth face covering.

Monitor Your Symptoms

- Symptoms of COVID-19 fever, cough, or other symptoms.

- Follow care instructions from your healthcare provider and local health department. Your local health authorities may give instructions on checking your symptoms and reporting information.

When to Seek Emergency Medical Attention

Look for emergency warning signs* for COVID-19. If someone is showing any of these signs, seek emergency medical care immediately:

- Trouble breathing.
- Persistent pain or pressure in the chest.
- New confusion.
- Inability to wake or stay awake.
- Bluish lips or face.

Call the Emergence Number or Your Doctor

Notify that you are seeking care for someone who has or may have COVID-19.

Call Ahead Before Visiting Your Doctor

- Call ahead. Many medical visits for routine care are being postponed or done by phone or telemedicine.
- If you have a medical appointment that cannot be postponed, call your doctor's office, and tell them you have or may have COVID-19. This will help the office protect themselves and other patients.

We also presented here the new section of the CDC about the Guidelines for pharmacological adjuvant treatment for COVID-19 (reviewed by CDC in May 12, 2020) [11].

Management of Persons with COVID-19

(Last updated June 11, 2020)

In general, adults with COVID-19 can be grouped into the following severity of illness categories, although the criteria in each category may overlap or vary across guidelines and clinical trials:

*This list is not all possible symptoms. Please call your medical provider for any other symptoms that are severe or concerning to you.

- **Asymptomatic or Presymptomatic Infection:** Individuals who test positive for SARS-CoV-2 by virologic testing using a molecular diagnostic (e.g., polymerase chain reaction) or antigen test, but have no symptoms.
- **Mild Illness:** Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging.
- **Moderate Illness:** Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SpO_2) $\geq 94\%$ on room air at sea level.
- **Severe Illness:** Individuals who have respiratory frequency >30 breaths per minute, $\text{SpO}_2 < 94\%$ on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) < 300 mmHg, or lung infiltrates $> 50\%$.
- **Critical Illness:** Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

In pediatric patients, radiographic abnormalities are common and, for the most part, should not be used as the sole criteria to define COVID-19 illness category. Normal values for respiratory rate also vary with age in children, thus hypoxia should be the primary criteria to define severe illness, especially in younger children.

CDC Guidelines for Pharmacological Treatment of Patients

Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can experience a range of clinical manifestations, from no symptoms to critical illness.

Currently, the Food and Drug Administration has not approved any drugs for the treatment of COVID-19. However, an array of drugs approved for other indications, as well as multiple investigational agents, are being studied for the treatment of COVID-19 in several hundred

clinical trials around the globe. Some drugs can be accessed through Emergency Use Authorization, expanded access programs, or compassionate use mechanisms.

Antithrombotic Therapy in Patients with COVID-19

COVID-19 has been associated with inflammation and a prothrombotic state, with increases in fibrin, fibrin degradation products, fibrinogen, and D-dimers. Although the true incidence of thrombosis is unknown, there have been reports of increased incidence of thromboembolic disease associated with COVID-19 in patients in the intensive care unit.

A new section titled Antithrombotic Therapy in Patients with COVID-19 has been added to the guidelines to address many questions related to the role of coagulation markers and thrombolytic, anticoagulant, and antiplatelet agents in those with COVID-19. The COVID-19 Treatment Guidelines Panel (the Panel) provides recommendations on the use of antithrombotic agents for the prevention of venous thromboembolic events in hospitalized patients with COVID-19. In addition, the Panel recommends carefully monitoring, evaluating, and treating hospitalized patients with COVID-19 for incident thrombotic events when indicated.

Potential Antiviral Drugs Under Evaluation for the Treatment of COVID-19

Study descriptions were updated to clearly indicate a study's publication status and to provide an assessment of a study's limitations and results. Data were also updated as needed based on changes to preprints or post-publication changes.

The following recommendations were added or revised in this section:

Remdesivir

The COVID-19 Treatment Guidelines Panel recommends the investigational antiviral

agent remdesivir for treatment of COVID-19 in hospitalized patients with $\text{SpO}_2 \leq 94\%$ on ambient air (at sea level) or those who require supplemental oxygen, as well as who are on mechanical ventilation or extracorporeal membrane oxygenation (ECMO), or not intubated receive 5 days of remdesivir. If the patients have not shown adequate improvement after 5 days of therapy, besides there are insufficient data on the optimal duration of therapy for mechanically ventilated patients, patients on ECMO, or patients who have not shown adequate improvement after 5 days of therapy, in these groups, some experts extend the total remdesivir treatment duration to up to 10 days.

