COVID-19: Interim Guidance on Management Pending Empirical Evidence. *From an American Thoracic Society-led International Task Force*

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on behalf of the International Task Force on COVID-19

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Disclosures: KCW is co-developer of the Convergence of Opinion on Recommendations and Evidence (CORE) process that is utilized in the guidance document and serves at the Chief of Guidelines and Documents for the American Thoracic Society. SHC, CB, and JR have nothing to disclose.

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Note to readers: There is little empirical evidence to guide management of COVID-19. However, with 80,000 new cases being confirmed daily and the rate still increasing, clinicians taking care of patients with COVID-19 need guidance now. We convened an international task force of clinicians from academic centers on the frontline of COVID-19 management to make consensus suggestions on controversial topics. The suggestions are based upon scarce direct evidence, indirect evidence, and clinical observations. The goal is to improve outcomes and facilitate research by standardizing care. The suggestions provided in this document do not constitute official positions of the American Thoracic Society or the institutions of the participants, and they should never be considered mandates as no suggestion can incorporate all potential clinical circumstances. The suggestions are interim guidance and will be reevaluated as evidence accumulates.

Abstract

Background: Coronavirus Disease 2019 (COVID-19) is an acute respiratory disease caused by the coronavirus, SARS-CoV-2. There is a paucity of empirical evidence to guide the management of COVID-19, but clinical observations are accumulating. Consensus recommendations can help standardize care and improve outcomes.

Methods: An International Task Force was composed, consisting of clinicians from academic centers active in COVID-19 patient care. Consensus suggestions were derived using the electronic decision-making portion of the Convergence of Opinion on Recommendations and Evidence (CORE) process.

Results: The task force recommended collecting data and comparing outcomes among COVID-19 patients who received an intervention to those who did not receive the intervention using appropriate methods for causal inference and control of confounders. Suggestions were made to treat hospitalized patients who have COVID-19 and severe pneumonia with hydroxychloroquine or chloroquine on a case-by-case basis if certain requirements are present, and to utilize prone ventilation and extracorporeal membrane oxygenation (ECMO) in patients with refractory hypoxemia due to COVID-19 pneumonia (i.e., acute respiratory distress syndrome [ARDS]). The task force made no suggestions for or against treatment with remdesivir, lopinavir-ritonavir, tocilizumab, or systemic corticosteroids.
Conclusions: The task force made suggestions based upon scarce direct evidence, indirect evidence, and clinical experience. Each suggestion will be reconsidered as relevant evidence, particularly randomized trials, are published.
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Introduction

Coronavirus Disease 2019 (COVID-19) is an acute respiratory disease caused by the coronavirus, SARS-CoV-2. There is little direct evidence to inform management of COVID-19. The International Task Force strongly agrees with prevailing sentiment that clinical trials are urgently needed to effectively guide management. However, most patients do not have access to clinical trials, trials take time, and speculation is that results will not be available until late spring or early fall. As a result, institutions and clinicians on the frontline are utilizing a variety of approaches to manage COVID-19 patients outside of a clinical trial, ranging from supportive care alone to prescribing unproven medications.

Pending the results of clinical trials, this document is aimed at providing interim guidance for therapeutic interventions to frontline clinicians, based upon scarce direct evidence, indirect evidence, and the observations and experiences of clinicians around the world who have battled COVID-19; they are not based upon systematic reviews of the evidence. Such consensus guidance may standardize care and improve outcomes. The suggestions provided in this document do not constitute official positions of the American Thoracic Society or the institutions of the participants. They should not be considered mandates, as no suggestion can incorporate all potential clinical circumstances. All suggestions will be revisited as evidence accumulates.

Methods

An International Task Force was composed from March 19-22, 2020. Invitations were initially sent to members of the American Thoracic Society (ATS) who are clinically active in medical centers that are involved in COVID-19 patient care. Those invitees were asked to suggest additional participants on the frontlines, with an emphasis on pulmonologists, medical intensivists, and infectious disease experts from areas most stricken by COVID-19. Clinicians were asked to abstain from questions outside their expertise. Invitations were sent to 95 individuals and 80 agreed to participate (84% acceptance rate). The lone reason for declining was being too busy with patient care responsibilities.

