Clinical Management of Critically Ill Adults with COVID-19

Clinician Outreach and Communication Activity (COCA) Webinar

Thursday, April 2, 2020
Continuing Education

Continuing Education is not offered for this COCA Call.
To Ask a Question

- Using the Webinar System
  - Click the Q&A button.
  - Type your question in the Q&A box.
  - Submit your question.

- If we are unable to get to your question during the call, you may also email your question to coca@cdc.gov.

- For media questions, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.
For More Clinical Care Information on COVID-19

- **Call** COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
- **Refer** patients to state and local health departments for COVID-19 testing and test results.
  - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19, OR to get COVID-19 test results.
- **Visit** CDC’s Coronavirus (COVID-19) website: https://www.cdc.gov/coronavirus
- **Visit** emergency.cdc.gov/coca over the next several days to learn about future COCA Calls.
Today’s Presenters

- **CAPT Tim Uyeki, MD**
  Clinical Team Lead
  COVID-19 Response
  Centers for Disease Control and Prevention

- **Michael Bundesmann, MD, FCCP**
  Medical Director of Respiratory Therapy
  Pulmonary and Critical Care Medicine
  EvergreenHealth
  Kirkland, WA

- **Waleed Alhazzani, MD, MSc, FRCPC**
  Associate Professor Department of Medicine,
  McMaster University
  Hamilton, Ontario, Canada
COVID-19 Overview for Clinicians

Tim Uyeki MD, MPH
Clinical Team
CDC COVID-19 Response
April 2, 2020

For more information: www.cdc.gov/COVID19
Median incubation period is 4-5 days (range: 2-14 days)

**COVID-19: Wide spectrum of disease**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Illness</td>
<td>Uncomplicated upper respiratory tract viral infection</td>
</tr>
<tr>
<td>Moderate Pneumonia</td>
<td>Pneumonia without the need for supplemental oxygen</td>
</tr>
<tr>
<td>Severe Pneumonia</td>
<td>Pneumonia with dyspnea, respiratory distress, SpO2≤93% on RA, P/F ratio &lt;300</td>
</tr>
<tr>
<td>Critical Illness</td>
<td>Respiratory failure, septic shock, multiple organ dysfunction/failure</td>
</tr>
</tbody>
</table>

Link: [WHO Guidelines 2020](#)
Most patients had mild to moderate disease, but nearly 20% had severe or critical illness.

COVID-19 - China through 11-Feb-2020 (N=44,415)

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/Mod</td>
<td>81%</td>
</tr>
<tr>
<td>Severe</td>
<td>14%</td>
</tr>
<tr>
<td>Critical</td>
<td>5%</td>
</tr>
</tbody>
</table>

Of 1,099 hospitalized COVID-19 patients (through 29-Jan-2020), 5% were admitted to the ICU. (Guan et al. NEJM 2020)

Links: [Wu JAMA 2020](#)
Potential for patients to have acute deterioration in the second week of illness

COVID-19 - China through 2-Jan-2020 (N = 41)

Figure 2: Timeline of 2019-nCoV cases after onset of illness

Link: Huang Lancet 2020
But the case-fatality is disproportionately higher among older adults

COVID-19 - United States, February 12–March 16, 2020 (N = 4,226)

Links: MMWR 2020
Older adults: More likely to require ICU care and die, but hospitalizations and ICU admissions also occur among non-elderly adults

COVID-19 United States, February 12–March 16, 2020 (N = 4,226)

Links: MMWR 2020
Mortality from COVID-19 is highest among persons with underlying medical conditions

COVID-19 - China through 11-Feb-2020

- Cardiovascular Disease: 10.5%
- Diabetes: 7.3%
- Chronic Respiratory Disease: 6.0%
- Cancer: 5.6%

Link: China COVID-19 Epi Team 2020
Most, but not all patients have fever, cough, or shortness of breath on hospital admission (China, Singapore, U.S.)

- Fever: 50-52% had fever at admission
- Cough: 80-90% had cough at admission
- Dyspnea: 20-30% had shortness of breath at admission

Lower respiratory specimens may have higher virus yield than upper respiratory specimens, China (N = 205) Jan 1-Feb 17 2020

