Philippine COVID-19 Living Recommendations

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By:

Institute of Clinical Epidemiology,
National Institutes of Health, UP Manila

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IMPORTANT NOTICE: These living recommendations will be updated as new evidence are published in the medical literature. It is critical that you take note of the date when the evidence was last reviewed. Additional recommendations may have to be developed as needed.

INTRODUCTION

Given the magnitude of the impact of COVID-19 in the country and the current priority given to it by health care providers, public health officials and the government, the need for clinical practice guidelines to optimize health care through effective management and control of the spread of this disease is imperative. Furthermore, an *infodemic* from the rapid pace of scientific developments on COVID-19 management is running side-by-side with the pandemic. We offer these living recommendations to health care providers to guide their diagnosis and treatment decisions on individual patient care. For policy makers and program managers, these living recommendations can serve to inform policy and provide timely guidance on effective interventions to be prioritized, implemented and made accessible to health care providers and the public.

While there are existing international guidelines and living systematic reviews on COVID-19, there is a need to localize the recommendations from the evidence in our setting by local experts, end-users and other relevant stakeholders. With the rapidly evolving science, the Living CPG development process is used wherein recommendations are switched to a living status based on the likelihood of new evidence and the importance of the recommendation in health care policy decision making. Living systematic reviews will be maintained to provide up-to-date, evidence-based living recommendations on the treatment, diagnosis, prevention and control of COVID-19.

DISCLAIMER

As a living guideline, the recommendations will be updated, and new recommendations will be added as the evidence evolves. The living recommendations are based on the best evidence available in scientific literature at the time of its formulation. However, this living CPG is not a comprehensive guide to all practice questions and management options on COVID-19. This is not meant to restrict the practitioner in using sound clinical judgement and sharing the decision with the patient, and from considering other management options according to the patient's particular needs and preferences. This CPG can serve to inform policy, but it is not meant to serve as a basis for approving or denying financial coverage or insurance claims merely because of nonconformance with recommendations. Neither are the recommendations supposed to be considered as legal rules for dictating certain modes of action to the exclusion of others.

LIVING CPG DEVELOPMENT METHODS

The development process of the Philippine Living CPG follows the Philippine Department of Health's Manual for Clinical Practice Guideline Development [DOH 2018] and the Grading of Recommendations, Assessment, Development and Evaluation or GRADE Approach [Schünemann et al 2013].

The specific phases of the CPG development process are as follows:

1. Guideline Preparation – The Steering Committee identified and convened members of the Living CPG task force: Lead CPG Developer (Steering Committee), Evidence Review Experts or Technical Working Group (TWG) and the Consensus Panel. A total of 20 specialty societies and stakeholders are represented in the task force.

   The Steering Committee, together with the TWG and other key stakeholders, finalized the health questions to be addressed in the CPG. The Steering Committee selected the members of the Consensus Panel based on their knowledge and experience, and potential conflicts of interest in consultation with the heads of the professional medical societies and stakeholder organizations. The Consensus Panel is composed of multi-sectoral representatives such as practitioners, both specialists and non-specialists, and patient advocates. The panel members were selected from the designated representatives of the relevant specialty groups. Some stakeholders, such as nurses, acted as patient advocates to reflect patients' and public's views and preferences.

   Several orientation sessions were conducted for the technical reviewers and consensus panel members on the COVID CPG development process. Technical reviewers were re-trained on evidence synthesis and the GRADE methodology. Consensus panel members were oriented on how to interpret the evidence summaries and generate the GRADE evidence-to-decision framework.

2. Evidence Synthesis - Evidence Review Experts reviewed and appraised existing CPGs and published literature, prepared evidence summaries, and drafted evidence-based recommendations. They are composed of members with one or more of the following expertise: methodologists, clinical epidemiologists, evidence-based practitioners, etc. They ideally have attended previous training on CPG development and evidence synthesis, or have previous experience on CPG development.

   For each health question, a systematic literature search was done. All eligible studies were critically appraised independently by the assigned reviewers.

Evidence tables and evidence summaries were generated by the TWG using the GRADE approach. Draft recommendations were formulated based on the quality of the evidence. All these steps were done by at least two independent reviewers.

During this stage of development, several technical coordinators with expertise on CPG Development and Evidence-Based Medicine oversee the retrieval and appraisal of evidence and the creation of the draft recommendations. A writer ensured that the draft recommendations are uniform, concise and clear. The Steering Committee organized several practice sessions for the ERE to finalize their presentations, and discuss them with other EREs, Steering Committee and technical experts. Evidence summaries were collated, formatted and prepared for presentation to the consensus panel.

3. Evidence to Decision - Upon completion of the evidence summaries by the ERE, several en banc meetings with the Consensus Panel were conducted wherein the evidence summaries and draft recommendations were presented for discussion and consensus voting. The Consensus Panel ranked the outcomes for each set of clinical questions according to whether they were critical, important but not critical or of low importance for decision making. Critical outcomes were primary factors that should influence a recommendation, while those with lower importance did not bear on these recommendations. In a scale of 1-9, those rated 7-9 were critical outcomes, 4-6 were important but not critical outcomes and 1-3 were outcomes of limited importance. Grading of the strength of recommendations are based on the overall quality of the evidence, trade-offs between benefits and harms, values and preferences of patients, resource implications and impact on equity. A skilled facilitator moderated the discussions during this meeting.

   Each member voted on the draft recommendation as follows: yes, no or abstain. Consensus was defined as at least 75% agreement among the members for both the direction and strength of recommendation. If consensus was not reached, members discussed the reasons in support of their votes for or against the recommendation. The voting was repeated, up to three rounds, until a consensus is reached. Any issues left unsettled after the en banc meeting were finalized through a modified Delphi activity.

4. Living CPG Process – From standard guideline development process above, several recommendations were prioritized to a *living status* according to the following: priority for decision making, reasonable chance that new evidence changes the existing recommendation, and likelihood of new research evidence [Akl et al, 2020]. Members of the EREs working on living recommendations (1) performed continual surveillance of literature to update the living systematic

review with new evidence and (2) updated the Evidence Summary tables and draft recommendations for panel discussion. The Steering Committee reviews the updated evidence summary and determines if the update will be presented to the Consensus Panel again. If so, the Consensus Panel is convened in an online meeting to discuss the new evidence and any changes in the living recommendation.