Consensus suggestions were derived using the electronic decision-making portion of the Convergence of Opinion on Recommendations and Evidence (CORE) process. The CORE process is a consensus-based approach to making clinical recommendations that has been shown to yield recommendations that are concordant with recommendations developed using Institute of Medicine-adherent methodology; it has been described in detail elsewhere.[1,2] Briefly, SurveyMonkey® software (SurveyMonkey, San Mateo, CA) was used to create a multiple-choice survey. Each survey question consisted of three parts: 1) presentation of the question in a modified PICO (Patient, Intervention, Comparator, Outcomes) format, 2) a multiple-choice question asking for a strong or weak recommendation for or against a course of action, or no

recommendation, and 3) a free-text box for comments.

The survey was initially administered from March 23-25, 2020. A second survey was then constructed that was identical to the first, except results from the first round were added: a) the proportion of participants who selected each multiple-choice option, b) representative comments from the participants, and c) references provided by the participants. The survey was re-administered from March 26-30, 2020. Seventy-three of the 80 task force members completed the surveys (91% response rate).

Agreement on directionality was tabulated for each multiple-choice question. For example, if 5, 20, 50, 13, and 12 individuals selected a strong recommendation for, weak recommendation for, no recommendation, weak recommendation against, and strong recommendation against, respectively, the results were reported as 25% for the intervention, 50% neither for nor against the intervention, and 25% against the intervention. At least 70% agreement on directionality was necessary to make a consensus suggestion. This threshold optimizes the concordance of CORE-derived consensus recommendations with Institute of Medicine-adherent guideline recommendations[1].

Following the tabulation of results, the manuscript was written. The suggestion was based upon the tabulated results, the rationale was extrapolated from participants' comments, and the description of what other organizations are saying was based upon a survey of other organizations' websites.

Suggestions

1. **The International Task Force suggests that data be collected from COVID-19 patients who receive one or more of the interventions suggested in this document, in a manner that enables studies that use valid methods for causal inference and control of confounders. The data should be assessed periodically so that patients who received the intervention can be compared those who did not receive the intervention. Management should be modified as-needed based upon the comparisons.**

Rationale. There is an immediate need to determine which interventions against COVID-19 are effective and safe. Ideally, this would be done through randomized trials and there are many such trials in progress. In the meantime, unproven therapies are being administered off-label or on a compassionate use basis. When data are not collected in such situations, it is a missed opportunity.

The International Task Force recommends that data be collected from COVID-19 patients who receive one or more of the interventions suggested in this document. Ideally, data collection will include detailed information about interventions, outcomes, and patient characteristics to enable analysis using appropriate methods of causal inference and to control for confounding. Important outcomes include mortality, ICU length of stay, hospital length of stay, intubation rate, length of mechanical ventilation, need for long-term oxygen therapy, and adverse events.

The data should be assessed periodically so that patients who received the intervention can be compared those who did not receive the intervention. This can be done at the institutional, local, national, or international level. Such data will provide interim guidance until superseded by randomized trial results when available.

For patients with COVID-19 who are well-enough to be managed as outpatients, we make <u>no suggestion</u> either for or against hydroxychloroquine (or chloroquine). 18% for intervention, 36% no suggestion, and 46% against intervention.

For hospitalized patients with COVID-19 who have no evidence of pneumonia, we make <u>no suggestion</u> either for or against hydroxychloroquine (or chloroquine). 8% for intervention, 50% no suggestion, and 42% against intervention.

For hospitalized patients with COVID-19 who have evidence of pneumonia, <u>*we suggest*</u> hydroxychloroquine (or chloroquine) on a case-by-case basis. Requirements include all of the following: a) shared decision-making in which the patient is informed about the possible benefits and potential side effects, b) collection of data in a manner that enables studies that use valid methods for causal inference and control of confounders for the purpose of interim assessment, c) the patient's clinical condition is sufficiently severe to warrant investigational therapy, and d) there is not a shortage of drug supply. 73% for intervention, 16% no suggestion, and 11% against intervention.

Evidence of pneumonia is defined as radiographic opacities or, if a chest radiograph has not been performed, an SpO2 of 94% or less accompanied by symptoms and signs of infection.