There are insufficient data for the Panel to recommend for or against remdesivir for the treatment of patients with mild or moderate COVID-19.

Lopinavir/Ritonavir and Other HIV Protease Inhibitors (Last updated May 12, 2020)

Rationale for Recommendation

The pharmacodynamics of HIV protease inhibitors raise concern regarding whether drug levels adequate to inhibit the SARS-CoV-2 protease can be achieved with oral dosing. Also, lopinavir/ritonavir was studied in a small randomized controlled trial in patients with COVID-19 with results that did not show efficacy.

Chloroquine or Hydroxychloroquine

The Panel recommends against the use of chloroquine or hydroxychloroquine for the treatment of COVID-19, except in a clinical trial.

Hydroxychloroquine plus Azithromycin (Last updated May 12, 2020)

The Panel recommends against the use of hydroxychloroquine plus azithromycin for the treatment of COVID-19, except in the context of a clinical trial.

Rationale for Recommendation

Chloroquine and hydroxychloroquine for COVID-19 have been used in small randomized

trials and in some case series with conflicting study reports. The combination of hydroxychloroquine and azithromycin is associated with QTc prolongation in patients with COVID-19. Given the long half-lives of both azithromycin (up to 72 hours) and hydroxychloroquine (up to 40 days), caution is warranted even when the two drugs are used sequentially instead of concomitantly.

New Sections of the Guidelines

Acute Kidney Injury and Renal Replacement Therapy

The Panel recommends continuous renal replacement therapy (CRRT) in critically ill patients with COVID-19 who have acute kidney injury and who develop indications for renal replacement therapy. If CRRT is not available or not possible due to limited resources, the Panel recommends prolonged intermittent renal replacement therapy rather than intermittent hemodialysis. The primary rationale for these recommendations is to reduce the risk of transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to health care workers, since there is no evidence that one modality is more beneficial than another.

Immune-Based Therapy

- There are insufficient data to recommend either for or against the use of COVID-19 convalescent plasma or SARS-CoV-2 immune globulins for the treatment of COVID-19.
- The COVID-19 Treatment Guidelines Panel (the Panel) recommends against the use of non-SARS-CoV-2-specific intravenous immune globulin (IVIG) for the treatment of COVID-19, except in the context of a clinical trial. This should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.
- There are insufficient data to recommend either for or against the use of the following agents for the treatment of COVID-19:
 - Interleukin-1 inhibitors (e.g., anakinra)

- Interleukin-6 inhibitors (e.g., sarilumab, siltuximab, tocilizumab)
- Except in the context of a clinical trial, the Panel recommends against the use of other immunomodulators, such as:
 - Interferons, because of the lack of efficacy in treatment of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and toxicity.
 - Janus kinase inhibitors (e.g., baricitinib), because of their broad immunosuppressive effect.

Interleukin-1 Inhibitors

New clinical data from a single-center case series and a single-center retrospective cohort study that evaluated the use of anakinra to treat of COVID-19 have been added. There is no change to the Panel's recommendation for interleukin-1 inhibitors.

There are no Food and Drug Administration-approved drugs for the treatment of COVID-19. Although reports have appeared in the medical literature and the lay press have claimed that patients with COVID-19 have been successfully treated with a variety of agents, definitive clinical trial data are needed to identify safe and effective treatments for this disease. Recommended clinical management of patients with COVID-19 includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. As in the management of any disease, treatment decisions ultimately reside with the patient and their health care provider.

Interleukin-6 Inhibitors

(Last updated June 11, 2020)

Recommendation

- There are insufficient data to recommend either for or against the use of interleukin-6 (IL-6) inhibitors (e.g., sarilumab, siltuximab, tocilizumab) for the treatment of COVID-19.

IL-6 is a pleiotropic, pro-inflammatory cytokine produced by a variety of cell types, including

lymphocytes, monocytes, and fibroblasts. Infection by the related SARS-associated coronavirus induces a dose-dependent production of IL-6 from bronchial epithelial cells. Elevations in IL-6 levels may be an important mediator when severe systemic inflammatory responses occur in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. COVID-19-associated systemic inflammation and hypoxic respiratory failure is associated with heightened cytokine release, as indicated by elevated blood levels of IL-6, C-reactive protein (CRP), D-dimer, and ferritin.