The Living CPG Development Process is summarized in the figure below:

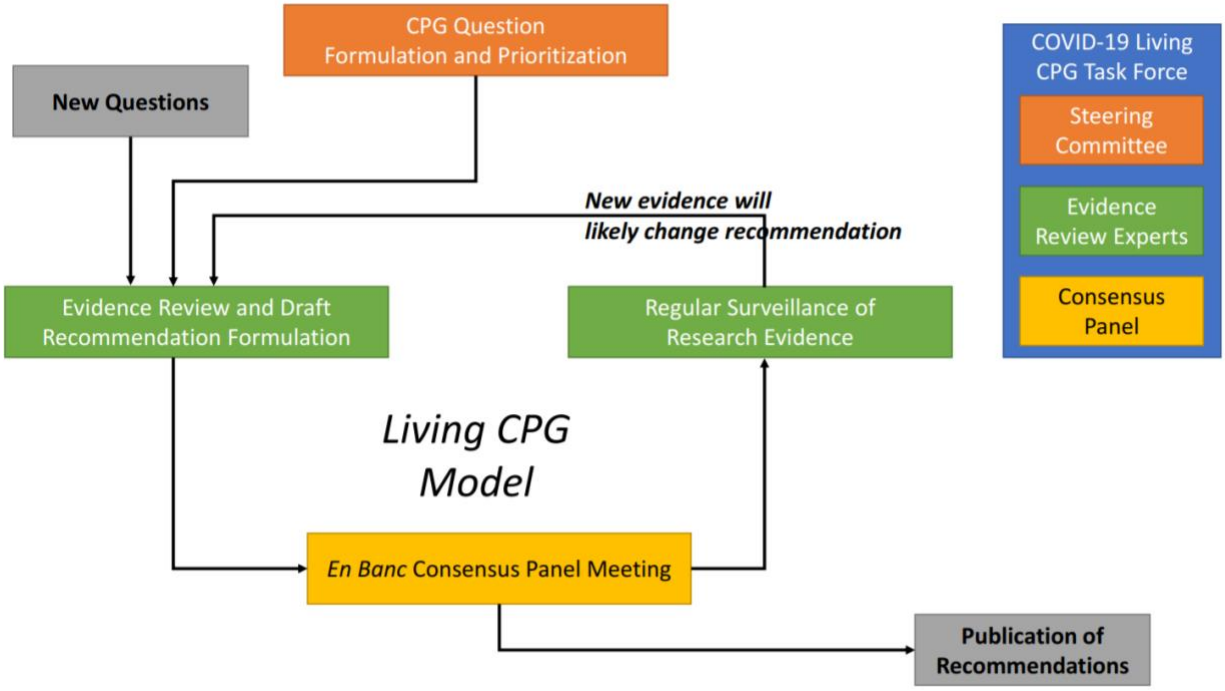

Figure 1. Process adapted by the Philippine COVID-19 Living Clinical Practice Guidelines.

This Living CPG tackles six central themes in COVID-19, and each theme is represented by a separate CPG Consensus Panel:

- Screening and diagnosis
- Treatment
- Critical care and respiratory management
- Non-pharmacologic interventions
- Vaccines and prophylactic interventions
- Adjunct interventions

MANAGEMENT OF CONFLICT OF INTEREST

All members involved in the creation of this Clinical Practice Guideline, including the Steering Committee, Technical Working Group and Consensus Panel, declared any conflicts of interest within the last 4 years, using a uniform Declaration of Conflict of Interest (DCOI) form. These were reviewed by the central project team and the Steering Committee, to screen and manage the COIs declared. Those without significant COIs were selected to be members of the consensus panel. Those with COIs which were not significant could participate, as long as their COIs were declared in the meetings and documented in the reports. Finally, those with significant personal and financial COIs related to COVID-19 were not selected to be involved in any part of the CPG project.

GRADE METHODOLOGY

The Consensus Panel evaluated the direction and strength of recommendation using the GRADE approach, based on the (1) over-all quality of evidence for each question, (2) balance between benefits and harms, (3) values, preferences, and burden on patients, (4) cost and resource use, and (5) other considerations.

The quality of evidence is one of the bases of the Consensus Panel in making the final recommendation. The following table shows the definition and implication of each:

Table 1. Definitions and Implications of each GRADE Quality of Evidence

GRADE Quality (Certainty) of Evidence	**Definition**	**Implication**
High	We are very confident that the true effect lies close to that of the estimate of the effect.	Further research is **very unlikely to change confidence** in the estimate of effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is **likely to have an important impact on confidence** in the estimate of effect and may change the estimate
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.	Further research is **very likely to have an important impact on confidence** in the estimate of effect and is likely to change the estimate
Very Low	We have very little confidence in the effect estimate: The true effect	Any estimate of effect is **very uncertain**

GRADE Quality (Certainty) of Evidence	Definition	Implication
	is likely to be substantially different from the estimate of effect	

The implications of strong and conditional recommendations are as follows [Schünemann et al 2013]:

Table 2. Implications of the Strength of Recommendation to Patients, Clinicians and Policymakers.

	Strong Recommendation	Conditional Recommendation
Patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
Clinicians	• Most individuals should receive the recommended course of action. • Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	• Recognize that different choices will be appropriate for different patients. • Clinicians must help each patient arrive at a management decision consistent with her or his values and preferences.
Policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions.

There are three reasons where the consensus panels were unable to make a recommendation:

- confidence in effect estimates is so low that the panels feel a recommendation is too speculative
- trade-offs are so closely balanced, and the values and preferences and resource implications not known or too variable
- management options have very different undesirable consequences, and individual patients' reactions to these consequences are likely to be variable

A strong recommendation is usually stated as "We recommend/ We recommend against…", while a conditional recommendation is worded "We suggest/ We suggest against…". Finally, when there is no recommendation that can be made, the sentence starts with "There is no/ insufficient evidence to recommend…"

CONTACT US

Send us an email at covidcpg.ph@gmail.com for any questions or clarifications on the outputs and process of this Living CPG. You may also suggest a clinical question for the consideration of the Living Clinical Practice Guidelines COVID-19 Taskforce.