Rationale for question. Hydroxychloroquine and chloroquine have been shown to have in vitro activity against SARS-CoV-2, with hydroxychloroquine being more potent[3,4]. Clinical trials, however, provide an inconsistent message. Small controlled clinical trials from more than ten hospitals in China reportedly indicate that chloroquine is superior to controls in preventing pneumonia, improving lung imaging findings, hastening conversion to a virus-negative state, and shortening the duration of disease[5]. However, two of the trials are now publicly available and they have important limitations: in a negative trial, both arms included patients who had undergone treatment with anti-viral drugs[6] and, in a positive trial, the arms of the trial had important baseline differences[7]. A small controlled trial from France reported that hydroxychloroquine hastens conversion to a virus-negative state, but important limitations included a lack of patients with severe illness, lack of blinding, no randomization, and loss to follow-up[8].

Results. The task force was roughly divided into two perspectives. Some members concluded that neither hydroxychloroquine nor chloroquine should be administered without proven benefit in COVID-19; rather, clinicians should wait until the results of randomized trials are known, otherwise there is a possibility that an ineffective and potentially harmful medication may be inappropriately administered on a large scale, potentially leading to shortages of these medications that are needed for other legitimate purposes. Other members extrapolated from the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework for making recommendations in the context of low or very-low quality evidence and concluded that treatment is reasonable because severe COVID-19 pneumonia is a potentially lethal disease, hydroxychloroquine or chloroquine might be beneficial, and the chance of harm is low[9]. The latter group emphasized that the adverse effects profile of hydroxychloroquine and chloroquine are well established including QT interval prolongation (less likely with hydroxychloroquine than chloroquine), hepatic and renal abnormalities, and immunosuppression. QT interval prolongation is more likely among patients who receive multiple medications with propensity to increase the QT interval, including azithromycin which many clinicians are using in combination with hydroxychloroquine or chloroquine. Patients can be monitored for adverse effects with routine tests; however, such testing increases patient-clinician interaction and laboratory personnel exposure, increasing the risk of transmission.

The results are notable for a shift toward treatment with hydroxychloroquine or chloroquine as the severity of COVID-19 increased, indicating that the perceived balance of potential benefits to harms changed as severity of illness increased. Fewer than 20% of the task force suggested using the medications in outpatients or hospitalized patients without pneumonia, but nearly 75% suggested prescribing hydroxychloroquine or chloroquine in hospitalized COVID-19 patients with severe pneumonia. This was adequate agreement to make a consensus suggestion for hydroxychloroquine or chloroquine in hospitalized patients with COVID-19 pneumonia given the *a priori* decision that 70% agreement would yield a suggestion; had we chosen a threshold of 75% or 80%, the result would have been no suggestion.

The trade-off between waiting for evidence before deciding whether to administer a therapy and utilizing a therapy while awaiting evidence isn't unique; however, it is magnified by the urgency of a pandemic[10]. The tension is probably best solved by creating evidence during routine patient care, while awaiting clinical trial results. The task force, therefore, concluded that data should be collected in a manner that enables studies that use valid methods for causal inference and control of confounders, so that interim assessment may occur, and management adjusted accordingly.

Comments by the task force during the survey and manuscript preparation provided essential conditions for the suggestion. The task force urged shared decision-making in which the patient is informed about the possible benefits and potential side effects. There were concerns that "hospitalized patients with COVID-19 and pneumonia" was too broad of a population; subsequent consensus was that the patient's illness should be severe enough to warrant investigational therapy. Several individuals who did not vote to suggest hydroxychloroquine or chloroquine in COVID-19 patients with pneumonia indicated that they would have voted

to use the medications if the illness was even more severe, such as the patient being severely hypoxemic or requiring high levels of conventional oxygen, high-flow oxygen, non-invasive mechanical ventilation, or invasive mechanical ventilation. The task force emphasized that patients should be monitored closely for adverse effects and a low threshold maintained for discontinuing the medications if adverse effects arise. Finally, the task force stated that the suggestion should be revised as-necessary as new evidence arises.

What others are saying. The World Health Organization (WHO) has warned against the use medications that have not been proven in an RCT; its SOLIDARITY trial includes a chloroquine arm. The United States Centers for Disease Control and Prevention (CDC) says, "There are no currently available data from RCTs to inform clinical guidance on the use, dosing, or duration of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection." The United States Food and Drug Administration (FDA) stated that there is insufficient evidence to support treatment of COVID-19 with hydroxychloroquine or chloroquine, but issued an emergency-use authorization to allow both donated drugs "to be distributed and prescribed by doctors to patients with COVID-19, as appropriate, when a clinical trial is not available or feasible." The Surviving Sepsis Campaign made no recommendation for or against hydroxychloroquine or chloroquine due to insufficient evidence[11].