Sarilumab

Sarilumab is a recombinant humanized anti-interleukin-6 receptor (IL-6R) monoclonal antibody that is approved by the Food and Drug Administration (FDA) for use in patients with rheumatoid arthritis. It is available as a subcutaneous (SQ) formulation and is not approved for cytokine release syndrome (CRS). A placebo-controlled clinical trial is evaluating the use of an intravenous (IV) formulation administered as a single dose for COVID-19.

The SQ formulation of sarilumab is not approved for CRS. The IV formulation is not approved by the FDA, but it is being studied in a clinical trial of hospitalized patients with COVID-19.

Siltuximab

Siltuximab is a recombinant human-mouse chimeric monoclonal antibody that binds IL-6 and that is approved by the FDA for use in patients with Castleman's disease. Siltuximab prevents the binding of IL-6 to both soluble and membrane-bound IL-6R, inhibiting IL-6 signaling. Siltuximab is dosed as an IV infusion. There are limited, unpublished data describing the efficacy of siltuximab in patients with COVID-19. There are no data describing clinical experiences using siltuximab for patients with other novel coronavirus infections (i.e., severe acute respiratory syndrome [SARS], Middle East respiratory syndrome).

Tocilizumab

Tocilizumab is a recombinant humanized anti-IL-6R monoclonal antibody that is approved by the FDA for use in patients with rheumatologic disorders and CRS induced by chimeric antigen receptor T cell (CAR-T) therapy. Tocilizumab can be dosed for IV or SQ injection. For CRS, the IV formulation should be used.

Immune-Based Therapy Under Evaluation for Treatment of COVID-19

Convalescent Plasma and Immune Globulins

New information has been added to the section on convalescent plasma and SARS-CoV-2-specific immune globulins. A new section for non-SARS-CoV-2 intravenous immune globulin (IVIG) was created, in which the Panel recommends against the use of non-SARS-CoV-2-specific IVIG for the treatment of COVID-19, except in the context of a clinical trial (AIII). This should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.

Corticosteroids

Preliminary clinical trial data from a large, randomized, open-label trial suggest that dexamethasone reduces mortality in hospitalized patients with COVID-19 who require mechanical ventilation or supplemental oxygen.

The recommendations for using corticosteroids in patients with COVID-19 depend on the severity of illness. Before initiating dexamethasone, clinicians should review the patient's medical history and assess the potential risks and benefits of administering corticosteroids to the patient.

Recommendations

- The Panel recommends using dexamethasone (at a dose of 6 mg per day for up to 10 days) in patients with COVID-19 who are mechanically ventilated and in patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated.

- The Panel recommends against using dexamethasone in patients with COVID-19 who do not require supplemental oxygen.

It has been proposed that the anti-inflammatory effects of corticosteroids have a potential therapeutic role in suppressing cytokine-related lung injury in patients with COVID-19. Data from other respiratory infections have shown that systemic corticosteroids can affect the pathogenesis of these infections in various ways. In outbreaks of other novel coronavirus infections⁵ (i.e., Middle East respiratory syndrome [MERS] and severe acute respiratory syndrome [SARS]), corticosteroid therapy was associated with delayed virus clearance. In severe pneumonia caused by influenza, corticosteroid therapy may worsen clinical outcomes, including secondary bacterial infection and mortality.

For Management of COVID-19

- The Panel recommends using dexamethasone (at a dose of 6 mg per day for up to 10 days) in patients with COVID-19 who are mechanically ventilated and in patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated.
- The Panel recommends against using dexamethasone in patients with COVID-19 who do not require supplemental oxygen.

Usefull Links

In the section below we presented the links for interventions, protocols, guidelines and guidance for COVID-19 followed by the majority of countries – International and government guidelines for general care – as well as other usefull links.

General

World Health Organization. Coronavirus disease (COVID-19) pandemic
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.

Centers for Disease Control and Prevention. United States Department of Health and Human Services. Coronavirus (COVID-19)
<https://www.cdc.gov/coronavirus/2019-ncov/index.html>.

Food and Drug Administration. United States Department of Health and Human Services. Coronavirus Disease 2019 (COVID-19)
<https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-COVID-19>.