<table>
<thead>
<tr>
<th>Specimens and values</th>
<th>Bronchoalveolar lavage fluid (n = 15)</th>
<th>Fibrobronchoscope brush biopsy (n = 13)</th>
<th>Sputum (n = 104)</th>
<th>Nasal swabs (n = 8)</th>
<th>Pharyngeal swabs (n = 398)</th>
<th>Feces (n = 153)</th>
<th>Blood (n = 307)</th>
<th>Urine (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive test result, No. (%)</td>
<td>14 (93)</td>
<td>6 (46)</td>
<td>75 (72)</td>
<td>5 (63)</td>
<td>126 (32)</td>
<td>44 (29)</td>
<td>3 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Cycle threshold, mean (SD)</td>
<td>31.1 (3.0)</td>
<td>33.8 (3.9)</td>
<td>31.1 (5.2)</td>
<td>24.3 (8.6)</td>
<td>32.1 (4.2)</td>
<td>31.4 (5.1)</td>
<td>34.6 (0.7)</td>
<td>ND</td>
</tr>
<tr>
<td>Range</td>
<td>26.4-36.2</td>
<td>26.9-36.8</td>
<td>18.4-38.8</td>
<td>16.9-38.4</td>
<td>20.8-38.6</td>
<td>22.3-38.4</td>
<td>34.1-35.4</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>28.9-33.2</td>
<td>29.8-37.9</td>
<td>29.3-33.0</td>
<td>13.7-35.0</td>
<td>31.2-33.1</td>
<td>29.4-33.5</td>
<td>0.0-36.4</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: ND, no data.

Link: [Wang JAMA 2020](http://example.com)
Laboratory findings at hospital admission

- **Lymphopenia** (83%)
  - Thrombocytopenia (36%)
  - Leukopenia (34%)
  - C-reactive protein ≥10 mg/L: (61%)
  - Elevated AST, ALT: (20-39%) - higher with severe disease
  - Procalcitonin - typically normal on admission

- **Co-infections:**
  - Sporadic viral co-infections reported (e.g., influenza, parainfluenza)
  - Community-acquired secondary bacterial infection not reported in published case series (blood cultures: negative)

Link: [CDC Clinical Guidance 2020](https://www.cdc.gov)
Laboratory abnormalities in severe disease

- **Associated with severe or critical illness:**
  - ↓ lymphocytes, ↑ neutrophils
  - ↑ alanine aminotransferase and ↑ aspartate aminotransferase levels
  - ↑ lactate dehydrogenase, ↑ PCT, ↑ CRP, ↑ ferritin levels
  - ↑ serum levels of pro-inflammatory cytokines and chemokines

- **Evidence of immune dysregulation:** Higher plasma levels of pro-inflammatory cytokines (TNFα, IL-1, IL-6) and chemokines (IL-8) in severe/critically ill patients vs less severely ill patients

- **Associated with mortality:** ↑ D-dimers and lymphopenia

Link: [Qin CID 2020](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7213508/); [Huang Lancet 2020](https://www.lancet.com/journal/lancet); [Wang JAMA 2020](https://www.jama.com/jama); [Yang Lancet 2020](https://www.lancet.com/journal/lancet); [Arentz JAMA 2020](https://www.jama.com/jama)
Leukocytosis, specifically neutrophilia, during hospitalization is associated with death (N = 138, China, Jan 1-28, 2020)

Link: Wang JAMA 2020
Lymphopenia is common in all patients, but may be lower in non survivors than survivors (N = 138, China, Jan 1-28, 2020)

Link: Wang JAMA 2020
D-dimer is a strong predictor of death when compared with other markers of COVID-19 severity (N = 191), China, Dec 28, 2019 - Jan 28, 2020

Table 3: Risk factors associated with in-hospital death

<table>
<thead>
<tr>
<th>Demographics and clinical characteristics</th>
<th>Univariable OR (95% CI)</th>
<th>p value</th>
<th>Multivariable OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years *</td>
<td>1.14 (1.09-1.18)</td>
<td>&lt;0.0001</td>
<td>1.10 (1.03-1.17)</td>
<td>0.0043</td>
</tr>
<tr>
<td>SOFA score</td>
<td>6.14 (3.48-10.85)</td>
<td>&lt;0.0001</td>
<td>5.65 (2.61-12.23)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>D-dimer, μg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤0.5</td>
<td>1 (ref)</td>
<td></td>
<td>1 (ref)</td>
<td></td>
</tr>
<tr>
<td>&gt; 0.5 (0.52-7.43)</td>
<td>1.96 (0.32)</td>
<td></td>
<td>2.14 (0.21-21.39)</td>
<td>0.52</td>
</tr>
<tr>
<td>&gt; 1 (0.52-61.56)</td>
<td>20.04 (0.0001)</td>
<td></td>
<td>18.42 (2.04-128.55)</td>
<td>0.0033</td>
</tr>
</tbody>
</table>

Link: Zhou Lancet 2020
Adult ICU Case Series, U.S.
(N = 21) Feb 20-March 5, 2020; (N=24) Feb 24-March 9, 2020

- Common co-morbidities
  - Heart failure (0-43%)
  - COPD (4-33%)
  - Diabetes (33-58%)
  - Kidney disease (21-48%)
  - Obstructive sleep apnea (21-29%)