Contents

STEERING COMMITTEE

Jemelyn U. Garcia. MD, FPCP, FPSMID

Evalyn A. Roxas, MD, MPH, FPCP, FPSMID

Mario M. Panaligan, MD, FPCP, FACP, FPSMID, FIDSA

Noel L. Espallardo, MD, MSc, FPAFP

Ivan N. Villespin, MD, MBA, FPCP, FPCCP, FCCP

Aileen R. Espina, MD, MPH, MHA, FPAFP

Antonio L. Dans, MD, MSc, FPCP

Maria Rosario S. Vergeire, MD, MPH, CESO IV

Project Lead Convenors

Marissa M. Alejandria, MD, MSc, FPCP, FPSMID

Leonila F. Dans, MD, MSc, FPPS, FPRA

CONSENSUS PANEL

Screening and Diagnosis

Clemencia D. Bondoc, MD

Alpha Grace B. Cabic, MD, DPSP

Jocelyn Myra R. Caja, MD, FPSP

Virgina de los Reyes, MD, FPCP, FPCCP

Mary Ann D. Lansang, MD, MSc, FPCP, FPSMID

Jane Eflyn L. Lardizabal-Bunyi, RPh, MD, OHP, DFM, FPAFP, CSPSH

Imelda B. Mateo, MD, MBAH, FPCP, FPCCP

Vernon M. Serafico, MD, FPCP

Treatment

Maria Elinore Alba-Concha, MD, FPAFP

Mary Ann C. Bunyi, MD, FPPS, FPIDSP

Erwin R. De Mesa, MD, FPOGS, FPIDSOG

Karl Evans R. Henson, MD, FPCP, FPSMID

Faith Joan C. Mesa-Gaerlan, MD, MS, FPCEM

Roland M. Panaligan, MD, LLM, FPCP, FPCCP

Rommel B. Punongbayan, RMT, MD, MBA, FPCP, FPSMS, CSPSH, DPCOM

Iris Conela A. Tagaro, MD, DPPS, MPM-MHSD

Critical Care and Respiratory Management

Joseph Adrian L. Buensalido, MD, FPCP, FPSMID

Pauline F. Convocar, MD, MCHM, DPBEM, FPCEM, DPCOM

Ricardo A. Francisco, Jr, MD, MHA, FPCP, FPSN

Mark Kristoffer U. Pasayan, MD, FPCP, FPSMID

Chito C. Permejo, MD, FPCP, FPCC, FPSCCM

Albert L. Rafanan, MD, FPCCP, FPCP, FCCP, FASSM, FPSSM

Rowena Marie T. Samares, MD, FPAFP, FPSHPM

Paul Michael S. Tan, RN, MAN, PhD

Non-Pharmacologic Interventions

Regina P. Berba, MD, MSc, FPCP, FPSMID

Vivien Fe F. Fadrilan-Camacho, MD, MPH, FPAFP

Rodley Desmond Daniel M. Carza, MPH, RN

Dominga Calalang-Gomez, RN

Anna Sofia Victoria S. Fajardo, MD, MBAH, DPCOM

Victoria Isla-Ching, RN, MGM-ESP

Nenacia Ranali Nirena P. Mendoza, MD, FPAFP

Ruth S. Punzalan, MD, MPH, FPAFP

Vaccines and Prophylactic Interventions

Maria Rhona G. Bergantin, MD, MSc, FPCP, FPSMID

Fatima Ignacio Gimenez, MD, FPPS, FPIDSP

Dax Ronald O. Librado, MD, FPCP, FACP

Anna Guia O. Limpoco, MD, MSCM, FPAFP

Edmyr M. Macabulos, MD, MPH, FPCOM

Rosally P. Zamora, MD, FPCP

Gian Carlo Torres, PhD, MAN, RN

Katrina Descartin, MD, MS, MPH, DIMPH, RSPH

Adjunct Interventions

Anthony F. Cortez, MD

Katrina G. Gomez-Chua, MD, MPH

Ana Melissa S. Guererro, MD, MPH (HTA)

Joan Mae M. Oliveros, MD, FPAFP

Maria Sonia Salamat, MD, MPH, FPCP, FPSMID

Julie Christie Gutierrez Visperas, MD, MHPEd, FPCP, FPCCP

Shirley P. Whisenhunt DNM, RN

Evidence Review Experts

Eva I. Bautista, MD, MSc, FPPS

John Jefferson V. Besa, MD

Julian M. A. Buban

Aldrich Ivan Lois D. Burog, MD, MSc (cand.)

Ian Theodore Cabaluna, RPh, MD, GDip (Epi)

Marie Gene D. Cruz, MD

Patricia Maria Gregoria M. Cuaño, MD

Lea Roselle O. De Castro, MD

Namnama P. Villarta-De Dios, MD, MSc, DPPS

Belen L. Dofitas, MD, MSc

Valentin C. Dones III, PhD

Gina Antonina S. Eubanas, MD, FPDS, D Clin Epi

Antonio L. Faltado Jr., MD, FPCP, FPSEDM

Anna Maria Vida P. Garcia, RPh, D Clin Epi

Rowena F. Genuino, MD, MSc

Germana Emerita V. Gregorio, MD, PhD

Myzelle Anne J. Infantado, PTRP, MSc (cand.)

Racquel Ibanez, MD, FPCP, DPCCP

Marquis Von Angelo Syquio Go Joson, MD

Anna Angelica Macalalad Josue, MD, FPCP, DPSEDM, MSc (cand)

Marie Carmela Lapitan, MD, MS, FPUA, FPCS

Christopher G. Manalo, MD, DPBEM

Patricia Pauline M. Remalante, MD, FPCP, DPRA

Evelyn O. Salido, MD, MSc, FPCP, FPRA

Maria Cristina Z. San Jose, MD, FPNA

Maria Vanessa V. Sulit, BSN, RN, MSc

Frangelo Conrad Tampus, MD

Cary Amiel G. Villanueva, MD

Paoline Nicole P. Villanueva, RMT, MD

Project Staff

Project Manager
Dan Louie Renz P. Tating, MS(cand), RN

Technical Coordinators
Howell Henrian G Bayona, MSc, CSP-PASP
Maria Teresa S. Tolosa, MD, FPDS, D Clin Epi
Dan Louie Renz P. Tating, MS(cand), RN

Copy Writers
Kate D. Dunlao, RPh
Joyce Anne Ceria-Pereña, RPh, MPM
Mikarla M. Lubat, RND

Project Staff
Maria Eleanor L. Candelaria, MPH, RN
Kate D. Dunlao, RPh

Facilitators

Screening and Diagnosis
Lia Aileen M. Palileo-Villanueva, MD, MSc

Treatment
Diana R. Tamondong-Lachica, MD, FPCP

Critical Care and Respiratory Management
Bernadette Heizel Manapat-Reyes, MD, MHPEd, FPCP, FPRA

Non-Pharmacologic Interventions
Carol Stephanie C. Tan-Lim, MD, MSc

Vaccines and Prophylactic Interventions
Maria Asuncion A. Silvestre, MD, FPSNbM

Adjunct Interventions
Carlo Irwin Panelo, MD, MA

Living Recommendations on Screening and Diagnosis of COVID-19

14-day Symptom-based Test

Should the 14-day symptom-based test be used in screening for COVID-19 infection in apparently healthy adults?

We suggest an initial screen for COVID-19 by checking for any influenza-like illness symptoms and typical COVID-19 symptoms* within the past 14 days in apparently healthy adults. *(Low quality of evidence; Conditional recommendation)*

Symptoms include fever, cough, sore throat, runny nose, myalgia, headache, fatigue/malaise, diarrhea, nausea/vomiting, anosmia, ageusia, shortness of breath/dyspnea.

Clinical Specimen

Which clinical specimens can be used as an alternative to nasopharyngeal swab RT-PCR* for the diagnosis of COVID-19?

We recommend the use of the following specimens as alternative specimens to nasopharyngeal swab RT-PCR for the diagnosis of COVID-19 among symptomatic and asymptomatic patients suspected of COVID-19 in hospital and outpatient settings:.

- oropharyngeal swab *(Moderate quality of evidence; Strong recommendation)*
- saliva drool/spit and oral saliva (*Moderate quality of evidence; Strong recommendation*)
- nasal swab/wash *(Moderate quality of evidence; Strong recommendation)*
- throat swab *(Low quality of evidence; Strong recommendation)*

We suggest the use of saliva swab and posterior oropharyngeal saliva specimens as an alternative specimen to nasopharyngeal swab RT-PCR for the diagnosis of COVID-19 among symptomatic and asymptomatic patients with suspected COVID-19 in hospital and community/outpatient settings. *(Low quality of evidence; Conditional recommendation)*

We recommend against the use of sputum as an alternative specimen to nasopharyngeal swab RT-PCR for the diagnosis of COVID-19. *(Very low quality of evidence; Strong recommendation)*

There is no evidence to recommend the use of bronchoalveolar lavage as an alternative specimen to nasopharyngeal swab RT-PCR for the diagnosis of COVID-19.