2. **For hospitalized patients with COVID-19 who have evidence of pneumonia we make <u>no suggestion</u> either for or against treatment with remdesivir.** 68% for intervention, 26% no suggestion, and 5% against intervention.

Rationale for question. Remdesivir has in vitro activity against SARS-CoV-2[3] and related viruses including MERS-CoV[12,13], SARS-CoV[13], and other coronaviruses[13].

Results. The differing perspectives described above for hydroxychloroquine and chloroquine also existed with remdesivir. Supporting the perspective that favored waiting for randomized trial data before deciding whether to prescribe remdesivir in COVID-19 pneumonia were concerns about the unknown adverse effect profile of remdesivir (in contrast to hydroxychloroquine and chloroquine for which there are decades of clinical experience) and the uncertainty regarding timing of initiation and duration of therapy.

It is noteworthy that 68% of the task force favored treatment remdesivir, if available, which was one vote shy of enough agreement to make a consensus suggestion. Several task force members indicated that radiographic evidence of pneumonia alone was insufficient to warrant a suggestion to initiate remdesivir; however, they would have voted to use the medication in conditions severe enough to warrant investigational therapy, such as patients who are severely hypoxemic or requiring high levels of conventional oxygen, high-flow oxygen, non-invasive mechanical ventilation, or invasive mechanical ventilation.

What others are saying. The WHO has not taken a position on the use of remdesivir in COVID-19 but its SOLIDARITY trial includes a remdesivir arm. The CDC has not taken a position on remdesivir but describes options for obtaining it for hospitalized patients with COVID-19 and pneumonia. The FDA reports that it has been working with the maker of remdesivir to find multiple pathways to study the drug under the FDA's investigational new drug requirements and to provide the drug to patients under emergency use. The Surviving Sepsis Campaign made no recommendation for or against remdesivir due to insufficient evidence[11].

3. **For hospitalized patients with COVID-19 who have evidence of pneumonia, we make <u>no suggestion</u> either for or against treatment with lopinavir-ritonavir.** 30% for intervention, 26% no suggestion, and 43% against intervention.

Rationale for question. Lopinavir has both in vitro and in vivo activity against MERS-CoV[14,15], while the lopinavir-ritonavir combination has in vitro activity against SARS-CoV[16,17]. In humans with SARS, lopinavir-ritonavir reduces viral load and the risk of acute respiratory distress syndrome (ARDS) or death[18]. In a randomized trial of 199 patients with COVID-19, patients who received lopinavir-ritonavir improved more quickly, had a shorter length of ICU stay, and had lower mortality than patients who received standard care; however, while the differences would have been clinically important if real, the trial was too small to definitively confirm or exclude an effect (i.e., the findings were not statistically significant)[19].

Results. A plurality of the task force was against the administration

of lopinavir-ritonavir to hospitalized patients with COVID-19 and pneumonia, reflecting the lack of definitive benefit and evidence of frequent gastrointestinal side effects in the RCT. However, the amount of agreement was insufficient to reach consensus on a formal suggestion against lopinavir-ritonavir, reflecting the opinion of some task force members that, if the RCT had been larger, some of the favorable point estimates may have reached statistical significance.

What others are saying. The WHO has not taken a position on the use of lopinavir-ritonavir in COVID-19 but its SOLIDARITY trial includes a lopinavir-ritonavir arm. The CDC states that "lopinavir-ritonavir did not show promise for treatment of hospitalized COVID-19 patients with pneumonia in a recent clinical trial in China. This trial was underpowered…". The FDA has not taken a position on the use of lopinavir-ritonavir in COVID-19. The Surviving Sepsis Campaign made a weak recommendation against the routine use of lopinavir-ritonavir[11].

4. For hospitalized patients with COVID-19 who have evidence of pneumonia, we make <u>no suggestion</u> either for or against treatment with tocilizumab. 30% for intervention, 56% no suggestion, and 14% against intervention.

Rationale for question. Patients with COVID-19 have elevated levels of the pro-inflammatory cytokine, IL-6, with the most severely ill patients exhibiting the highest levels[20-22]. Tocilizumab is an anti-IL-6 monoclonal antibody that has proven effective in other IL-6 mediated diseases. It is recommended by China's National Health Commission for use in COVID-19 patients with elevated IL-6 levels.