European Centre for Disease Prevention and Control. An agency of the European Union. COVID-19
<https://www.ecdc.europa.eu/en/COVID-19-pandemic>.

Pandemic Preparedness
<https://www.ecdc.europa.eu/en/seasonal-influenza/preparedness/why-pandemic-preparedness>.
<https://www.who.int/docs/default-source/coronavirus/covid-19-sprp-unct-guidelines.pdf>.
https://www.who.int/influenza/preparedness/pandemic/WHO_Guidance_for_surveillance_during_an_influenza_pandemic_082017.pdf.

Diagnostic
<https://www.finndx.org/COVID-19>.
<https://ourworldindata.org/coronavirus-testing-source-data>.
 Epidemiological surveillance (https://wwwnc.cdc.gov/eid/article/25/1/17-1901_article)

Cochrane Database of Systematic Reviews
<https://www.cochranelibrary.com>.

Internacional

World Health Organization (WHO): Country and technical guidance – Coronavirus disease (COVID-19)
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications>

- Surveillance protocol for SARS-CoV-2 infection among health workers
https://www.who.int/publications-detail/WHO-2019-nCoV-HCW_Surveillance_Protocol-2020.1
- Interim guidance on clinical management of COVID-19

<https://www.who.int/publications-detail/clinical-management-of-COVID-19>

- Cleaning and disinfection of environmental surfaces in the context of COVID-19
<https://www.who.int/publications-detail/cleaning-and-disinfection-of-environmental-surfaces-in-the-context-of-COVID-19>
- Immunization in the context of COVID-19 pandemic
<https://www.who.int/publications/i/item/immunization-in-the-context-of-COVID-19-pandemic>
- Laboratory biosafety guidance related to coronavirus disease 2019 (COVID-19)
[https://www.who.int/publications/i/item/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-\(COVID-19\)](https://www.who.int/publications/i/item/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-(COVID-19))
- Contact tracing in the context of COVID-19
<https://www.who.int/publications/i/item/contact-tracing-in-the-context-of-COVID-19>
- Community-based health care, including outreach and campaigns, in the context of the COVID-19 pandemic
 - o <https://www.who.int/publications/i/item/community-based-health-care-including-outreach-and-campaigns-in-the-context-of-the-COVID-19-pandemic>
- Clinical care of severe acute respiratory infections – Tool kit
<https://www.who.int/publications/i/item/clinical-care-of-severe-acute-respiratory-infections-tool-kit>
- Interim guidance on the rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages
[https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-\(COVID-19\)-and-considerations-during-severe-shortages](https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-(COVID-19)-and-considerations-during-severe-shortages)
- Interim guidance on advice on the use of masks in the context of COVID-19
[https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak](https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak)
- Interim guidance on global surveillance (with case definitions) for human infection with coronavirus disease (COVID-19)
[https://www.who.int/publications/i/item/global-surveillance-for-human-infection-with-novel-coronavirus-\(2019-ncov\)](https://www.who.int/publications/i/item/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov))

- Interim guidance on infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected
[https://www.who.int/publications/i/item/infection-prevention-and-control-during-health-care-when-novel-coronavirus-\(ncov\)-infection-is-suspected-20200125](https://www.who.int/publications/i/item/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125)
 - Technical documentation on considerations for quarantine of individuals in the context of containment for coronavirus disease (COVID-19)
[https://www.who.int/publications/i/item/considerations-for-quarantine-of-individuals-in-the-context-of-containment-for-coronavirus-disease-\(COVID-19\)](https://www.who.int/publications/i/item/considerations-for-quarantine-of-individuals-in-the-context-of-containment-for-coronavirus-disease-(COVID-19))
 - Interim guidance on laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases
<https://www.who.int/publications/i/item/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117>
 - Interim guidance on risk assessment and management of exposure of health care workers in the context of COVID-19
<https://www.who.int/publications/i/item/risk-assessment-and-management-of-exposure-of-health-care-workers-in-the-context-of-COVID-19-interim-guidance>
 - Interim guidance on home care for patients with COVID-19 presenting with mild symptoms and management of their contacts
[https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)
 - Protocol for assessment of potential risk factors for 2019-novel coronavirus (2019-nCoV) infection among health care workers in a health care setting
[https://www.who.int/publications/i/item/protocol-for-assessment-of-potential-risk-factors-for-2019-novel-coronavirus-\(2019-ncov\)-infection-among-health-care-workers-in-a-health-care-setting](https://www.who.int/publications/i/item/protocol-for-assessment-of-potential-risk-factors-for-2019-novel-coronavirus-(2019-ncov)-infection-among-health-care-workers-in-a-health-care-setting)
 - Coronavirus disease (COVID-19) travel advice
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/travel-advice>
- United States**
- Centers for Disease Control and Prevention (CDC): Coronavirus (COVID-19)
<https://www.cdc.gov/coronavirus/2019-ncov/index.html>
- Information for healthcare professionals about coronavirus (COVID-19)
<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>
 - Evaluating and testing persons for coronavirus disease 2019 (COVID-19)
https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fclinical-criteria.html
 - Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
 - Information for clinicians on investigational therapeutics for patients with COVID-19
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>
 - Discontinuation of isolation for persons with COVID-19 not in healthcare settings (interim guidance)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>
 - Interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)
https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fguidance-home-care.html
 - Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings (interim guidance)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html>
 - Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>
 - Using personal protective equipment (PPE)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/using-ppe.html>