*SARS COV-2 RT-PCR of nasopharyngeal swabs remains the diagnostic test of choice to confirm the diagnosis of COVID-19 among suspected individuals.

Rapid Antigen Tests

Should rapid antigen tests be used in the diagnosis of COVID-19 in clinically suspected patients?

We recommend the use of rapid antigen test in patients suspected of COVID-19 infection meeting all the following conditions: *(Moderate quality of evidence; Strong recommendation)*

- Symptomatic AND
- Early phase </=7 days from onset of symptoms AND
- Specific brands that demonstrated sensitivity ≥80% and have very high specificity (≥97-100%))

We recommend against the use of saliva as specimen for rapid antigen test in patients suspected of COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

We recommend against the use of rapid antigen test alone in asymptomatic patients suspected of COVID-19 infection. *(Moderate to high quality of evidence; Strong recommendation)*

Pooled Testing using RT-PCR

Should pooled testing using RT-PCR for SARS-CoV-2, versus individual testing using RT-PCR, be used for screening and surveillance for SARS-CoV-2 in patients with suspected COVID-19 infection?

We suggest the use of pooled RT-PCR testing in targeted* low-risk and low-prevalence populations using a pool size of 5 in individuals suspected of COVID-19 infection. *(Moderate quality of evidence; Conditional recommendation)*

**Target population refer to the list of PSP and DOH*

Repeat Testing using RT-PCR

Should repeat RT-PCR testing after an initial negative RT-PCR (versus single RT-PCR testing) be done to diagnose COVID-19 in symptomatic patients?

We suggest to repeat RT-PCR testing when the initial RT-PCR test is negative among symptomatic patients with highly suspected to have COVID-19 infection. *(Low quality of evidence; Conditional recommendation)*

Clinical risk assessment for surgery

Among asymptomatic individuals scheduled for non-urgent, non-emergency surgery, should RT-PCR and clinical risk assessment vs clinical risk assessment alone be done to screen for COVID-19?

We recommend the use of both clinical risk assessment and RT-PCR* to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery *(Very low quality of evidence; Strong recommendation)*.

We recommend the use of both clinical risk assessment and Antigen-Rapid Diagnostic Test (Ag-RDT)** to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery when RT-PCR testing is not available or when prolonged turnaround time is considered *(Very low quality of evidence; Strong recommendation)*.

**Use high-risk PPE regardless of RT-PCR or Ag-RDT test results in areas with prevalence of 1% or higher.*
***Ag-RDT should have a Sn of 80% and Sp of 97%*

Antibody tests for seroprevalence

Should antibody tests be used for COVID-19 seroprevalence studies among adult populations?

We suggest using laboratory-based antibody tests with high sensitivity and specificity (e.g., total antibody or IgG assays, ELISA, ECLIA) to determine COVID-19 seroprevalence among adults *(Very low quality of evidence; Conditional recommendation)*.

We recommend against using antibody tests detecting IgM to determine COVID-19 seroprevalence among adults *(Very low quality of evidence; Strong recommendation).*

We recommend against using rapid antibody tests (e.g., Lateral flow immunoassays) to determine COVID-19 seroprevalence among adults *(Very low quality of evidence; Strong recommendation).*

Antibody test for reinfection

Among symptomatic individuals previously diagnosed with COVID-19, should antibody testing be done to diagnose presumptive COVID-19 reinfection?

We recommend against the use of SARS-CoV-2 Ab testing to diagnose presumptive COVID-19 reinfection among symptomatic patients previously diagnosed with COVID-19* *(Very low quality of evidence; Strong recommendation)*.

**NAAT (RT-PCR) and Genomic sequencing are the recommended diagnostic tests to confirm COVID-19 reinfection.*

Return to work

What criteria should be used for allowing workers who were previously infected with COVID-19 to return to work?

We recommend the use of **symptom-based strategy** for the discontinuation of isolation and return to work clearance of the following:

1. **Asymptomatic adults who are not severely immunocompromised if they fulfill the following *(Very low quality of evidence; Strong recommendation):***
   - remained asymptomatic throughout their infection
   - 10 days have passed from the first positive viral diagnostic test (RT-PCR or rapid antigen)

2. **Adults who had mild to moderate COVID-19 who are not severely immunocompromised if they fulfill the following *(Very low quality of evidence; Strong recommendation):***
   - Afebrile for at least 24 hours without use of antipyretic medications
   - Respiratory symptoms have improved (cough, shortness of breath)
   - 10 days have passed from symptom onset

3. **Adults who had severe to critical COVID-19 who are not severely immunocompromised if they fulfill the following *(Very low quality of evidence; Strong recommendation):***
   - Afebrile for at least 24 hours without use of antipyretic medications
   - Respiratory symptoms have improved (cough, shortness of breath)
   - 21 days have passed from symptom onset

A repeat negative RT-PCR test is no longer needed for discharge of immunocompetent patients with probable or confirmed COVID-19 regardless of severity, *because, in most cases, it results in prolonged isolation of patients who continue to shed detectable SARS-CoV-2 RNA but are no longer infectious.*

We suggest **test-based** strategy using RT-PCR for the discontinuation of isolation and return to work clearance of the following:

1. **Severely immunocompromised adults**
2. **Health care workers**

if they fulfill the following:

- Afebrile for at least 24 hours without use of antipyretic medications
- Respiratory symptoms have improved (cough, shortness of breath)
- With at least one negative RT-PCR test of a respiratory specimen

(Very low quality of evidence; Conditional recommendation)

Severely immunocompromised: Ongoing chemotherapy for cancer, or within one year from receiving a hematopoietic stem cell or solid organ transplant; untreated HIV infection with CD4 count < 200, combined primary immunodeficiency disorder, and receipt of prednisone >20mg/day for more than 14 days, may cause a higher degree of immunocompromise and require actions such as prolonging the duration of work restrictions. Other less immunocompromising conditions include advanced old age, DM, CKD. The degree of

immunocompromise is determined by the health care provider, and preventive actions are adapted to each individual and situation.

Chest X-Ray

Should Chest X-Ray be used to diagnose COVID-19 among suspected patients?
We suggest against the use of chest x-ray to diagnose COVID 19 infection among asymptomatic individuals *(Very low quality of evidence, Conditional recommendation).*

We suggest Chest x-ray to facilitate rapid triage, infection control and clinical management among any of the following *(Very low quality of evidence, Conditional recommendation)*:

- patients with mild features of COVID 19 at risk for progression
- patients with moderate to severe features of COVID 19
- patients with symptoms of at least 5 days duration

Chest CT Scan

Should Chest CT Scan be used to diagnose COVID-19 among suspected patients?
We suggest against the routine use of CT scan for diagnosing COVID-19 among suspected patients with COVID-19 presenting at the emergency department if RT-PCR testing is readily available with timely results. *(Very low quality of evidence, Conditional recommendation).*

If RT-PCR test is not available, we suggest using non-contrast chest CT scan for symptomatic patients suspected of having COVID-19 to guide early triage and management under the following conditions:

- patients with mild COVID-19 who are at risk for progression (elderly, with comorbidities)
- patients with moderate to severe COVID-19

(Very low quality of evidence, Conditional recommendation)

Lung Ultrasound

Should Lung Ultrasound be used to diagnose COVID-19 among suspected patients?
We suggest against the use of lung ultrasound alone in diagnosing patients with suspected COVID-19 infection.
(Low quality of evidence, Conditional recommendation)

Prognostic Models

Among adult patients diagnosed with COVID-19, should prognostic models be used to predict the likelihood of severe disease and mortality?