Results. Most task force members elected to make no suggestion, concluding that evidence of beneficial effects in other IL-6 mediated diseases is insufficient to warrant use in COVID-19 at this time. The task force agreed, however, that clinical trials are worthwhile.

What others are saying. The WHO, CDC, and FDA have not taken a position on the use of tocilizumab in COVID-19, although the FDA approved an RCT comparing tocilizumab to standard care. The Surviving Sepsis Campaign made no recommendation for or against tocilizumab due to insufficient evidence[11].

5. For hospitalized patients with COVID-19 who have evidence of pneumonia, we make <u>no suggestion</u> either for or against treatment with systemic corticosteroids. 15% for intervention, 18% no suggestion, and 67% against intervention.

Rationale for question. Patients with COVID-19 have elevated levels of pro-inflammatory cytokines and other inflammatory biomarkers[20-22], leading some clinicians to postulate that systemic corticosteroid therapy may be beneficial. However, studies from patients with other viral infections suggest that systemic corticosteroids may confer no benefit or may have harmful effects, including increased viral replication and prolonged viral shedding[23-26].

Results. Sixty-seven percent of the task force favored a suggestion against systemic corticosteroids for the treatment of COVID-19. This was only two votes shy of enough agreement to make a consensus suggestion against systemic corticosteroids. The task force emphasized that the question was about systemic corticosteroids for the specific treatment of COVID-19 in general. The task force did not address systemic steroids administered at different points during the disease course or systemic steroids administered for the treatment of comorbid conditions, such as COPD exacerbations or ARDS; some clinical practice guidelines recommend systemic corticosteroids for moderate to severe early ARDS[11,27].

What others are saying. The WHO says that clinicians should "not routinely give systemic corticosteroids for the treatment of viral pneumonia outside clinical trials." The CDC says "corticosteroids should be avoided unless indicated for other reasons, such as management of chronic obstructive pulmonary disease exacerbation or septic shock." The FDA has not taken a position on the use of systemic corticosteroids in COVID-19. The Surviving Sepsis Campaign made a weak recommendation against systemic corticosteroids in mechanically ventilated COVID-19 patients without ARDS, but a weak recommendation for systemic corticosteroids in mechanically ventilated COVID-19 patients with ARDS[11].

6. For patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS), <u>*we suggest*</u> prone ventilation. 99% for intervention, 1% no suggestion, and 0% against intervention.

Refractory hypoxemia refers to an SpO2 consistently less than 90%

despite maximal ventilator interventions to increase the SpO2.

Rationale for question. Patients with COVID-19 may develop viral pneumonia, which can progress to ARDS. Clinical practice guidelines make a strong recommendation for prone ventilation for more than 12 hours in patients with severe ARDS[28]; however, prone ventilation has not been studied in COVID-19 patients.

Results. The task force agreed that patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS) should undergo prone ventilation. This was based upon the assumption that ARDS due to COVID-19 behaves like ARDS due to other causes for which the benefits of prone ventilation are well established. Agreement with the assumption of similarity was not universal, however, as several task force members argued that ARDS in COVID-19 is unique because lung compliance is maintained and the effects of prone ventilation more modest than in typical ARDS, a view supported by a recent research letter[29]. Nevertheless, the task force concluded that prone ventilation is worth a trial since it is low risk and low cost. However, they warned that placing the patient in the prone position must be done with caution since there is a risk of transmitting infection to healthcare staff due to aerosolized secretions.

What others are saying. The WHO, CDC, and FDA have not addressed prone ventilation. The Surviving Sepsis Campaign made a weak recommendation for prone ventilation in patients with moderate to severe ARDS[11].

6. **For patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS), *we suggest* that extracorporeal membrane oxygenation (ECMO) be considered if prone ventilation fails.** 75% for intervention, 23% no suggestion, and 1% against intervention.

Rationale for question. Patients with COVID-19 may develop viral pneumonia, which can progress to ARDS. Clinical practice guidelines declined to make a recommendation for or against ECMO in ARDS[28] and ECMO has not been studied in COVID-19 patients.