- o Hand hygiene recommendations – Guidance for healthcare providers about hand hygiene and COVID-19
https://www.cdc.gov/coronavirus/2019-ncov/hcp/hand-hygiene.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Finfection-control%2Fhcp-hand-sanitizer.html
- o Outpatient and ambulatory care settings – Responding to community transmission of COVID-19 in the United States
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/ambulatory-care-settings.html>
- o Preparing for COVID-19 – Long-term care facilities, nursing homes
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html>
- o Strategies to optimize the supply of PPE and equipment
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/index.html>
- o Interim US guidance for risk assessment and public health management of healthcare personnel with potential exposure in a healthcare setting to patients with coronavirus disease 2019 (COVID-19)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html>
- o Criteria for return to work for healthcare personnel with confirmed or suspected COVID-19 (interim guidance)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/return-to-work.html>
- o Preparedness tools for healthcare professionals and facilities responding to coronavirus (COVID-19)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/preparedness-checklists.html>
- Healthcare facilities – Preparing for community transmission
https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-hcf.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhealthcare-facilities%2Fguidance-hcf.html
- o Prepare your practice for COVID-19
https://www.cdc.gov/coronavirus/2019-ncov/hcp/preparedness-resources.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhealthcare-facilities%2Fpractice-preparedness.html
- Health departments
<https://www.cdc.gov/coronavirus/2019-ncov/php/index.html>
- o Contact tracing
https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/contact-tracing-resources.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fphp%2Fopen-america%2Fcontact-tracing.html
- o Public health guidance for potential COVID-19 exposure associated with international travel or cruise travel
<https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html>
- o Public health recommendations for community-related exposure
<https://www.cdc.gov/coronavirus/2019-ncov/php/public-health-recommendations.html>
- o Interim guidance for public health professionals managing people with COVID-19 in home care and isolation who have pets or other animals
https://www.cdc.gov/coronavirus/2019-ncov/animals/interim-guidance-managing-people-in-home-care-and-isolation-who-have-pets.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fphp%2Finterim-guidance-managing-people-in-home-care-and-isolation-who-have-pets.html
- Information for laboratories about coronavirus (COVID-19)
<https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html>
- o Interim guidelines for COVID-19 antibody testing
<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>
- o Interim guidelines for collecting, handling, and testing clinical specimens from persons for COVID-19
<https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>

- o Interim laboratory biosafety guidelines for handling and processing specimens associated with coronavirus disease 2019 (COVID-19)
<https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html>
- Communities, schools, workplaces, and events
<https://www.cdc.gov/coronavirus/2019-ncov/community/index.html>
 - o Interim guidance for general population disaster shelters during the COVID-19 pandemic
https://www.cdc.gov/coronavirus/2019-ncov/downloads/Guidance-for-Gen-Pop-Disaster-Shelters-a-Pandemic_cleared_JIC_ADS_final.pdf
 - o Interim guidance on implementing safety practices for critical infrastructure workers who may have had exposure to a person with suspected or confirmed COVID-19 – Interim guidance
<https://www.cdc.gov/coronavirus/2019-ncov/community/critical-workers/implementing-safety-practices.html>
 - o Cleaning and disinfecting your facility
https://www.cdc.gov/coronavirus/2019-ncov/community/disinfecting-building-facility.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019ncov%2Fprepare%2Fdisinfecting-building-facility
 - o Resources to support people experiencing homelessness
<https://www.cdc.gov/coronavirus/2019-ncov/community/homeless-shelters/index.html>
 - o Interim guidance on management of coronavirus disease 2019 (COVID-19) in correctional and detention facilities
<https://www.cdc.gov/coronavirus/2019-ncov/community/correction-detention/guidance-correctional-detention.html>
- Travel
<https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html>