<u>To guide the decision to admit patients with COVID-19 to the hospital:</u>
We suggest the use of the following scoring systems:

- Age, BUN, number of Comorbidities, CRP, SpO2/FiO2 ratio, Platelet count, Heart rate (ABC2-SPH) risk score,
- Confusion Urea Respiration Blood Pressure (CURB-65) severity score,
- Risk Stratification in the Emergency Department in Acutely Ill Older Patients (RISE-UP) score, and
- Rapid Emergency Medicine Score (REMS).

(Low quality of evidence; Conditional recommendation)

There is insufficient evidence to recommend the use of the 4C Mortality Score, COVID Outcome Prediction in the Emergency Department (COPE) model, and Quick Sepsis-related Organ Failure Assessment (qSOFA) score. *(Very low quality of evidence)*

To guide in the expectant monitoring of hospitalized patients:
We suggest the use of the 4C Deterioration model. *(Low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend the use of the Modified Early Warning Score (MEWS) and National Early Warning Score 2 (NEWS2) scoring systems . *(Very low quality of evidence)*

Severity Classification of COVID-19

Non-severe COVID-19

Mild COVID-19 – no pneumonia or hypoxia, acute onset of fever and cough or any three or more of the following: fever, cough, coryza, sore throat, diarrhea, anorexia/nausea/vomiting, loss of sense of smell or taste, general weakness/body malaise/fatigue, headache, myalgia

Moderate COVID-19

a. With pneumonia, no difficulty of breathing, RR < 30 breaths/min, oxygen saturation >/= 94%
b. Without pneumonia but with risk factors for progression: elderly and/or with comorbidities

Severe COVID-19 – with pneumonia and signs of respiratory distress, oxygen saturation < 94%. RR >30 breaths/minute, requiring oxygen supplementation

Critical COVID-19 – with pneumonia and impending respiratory failure requiring high flow oxygen, non-invasive or invasive ventilation, acute respiratory distress syndrome, sepsis or shock, deteriorating sensorium, multi-organ failure

Hydroxychloroquine/Chloroquine

Should hydroxychloroquine/ chloroquine, with or without azithromycin be used in the treatment of patients with COVID-19 infection?

We recommend against the use of hydroxychloroquine/chloroquine, with or without azithromycin among patients with COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

Azithromycin

Should azithromycin be used in the treatment of patients with COVID-19 infection?

We recommend against the use of azithromycin among patients with COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

Favipiravir

Should favipiravir be used in the treatment of patients with COVID-19 infection?

There is insufficient evidence to recommend the use of favipiravir among patients with COVID-19. *(Very low quality of evidence)*

Remdesivir

Should remdesivir be used in the treatment of patients with COVID-19 infection?

We suggest against the use of remdesivir in patients with COVID-19 infection who have O2 saturation ≥94% and do not require oxygen supplementation. *(Low quality of evidence; Conditional recommendation)*

We suggest the addition of remdesivir to dexamethasone in patients with COVID-19 infection who have O2 saturation < 94% and/or requiring oxygen supplementation. *(Low quality of evidence; Conditional recommendation)*

We suggest against the use of remdesivir in patients with COVID-19 infection who are already on invasive mechanical ventilation or ECMO. *(Low quality of evidence, conditional recommendation)*

Tocilizumab

Should tocilizumab be used in the treatment of patients with COVID-19 infection?
We recommend the addition of tocilizumab to systemic steroids in patients with elevated biomarkers of inflammation (CRP), showing rapid respiratory deterioration and/or requiring high doses of oxygen (high-flow nasal cannula, noninvasive or invasive mechanical ventilation) and. *(Moderate quality of evidence; Strong recommendation)*

We recommend against the use of tocilizumab in patients with COVID-19 infection who do not require oxygen supplementation. *(Very low quality evidence, Strong recommendation)*

Convalescent Plasma

Should convalescent plasma be used in the treatment of patients with COVID-19 infection?
We recommend against the use of convalescent plasma among patients with COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

Ibuprofen

Should ibuprofen be used in the treatment of patients with COVID-19 infection?
We recommend against the use of ibuprofen as treatment among patients with COVID-19 infection. *(Very low quality of evidence; Strong recommendation)*

Virgin Coconut Oil

Should virgin coconut oil (VCO) be used in the treatment of patients with COVID-19 infection?
There is no evidence to recommend the use of VCO as treatment among patients with COVID-19 infection.

Lianhua

Should Lianhua be used in the treatment of patients with COVID-19 infection?
We recommend against the use of Lianhua as treatment among patients with COVID-19 infection. *(Very low quality of evidence; Strong recommendation)*

Ivermectin

Should ivermectin be used in the treatment of patients with COVID-19 infection?
There is insufficient evidence to recommend the use of ivermectin in the treatment of patients with mild-to-moderate COVID-19 *(Very low quality of evidence)*

We suggest against the use of ivermectin for the treatment of patients with severe COVID-19 *(Very low quality of evidence; Conditional recommendation)*

We suggest against the use of ivermectin combined with doxycycline for the treatment of patients with COVID-19 *(Very low quality of evidence; Conditional recommendation)*

Colchicine

Should colchicine be used in the treatment of patients with COVID-19 infection?

We suggest against the use of colchicine in the treatment of COVID-19 *(Low quality of evidence; Conditional recommendation)*

Interferon

Should interferon be used in the treatment of patients with COVID-19 infection?

We suggest against the use of interferon in the treatment of hospitalized patients with moderate to critical COVID-19. *(Very low quality of evidence; Conditional recommendation)*

Baricitinib

Should baricitinib with or without remdesivir be used in the management of hospitalized patients with COVID-19?

We suggest the use of baricitinib in combination with remdesivir in hospitalized COVID-19 patients who cannot take corticosteroids and require oxygen supplementation. *(Low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend the use of baricitinib in combination with remdesivir and corticosteroids in hospitalized COVID-19 patients. *(Very low quality of evidence)*

There is no evidence to recommend the use of baricitinib alone in hospitalized COVID-19 patients.

Inhalational Corticosteroids

Should inhaled corticosteroids be used in the treatment of patients with COVID-19 infection?

There is insufficient evidence to recommend the use of inhaled corticosteroids as treatment for non-hospitalized patients with mild to moderate COVID-19 infection *(Very low quality of evidence)*

Lopinavir/Ritonavir

Should lopinavir/ritonavir be used in the treatment of COVID-19?