Results. Seventy-five percent of the task force agreed that patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS) should be considered for ECMO; this was adequate agreement for a consensus suggestion in favor of ECMO. The task force emphasized that ECMO should be contemplated only after failing prone ventilation. The task force acknowledged that ECMO may not be feasible during much of a pandemic because it is resource intensive, challenging from an infection control perspective, and requires frequent blood transfusions at a time when blood may be in shortage.

What others are saying. The WHO, CDC, and FDA have not addressed ECMO. The Surviving Sepsis Campaign made a weak recommendation for veno-venous ECMO or referral to an ECMO center in patients with refractory hypoxemia despite recruitment maneuvers[11].

Discussion

The task force's goal was to provide interim guidance for therapeutic interventions to frontline clinicians, based upon scarce direct evidence, indirect evidence, and the observations and experiences of other clinicians around the world who have battled COVID-19, using a consensus-building process called the CORE process[1,2]. The task force suggests prone ventilation for COVID-19 patients with refractory hypoxemia, ECMO for COVID-19 patients with refractory hypoxemia who fail prone ventilation and, on a case-by-case basis, hydroxychloroquine or chloroquine in the context of shared decision-making, data collection for research, severe enough disease to warrant investigational therapy, and sufficient quantities of drug are available (Table).

This interim guidance has several important limitations. There may have been selection bias during task force composition, favoring those with professional connections with the American Thoracic Society and, therefore, pulmonary and critical care medicine. Since COVID-19 is a new disease being managed by a variety of specialties ranging from intensivists to infectious disease specialists, expertise in COVID-19 management was probably variable across task force members; this was enhanced by the inclusion of multiple specialties to ensure that we have appropriate expertise for future versions of the guidance, which may include infection control, radiological findings, and other topics. The document did not address the combination of hydroxychloroquine plus azithromycin, which is being used in many institutions currently. Finally, crude data was not collected in a

fashion that enabled comparison of different groups of task force members, such as North Americans versus Europeans, clinicians versus thought leaders, etc.

In conclusion, empirical evidence, particularly randomized trials, are desperately needed to guide therapy. Supportive care remains the mainstay of treatment and social distancing remains an important part of prevention. The suggestions provided in this document will be periodically reevaluated as new evidence emerges and modified accordingly.

Table- Interim Guidance on Management of COVID-19

Suggestions for	Vote from CORE process (>70% agreement to make suggestion)
For any COVID-19 patient who receives an intervention suggested in this document, data should be collected in a manner that enables studies that use valid methods for causal inference and control of confounders. The data should be assessed periodically so that patients who received the intervention can be compared those who did not receive the intervention. Management should be modified as-needed based upon the comparisons.	No vote
Hydroxychloroquine (HCQ) or chloroquine (CQ) for patients with confirmed COVID-19 and severe pneumonia if: • Shared decision-making is utilized, and • Data is collected for research comparing HCQ to no HCQ, or CQ to no CQ, and • Illness is severe enough to warrant investigational therapy, and • HCQ or CQ are not in short supply.	73% for HCQ or CQ 16% no suggestion 11% against HCQ or CQ
Prone ventilation for patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS)	99% for prone ventilation 1% no suggestion 0% against prone ventilation
Consideration of ECMO for patients with refractory hypoxemia due to progressive COVID-19 pneumonia (i.e., ARDS) who have failed prone ventilation	75% for ECMO 23% no suggestion 1% against ECMO
No suggestion for or against	
HCQ or CQ for outpatient COVID-19 patients	18% for HCQ or CQ 36% no suggestion 46% against HCQ or CQ
HCQ or CQ for hospitalized COVID-19 patients without pneumonia	8% for HCQ or CQ 50% no suggestion 42% against HCQ or CQ
Remdesivir for hospitalized COVID-19 patients with pneumonia	68% for remdesivir 26% no suggestion 5% against remdesivir
Lopinavir-ritonavir for hospitalized COVID-19 patients with pneumonia	30% for lopinavir-ritonavir 26% no suggestion 43% against lopinavir-ritonavir
Tocilizumab for hospitalized COVID-19 patients with pneumonia	30% for tocilizumab 56% no suggestion 14% against tocilizumab
Systemic corticosteroids for hospitalized COVID-19 patients with pneumonia	15% for intervention 18% no suggestion 67% against intervention

CORE= Convergence of Opinion on Recommendations and Evidence; ARDS= Acute Respiratory Distress Syndrome; ECMO= Extracorporeal Membrane Oxygenation

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