Centers for Medicare and Medicaid Services (CMS):
Coronavirus – Clinical and technical guidance
<https://www.cms.gov/About-CMS/Agency-Information/Emergency/EPRO/Current-Emergencies/Current>

National Institutes of Health (NIH): Coronavirus disease 2019 (COVID-19) treatment guidelines
<https://www.covid19treatmentguidelines.nih.gov/>

- Overview and spectrum of COVID-19
<https://www.covid19treatmentguidelines.nih.gov/overview/>
- Care of critically ill patients with COVID-19
<https://www.covid19treatmentguidelines.nih.gov/critical-care/>
- Potential antiviral drugs under evaluation for the treatment of COVID-19
<https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/>
- Immune-based therapy under evaluation for treatment of COVID-19
<https://www.covid19treatmentguidelines.nih.gov/immune-based-therapy/>
- Antithrombotic therapy in patients with COVID-19
<https://www.covid19treatmentguidelines.nih.gov/antithrombotic-therapy/>
- Considerations for certain concomitant medications in patients with COVID-19
<https://www.covid19treatmentguidelines.nih.gov/concomitant-medications/>

US Food and Drug Administration (FDA):
Coronavirus disease 2019 (COVID-19)
<https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-COVID-19>

Europe

European Centre for Disease Prevention and Control (ECDC): COVID-19
<https://www.ecdc.europa.eu/en/COVID-19-pandemic>

- Risk assessment on COVID-19
<https://www.ecdc.europa.eu/en/current-risk-assessment-novel-coronavirus-situation>
- Preparedness for COVID-19
<https://www.ecdc.europa.eu/en/COVID-19/preparedness-and-response>
 - o Infection prevention and control for COVID-19 in healthcare settings
<https://www.ecdc.europa.eu/en/publications-data/infection-prevention-and-control-and-preparedness-COVID-19-healthcare-settings>

- o Guidance for health system contingency planning during widespread transmission of SARS-CoV-2 with high impact on healthcare services
<https://www.ecdc.europa.eu/en/publications-data/guidance-health-system-contingency-planning-during-widespread-transmission-sars>
 - o Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19
<https://www.ecdc.europa.eu/en/publications-data/COVID-19-guidance-discharge-and-ending-isolation>
 - o Guidelines for the use of non-pharmaceutical measures to delay and mitigate the impact of 2019-nCoV
<https://www.ecdc.europa.eu/en/publications-data/guidelines-use-non-pharmaceutical-measures-delay-and-mitigate-impact-2019-ncov>
 - o Personal protective equipment (PPE) needs in healthcare settings for the care of patients with suspected or confirmed novel coronavirus (2019-nCoV)
<https://www.ecdc.europa.eu/en/publications-data/personal-protective-equipment-ppe-needs-healthcare-settings-care-patients>
- EU level surveillance of COVID19
<https://www.ecdc.europa.eu/en/COVID-19/surveillance>
 - o Case definition and European surveillance for COVID-19
<https://www.ecdc.europa.eu/en/COVID-19/surveillance/case-definition>
 - Laboratory support for COVID-19 in the EU/EEA
<https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support>
 - o Contact tracing – Public health management of persons, including healthcare workers, having had contact with COVID-19 cases in the European Union
<https://www.ecdc.europa.eu/en/COVID-19-contact-tracing-public-health-management>
 - o Guidance for wearing and removing personal protective equipment in healthcare settings for the care of patients with suspected or confirmed COVID-19
<https://www.ecdc.europa.eu/en/publications-data/guidance-wearing-and-removing-personal-protective-equipment-healthcare-settings>
 - o Disinfection of environments in healthcare and non-healthcare settings potentially contaminated with SARS-CoV-2
<https://www.ecdc.europa.eu/en/publications-data/disinfection-environments-COVID-19>
 - o Using face masks in the community – Reducing COVID-19 transmission from potentially asymptomatic or pre-symptomatic people through the use of face masks
<https://www.ecdc.europa.eu/en/publications-data/using-face-masks-community-reducing-COVID-19-transmission>