We recommend against the use of lopinavir/ritonavir as treatment for COVID-19 infection *(Moderate quality of evidence; Strong recommendation)*

Bamlanivimab

Should bamlanivimab be used in the treatment of COVID-19?

We recommend against the use of bamlanivimab monotherapy as treatment for COVID-19 infection *(Very low quality of evidence; Strong recommendation)*

We suggest against the use of bamlanivimab - etesevimab in the treatment of non-hospitalized COVID-19 patients with mild-to-moderate COVID-19 at high risk of progression to severe disease *(Low quality of evidence; Conditional recommendation)*

Regeneron (casirivimab - imdevimab)

Should regeneron (monoclonal antibody cocktail) be used in the treatment of COVID-19?

There is insufficient evidence to recommend the use of REGN-COV2 (casirivimab/imdevimab) as treatment for COVID-19 infection *(Low quality of evidence)*

Leronlimab

Should leronlimab be used in the treatment of patients with COVID-19 infection?

There is insufficient evidence to recommend the use of leronlimab as treatment for COVID-19 *(Very low quality of evidence)*

Steam Inhalation

Should steam inhalation be used for the treatment of COVID-19?

We recommend against the use of steam inhalation alone in the treatment of COVID-19. *(Very low quality of evidence; Strong recommendation)*

Living Recommendations for the Critical Care and Respiratory Management of COVID-19

Systemic Corticosteroids

Should systemic corticosteroids be used in patients with COVID-19 infection?
We recommend the use of dexamethasone in patients with COVID-19 infection who require supplemental oxygenation (i.e., including high-flow device, non-invasive, invasive mechanical ventilation and ECMO). *(High quality of evidence; Strong recommendation)*

We recommend against the use of systemic corticosteroids among patients with COVID-19 infection who do not require oxygen supplementation. *(Moderate to high quality of evidence; Strong recommendation)*

Anticoagulation

Should anticoagulation be used in treating patients diagnosed with COVID-19 infection?
We suggest the use of prophylactic anticoagulation among hospitalized patients with COVID-19 infection, unless with contraindications. *(Very low quality of evidence; Conditional recommendation)*

We suggest the use of prophylactic dose anticoagulation rather than therapeutic anticoagulation in critically ill patients with COVID-19 infection. *(Low quality of evidence; Conditional recommendation)*

Empiric antimicrobials

Should empiric antimicrobial coverage be given to patients with severe and critical COVID-19?
We recommend against the routine use of antibiotics in patients with severe and critical COVID-19 infection, unless with suspicion of secondary bacterial co-infection. For patients on empiric antibiotics, they should be assessed daily for the need for discontinuation, continuation or escalation based on clinical and laboratory parameters. *(Very low quality of evidence; Strong recommendation)*

Hemoperfusion

Should hemoperfusion be used in patients with COVID-19 infection?
There is insufficient evidence on the use of hemoperfusion among patients with COVID-19 infection. *(Very low quality of evidence)*

Fluid Management

Should a conservative fluid management strategy be used in mechanically ventilated adult COVID-19 patients?
We suggest the use of conservative fluid management rather than liberal fluid management strategy in mechanically ventilated adult COVID-19 patients with acute respiratory distress syndrome who have been adequately resuscitated*. *(Low quality of evidence; Conditional recommendation)*
**without tissue hypoperfusion and fluid responsiveness*

Proning in Non-Intubated Patients

Should proning be used in non-intubated patients with COVID-19 infection?
We suggest self-proning to improve oxygenation status of non-intubated hospitalized patients with COVID-19 infection requiring oxygen supplementation. *(Very low quality of evidence; Conditional recommendation)*

High Flow Nasal Cannula

Should high flow nasal cannula be used in patients with COVID-19 infection?
We suggest the use of high-flow nasal cannula oxygenation rather than non-invasive ventilation (e.g., helmet CPAP, mask NIV) in patients with COVID-19 infection and acute hypoxemic respiratory failure who do not respond to conventional oxygen therapy. *(Very low quality of evidence; Conditional recommendation)*

Mechanical Ventilation

Should lung protective ventilation, high PEEP and driving pressure-limited strategies be used in the management of adult patients with COVID-19-associated acute respiratory distress syndrome?
We suggest the use of a lung protective ventilation strategy (tidal volume 4-8 mL/kg predicted body weight and plateau pressure less than 30 cmH2O) in patients with COVID-19 infection and ARDS. *(Very low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend the use of a higher PEEP strategy. We suggest to individualize PEEP or employ a PEEP strategy on respiratory mechanics (i.e., compliance) in patients with COVID-19 infection. *(Low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend a driving pressure limited strategy in patients with COVID-19 infection. We suggest to keep the driving pressure ≤ 14 cmH2O. *(Low quality of evidence; Conditional recommendation)*

Rapid Sequence Intubation

Should rapid sequence intubation or delayed sequence intubation be used for the management of COVID-19?
We suggest the use of rapid sequence intubation for COVID-19 patients to reduce infection among healthcare workers performing the procedure *(Very low quality of evidence; Conditional recommendation)*

Extracorporeal Membrane Oxygenation

Should Extracorporeal Membrane Oxygenation (ECMO) be used in the management of ARDS among COVID-19?
We suggest the use of VV-ECMO for judiciously selected COVID-19 patients with severe ARDS based on the Extracorporeal Life Support Organization (ELSO) criteria *(Very low quality of evidence; Conditional recommendation)*

Hyperbaric Oxygen Therapy

Should hyperbaric oxygen therapy be used in the management of COVID-19 patients?
There is insufficient evidence to recommend the use of hyperbaric oxygen therapy for the management of COVID-19 patients *(Very low quality of evidence)*

Etoposide

Should etoposide be given among patients with severe COVID-19 pneumonia in cytokine storm?
We recommend against the use of etoposide among patients with COVID-19 pneumonia in cytokine storm *(Very low quality of evidence; Strong recommendation)*

Pulmonary rehabilitation in patients with Long COVID-19

Should pulmonary rehabilitation be done among long COVID patients with residual pulmonary symptoms to improve pulmonary function and quality of life?

We recommend individualized pulmonary rehabilitation with pre-intervention medical clearance for long COVID patients who show residual respiratory symptoms *(Moderate quality of evidence; Strong recommendation)*

Living Recommendations on Non-Pharmacologic Interventions for Prevention and Control of COVID-19 Infection

Cloth Masks

Should cloth masks be used in the prevention and control of COVID-19 infection?
We recommend that healthcare workers not directly taking care of COVID-19 patients, and other persons with high risk of exposure to COVID-19 should use properly fitted surgical masks instead of cloth masks. *(Moderate quality of evidence; Strong recommendation)*

We suggest using a cloth mask that fits snugly on the face and made of at least two layers of cotton (e.g. t-shirt fabric) or non-woven nylon with aluminum nose bridge for the general public with low risk of exposure to COVID-19 in outdoor or indoor areas to prevent COVID-19 infections *(Low quality of evidence; Conditional recommendation)*

Ionizing Air Filter

Should ionizing air filter be used in the prevention and control of COVID-19 infection in public spaces with sustained community transmission?
We recommend against the use of ionizing air purifier to reduce COVID-19 transmission in the community. *(Low quality of evidence; Strong recommendation)*

Foot Baths

Should foot baths be used in the prevention and control of COVID-19 infection?
We recommend against the use of footbaths for the prevention and control of COVID-19 transmission. *(Very low quality of evidence; Strong recommendation)*

Misting Tents

Should misting tents or disinfection chambers be used in preventing and controlling COVID-19 transmission?
We recommend against the use of misting tents or disinfection chambers for preventing and controlling COVID-19 transmission. *(Very low quality of evidence; Strong recommendation)*

Ultraviolet (UV) Lamps

Should ultraviolet (UV) lamps be used in the prevention and control of COVID-19 infection in public spaces in locations with sustained community transmission?
We recommend against the use of UV lamps or other UV devices in any place outside of a controlled clinic or hospital setting to prevent and control COVID-19 transmission. *(Low quality of evidence; Strong recommendation)*

High Efficiency Particulate Air (HEPA) Filter

Should high efficiency particulate air (HEPA) filters be used in the prevention and control of COVID-19 infection in public spaces and locations with sustained community transmission?
We suggest the use of HEPA filter as an option to improve air quality for COVID-19 prevention and control in indoor spaces with inadequate ventilation. *(Low quality of evidence; Conditional recommendation)*

N95 Decontamination Techniques

What are effective decontamination techniques for N95 reuse?

In situations where there is shortage of filtering facepiece respirators (FFR), we suggest the use of Hydrogen Peroxide Vapor (HPV), Ultraviolet Germicidal Irradiation (UVGI), moist heat and peracetic acid dry fogging system (PAF) as options for N95 mask decontamination as recommended by the manufacturer based on their ability to reduce SARS-COV-2 load and infectivity while still maintaining N95 mask integrity. *(Low quality of evidence; Conditional recommendation)*

We recommend against the use of autoclave and alcohol as these methods alter filtering facepiece respirator's (N95) integrity and degrade filtration efficacy. *(Very low quality of evidence; Strong recommendation)*

PPE in Surgery

What is the appropriate PPE to be used use during surgeries to reduce the risk of virus transmission?

We recommend the use of appropriate PPE to include mask (N95 or higher standard), fluid repellent sealed well-fitting long gown, double gloves, apron, full face shield or goggles or visor, scrub hat, and disposable shoe covers or dedicated closed footwear among surgeons engaged in aerosol generating procedures of suspected or confirmed COVID-19 patients. *(Very low quality of evidence; Strong recommendation)*

PPE in Outpatient Settings

What is the appropriate PPE for healthcare workers in the outpatient setting to reduce the risk of virus transmission?

We recommend the use of at least surgical face mask and face shield for protection against COVID-19 infection among healthcare workers in the outpatient setting not performing aerosol generating procedures. Additional PPEs such as medical gowns and gloves should be worn as part of standard precautions during the performance of other procedures. *(Very low quality of evidence; Strong recommendation)*

PPE in Hospitals

What is the appropriate PPE for health care workers in the wards, ICU and emergency room to reduce the risk of virus transmission?

We recommend the use of the following PPE: disposable hat, medical protective mask (N95 or higher standard), goggles or face shield (anti-fog), medical protective clothing, disposable gloves and disposable shoe covers or dedicated closed footwear as an effective intervention in the prevention of COVID-19 among health care workers in areas with possible direct patient care of confirmed or probable COVID-19 patients and possible performance of aerosol generating procedures. *(Moderate quality of evidence; Strong recommendation)*

Face Mask and Face Shield or Goggles vs Face Mask Alone

Should facemask plus face shield be used rather than facemask alone to reduce SARS COV2 transmission?

We suggest the use of face mask plus protective eyewear in the form of face shield or goggles for the general public in areas with sustained community transmission of SARS-COV2. *(Very low quality of evidence; Conditional recommendation)*

We recommend the use of medical face mask plus face shield and standard personal protective equipment

among health care workers not directly involved in the care of COVID-19 patients in areas with sustained community transmission of SARS-COV2. *(Very low quality of evidence; Strong recommendation)*

Physical Barriers

Should protective physical barriers be used to prevent COVID-19?

We suggest against the use of protective physical barrier enclosures (ex. aerosol box) for the prevention of COVID-19 among health care providers who perform aerosol generating medical procedures*. *(Very low quality of evidence; Conditional recommendation)*

We suggest the use of protective physical barriers in the prevention of COVID-19 in areas where physical distancing cannot be adhered to (e.g., offices, reception desk)**. *(Very low quality of evidence; Conditional recommendation)*

*Proper PPEs should be used by health care providers when performing aerosol-generating procedures.
** Adequate ventilation, physical distancing, use of facemasks and personal hygiene should still be maintained to prevent COVID-19 infections. Regular cleaning and disinfection of physical barriers should be practiced.

Disinfection of Surfaces

Should surfaces be disinfected to prevent COVID-19 infection?

we recommend the practice of cleaning and disinfecting surfaces using the appropriate disinfecting chemical agents such as 0.5% sodium hypochlorite solution (bleach) or 70% alcohol to prevent COVID-19 infection.

For high touch surfaces and high traffic areas, such as in the workplace, disinfection should be done before shift, intermittently during shift and after the shift.

For household disinfection, once daily disinfection on high touch surfaces is recommended.

(Low quality of evidence; Strong recommendation)

Living Recommendations on Vaccines and Prophylactic Interventions for COVID-19

Vaccines

Are vaccines effective and safe in the prevention of COVID-19 infections?

We recommend the use of the following vaccines to prevent symptomatic SARS-CoV-2 infection in **adults**: *(Moderate quality of evidence; Strong recommendation)*

a. BNT162b2 (Pfizer/BioNTech) (given as 0.3ml (30ug) intramuscular injections, in 2 doses, 21 days apart)
b. mRNA-1273 (Moderna) (given as 0.5ml (100ug) intramuscular injections, in 2 doses, 28 days apart)
c. ChAdOx1 (AstraZeneca) (given as 0.5 ml (5×10^6 vp) intramuscular injections, in 2 doses, at least 12 weeks apart)
d. Gam-COVID-Vac (Gamaleya) (given as rAd-26 0.5ml intramuscular injection, then rAd-5S 0.5 ml intramuscular injection 21 days after)
e. Ad26.COV2.S (Janssen/Johnson&Johnson) (given as 0.5ml single dose intramuscular injection)

We recommend the use of CoronaVac (Sinovac) (given as 0.5ml (600SU) intramuscular injection, in 2 doses, at 28 days apart) to prevent symptomatic SARS-CoV-2 infection among **adults**. *(Low quality of evidence; Strong recommendation)*

We recommend the use of BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya) and Ad26.COV2.S (Janssen/ Johnson&Johnson) vaccines to prevent symptomatic SARS-CoV-2 infection in **older adults (>64 year old)**. *(Low quality of evidence; Strong recommendation)*

There is insufficient evidence to recommend the use of CoronaVac (Sinovac) to prevent symptomatic SARS-CoV-2 Infection in **older adults (>60 years old)**. *(Very low quality of evidence)*