World Health Organization (WHO) Europe: Interim guidance on preparedness, prevention and control of COVID-19 in prisons and other places of detention

<http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-COVID-19/technical-guidance/2020/preparedness,-prevention-and-control-of-COVID-19-in-prisons-and-other-places-of-detention,-15-march-2020>

Brasil

Ministério da Saúde do Brasil. Protocolo de Manejo Clínico do Corona Vírus (COVID-19) na Atenção Primária à Saúde (8ª versão)
http://189.28.128.100/dab/docs/portaldab/documentos/20200422_ProtocoloManejo_ver08.pdf.

Ministério da Saúde. Diretrizes para Diagnóstico e Tratamento da COVID-19 (4ª versão)
<https://portalarquivos.saude.gov.br/images/pdf/2020/May/08/Diretriz-Covid19-v4-07-05.20h05m.pdf>.

Anvisa

<https://www20.anvisa.gov.br/segurancadopaciente/index.php/alertas/category/COVID-19>

Discussion

Despite the presentation of the main international protocols and guidelines of referred Centers and

Organizations, concerning the adjuvante treatment of mild and severe patients, Xu and colleagues [12] presented seven clinical guidelines on the management of COVID-19 pneumonia (mild, severe and critical) by international or national professional:

1. WHO: Interim guidance on clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. World Health Organization. Clinical management of severe acute respiratory infection when COVID-19 is suspected 2020 [13];
2. Infectious Diseases Society of America (IDSA): Guidelines on the treatment and management of patients with COVID-19 [14];
3. Surviving Sepsis Campaign: Guidelines on the management of critically ill adults with COVID-19 [15];
4. People's Republic of China's National Health Commission (NHC): Guidelines on the treatment of COVID-19 (7th edition) [16];
5. The Lombardy Section of the Italian Society of Infectious and Tropical Diseases (Società Italiana di Malattie Infettive e Tropicali) (SIMIT Lombardy Section): Vademecum for the treatment of people with COVID-19. Edition 2.0, 13 March 2020 [17];
6. The Netherlands' Working Party on Antibiotic Policy (Stichting Werkgroep Antibiotica Beleid) (SWAB): Drug treatment options in patients with COVID-19 [18];
7. Belgium's Sciensano (scientific institute of public health): Interim clinical guidance for adults with suspected or confirmed COVID-19 in Belgium [19].

As there is no general consensus on the clinical classification of COVID-19 and each guideline tends to use its own defined clinical categories of COVID-19, the authors [12] compared each other and classified the categories across the several guidelines into “mild”, “pneumonia”, “severe” and “critical” groups according to case definitions put forth by the WHO [20], which led the classification “moderately severe” group

to re-categorized to “severe” category to match WHO's case definition, as we defined. So, the guidelines from the countries on the use of adjunctive treatments could then be compared based on fairly similar descriptions of clinical severity [12].

Conclusion

The COVID-19 pandemic is spreading fast and new informations about the disease comes up everyday so that the guidelines and protocols change all the time. However, all these guidelines or guidance as well as protocols can be easily find in the links we pointed in this paper pretending to facilitate the search of these importante informations. So, it doesn't matter if what we wrote here tomorrow will be outdated, because the links will address the reader to the novel status of the guidelines. And the rapid and effective enforcement of existing international and national action plans, as well as parallel review and improvisation, is facilitating the affected countries to contain transmission and possibly delay the peak of outbreak and mortality. Also, all guidelines and protocols tend to use WHO as a reference with particular differences between countries. However, the more the COVID-19 is known, the more the protocols and guidelines change. Although the global economy is suffering with the pandemic, it is important to review the current action plans and suitably improvise the future action plans to mitigate the disease and avoid potential recurrences.

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7. CDC. https://www.cdc.gov/flu/pandemic-resources/pdf/community_mitigation-sm.pdf.
8. PAHO. https://www.paho.org/hq/index.php?option=com_content&view=article&id=15740:paho-director-calls-on-countries-of-the-americas-to-intensify-COVID-19-preparedness-and-response-activities&Itemid=1926&lang=en.
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