We recommend the use of BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya), CoronaVac (Sinovac) and Ad26.COV2.S (Janssen/ Johnson&Johnson) vaccines in **pregnant and lactating women** after consultation with a physician. *(Very low quality of evidence; Conditional recommendation)*

We recommend the use of BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya) and Ad26.COV2.S (Janssen/ Johnson&Johnson) vaccines to prevent SARS-CoV-2 infection in **adults who have stable medical comorbidities and are at risk for severe infection**. *(Moderate quality of evidence; Strong recommendation)*

We suggest the use of CoronaVac (Sinovac) to prevent SARS-CoV-2 infection **in adults who have stable medical comorbidities and are at risk for severe infection**. *(Very low quality of evidence; Conditional recommendation)*

We recommend the use of BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya), CoronaVac (Sinovac) and Ad26.COV2.S (Janssen/ Johnson&Johnson) vaccines to prevent SARS-CoV-2 infection in **immunocompromised patients** (i.e., diagnosed with HIV, hepatitis B and C, those with cancer undergoing chemotherapy, transplant patients receiving immune-suppression) after medical clearance from a physician. *(Low quality of evidence; Strong recommendation)*

We recommend the use of BNT162b2 (Pfizer/BioNTech)vaccine in children 12 years old and above to prevent SARS-CoV-2 infection: *(Moderate quality of evidence, Strong recommendation)*

There is no evidence on the use of mRNA-1273 (Moderna), ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya), Ad26.COV2.S (Janssen/ Johnson&Johnson) and CoronaVac (Sinovac) among children <18 years old to prevent SARS-CoV-2 infection.

We recommend **against** the use of these vaccines for those **who have known allergies to the contents / excipients** of the vaccine, such as polysorbate (ChAdOx1 (Astrazeneca), Gam-COVID-Vac (Gamaleya) and Ad26.COV2.S (Janssen/ Johnson&Johnson)) and polyethylene glycol or PEG200 DMG (BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna)). *(Moderate to high quality of evidence; Strong recommendation)*

Melatonin

Should melatonin be used in the prevention of COVID-19 infection?
We recommend against the use of melatonin as prevention for COVID-19 infection. *(Very low quality of evidence; Strong recommendation)*

Vitamin D

Should Vitamin D supplementation be used in the prevention of COVID-19 infection?
We recommend against the use of Vitamin D supplementation to prevent COVID-19 infection. *(Very low quality of evidence; Strong recommendation)*

Zinc

Should zinc supplementation be used in the prevention of COVID-19 infection?
We recommend against the use of zinc supplementation to prevent COVID-19 infection. *(Very low quality of evidence; Strong recommendation)*

Hydroxychloroquine/Chloroquine

Should hydroxychloroquine/ chloroquine be used in the prevention of COVID-19?
We recommend against the use of HCQ for pre-exposure prophylaxis in adults who are at high risk of exposure to COVID-19 cases. *(Moderate quality of evidence; Strong recommendation)*

We recommend against the use of HCQ for post-exposure prophylaxis in adults who are exposed to COVID-19 cases. *(Low quality of evidence; Strong recommendation)*

Lopinavir/Ritonavir

Should lopinavir/ritonavir be used as prophylaxis for the prevention of COVID-19?
We recommend against the use of lopinavir/ritonavir for chemoprophylaxis in individuals exposed to COVID-19 patients. *(Very low quality of evidence; Strong recommendation)*

Saline Nasal Irrigation

Should saline nasal irrigation be used for the prevention of COVID-19?

There is insufficient evidence to recommend the use of saline nasal irrigation (SNI) to prevent COVID-19 in healthy individuals. *(Very low quality of evidence)*

Steam Inhalation

Should steam inhalation be used for the prevention of COVID-19?

We recommend against the use of steam inhalation in the prevention of COVID-19. *(Very low quality of evidence; Strong recommendation)*

Antiseptic Gargles

Should antiseptic gargles be used for the prevention of COVID-19?

There is insufficient evidence to recommend the use of antiseptic mouthwash or gargle to prevent COVID-19 in healthy individuals. *(Very low quality of evidence)*

Ivermectin

Should ivermectin be used as COVID-19 prophylaxis for the general population?

We recommend against the use of ivermectin as COVID-19 prophylaxis for the general population. *(Very low quality of evidence; Strong recommendation)*

We recommend against the use of ivermectin for COVID-19 as post-exposure prophylaxis for household contacts of confirmed COVID-19 patients. *(Very low quality of evidence; Strong recommendation)*

We recommend against the use of ivermectin for COVID-19 as prophylaxis for healthcare workers. *(Very low quality of evidence; Strong recommendation)*

Living Recommendations on Adjunct Interventions for Treatment of COVID-19

Zinc

Should zinc be given as an adjunct treatment to patients diagnosed with COVID-19 infection?
There is insufficient evidence to recommend the use of zinc as adjunct treatment for patients with COVID-19 infection both in the outpatient and in-patient setting. *(Very low quality of evidence)*

Vitamin B

Should B Vitamins be used as an adjunct in the treatment of COVID-19?
We suggest against the use of B vitamins as adjunct in the treatment of patients with COVID-19. *(Very low quality of evidence; Conditional recommendation)*

Vitamin C

Should Vitamin C be used as adjunct treatment for COVID-19?
There is insufficient evidence to recommend the use of intravenous Vitamin C as adjunct treatment for patients with COVID-19 infection. *(Low quality of evidence)*

Vitamin D

Should Vitamin D supplements be used as adjunct treatment for COVID-19?
There is insufficient evidence to recommend the use of Vitamin D supplementation as adjunct treatment for patients with COVID-19 infection. *(Very low quality of evidence)*

Melatonin

Should melatonin be used in the adjunctive treatment of COVID-19?
There is insufficient evidence to recommend the use of melatonin as adjunct treatment for patients with COVID-19 infection. *(Very low quality of evidence)*

Virgin Coconut Oil

Should virgin coconut oil be used in the adjunctive treatment of COVID-19?
There is no evidence to recommend the use of virgin coconut oil as adjunct treatment for patients with COVID-19 infection.

Fatty Acids

Should oral fatty acid supplements be used as adjunct treatment for patients with COVID-19?
There is insufficient evidence to recommend the use of fatty acid supplements as adjunctive treatment for patients with COVID-19. *(Low quality of evidence)*

N-acetylcysteine

Should N-acetylcysteine be used as an adjunct treatment for patients diagnosed with COVID-19?
We recommend against the use of intravenous N-acetylcysteine as adjunct treatment for patients with COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

Renin-Angiotensin-Aldosterone System Blockers (RAAS)

Should RAAS blockers be continued in patients with COVID-19?

We recommend continuing maintenance RAAS blockers for hypertension among patients with COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

Ibuprofen

Does the concurrent use of Ibuprofen worsen COVID-19 outcomes?

We suggest that ibuprofen may still be used as symptomatic treatment of patients with COVID-19 infection if clinically warranted. Concurrent use of ibuprofen is not associated with worsening of COVID-19 outcomes. *(Very low quality of evidence; Conditional recommendation)*