- Onset to ICU admission: @4.5-7 days
- Mean age: 70 years (43-92); 63 years (23-97)

- Complications
  - Respiratory failure requiring mechanical ventilation: (71-75%)
  - Shock requiring vasopressors: (67-71%)
  - Acute kidney failure: (0-19%)
  - Cardiomyopathy: (0-33%)
  - Bacterial co-infection (1/21; 0/20)

- Mortality: (50-52%)
COVID-19: Inpatient clinical management

- No proven FDA-approved treatment for COVID-19

- Management is supportive
  - Hypoxemic respiratory failure/ARDS
  - Septic shock
  - Cardiomyopathy/arrhythmia
  - Common critical care complications

COVID-19: Therapeutics

- No FDA-approved specific treatment for COVID-19 patients

  - Corticosteroids **should be avoided** unless indicated for other reasons
    - May prolong viral replication
    - Data supporting use is uncontrolled and not high quality

  - Several drugs under investigation:
    - Remdesivir
    - Hydroxychloroquine or chloroquine
    - Lopinavir/ritonavir
    - IL-6 blockers (e.g., tocilizumab, sarilumab)

Resources for Inpatient COVID-19 Management

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Waleed Alhazzani1,2, Morten Hylander Møller3,4, Yaseen M. Arabi5, Mark Loeb1,3, Michelle Ng Gong6, Eddy Fan7, Simon Ozckowski1,2, Mitchell M. Levy8, Lennie Derde9,10, Amy Dzierski9,11, Bin Du12, Michael Aboud6, Hannah Wunsch14,15, Maurizio Cecconi14,17, Younsouk Koh18, Daniel S. Chertow19, Kathryn Matland20, Fayeza Alshamsi21, Emilie Belley-Cote2,32, Massimiliano Greco18,17, Matthew Laundy23, Jill S. Morgan24, Jozef Kesecioglu29, Allison McGeer25, Leonard Merem26, Manoj J. Mammen26, Paul E. Alexander2,37, Amy Arrington26, John Centofanti29, Giuseppe Citerio10,21, Bandar Baw13,32, Ziad A. Memish33, Naomi Hammond34,35, Frederick G. Hayden4, Lauren Evans37, Andrew Rhodes31

<table>
<thead>
<tr>
<th>Recommendation Level</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>Must do or must avoid</td>
</tr>
<tr>
<td>Best Practice</td>
<td>Must do or must avoid</td>
</tr>
<tr>
<td>Weak</td>
<td>Consider doing or consider avoiding</td>
</tr>
<tr>
<td></td>
<td>![Strong recommendation or best practice]</td>
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<tr>
<td></td>
<td>![Consider in select patients]</td>
</tr>
<tr>
<td></td>
<td>![Intervention is harmful]</td>
</tr>
</tbody>
</table>

Link: [WHO Guidelines 2020, Surviving Sepsis Campaign 2020](#)
COVID-19 Case Examples

MICHAEL BUNDESMANN, MD, FCCP
MEDICAL DIRECTOR OF RESPIRATORY THERAPY
PULMONARY AND CRITICAL CARE MEDICINE
EVERGREEN HEALTH, KIRKLAND, WA
CDC COCA CALL, APRIL 2, 2020
Disclaimer

The views expressed in this presentation are those of the author and do not necessarily represent the opinion of the Centers for Disease Control and Prevention.
Case 1

47-year-old man with 7 days of URI, 3 days of worsening dyspnea

- HTN, obesity (BMI 36), untreated DM
- No tobacco
- Home medications included lisinopril, HCTZ, carvedilol
- At time of presentation, he was not tested for COVID-19
Hospital Course

- Intubation and institution of lung protective ventilation from day 2 through day 14
- Proned days 2-13 of hospitalization
  - Inhaled epoprostenol and NMB were not given’
  - Extubated to HFNC
- Ceftriaxone and azithromycin discontinued after 7 days (no initial procalcitonin checked)
- On day 6, compassionate use Remdesivir was given for 10-day course
- On day 10, hydroxychloroquine 400 BID, then daily x 5 days
- On day 21, weaned to room air, significant neuromuscular weakness
Notable Findings

- 3/2 Respiratory pathogen panel negative
- 3/2 NP sample drawn, SARS-CoV-2 detected 3/6
- 3/2 Bronchoscopy BAL 62% Ly, 13% PMN
- Abs lymphocyte 1.0x10^3/uL
- AST/ALT < 2x ULN
- CRP 15.93 on 3/8 decreased to 1.11
- Normal NT-proBNP, TnI
- SARS-CoV-2 remains positive 3 weeks into hospitalization
Lab Trends
Transthoracic Echocardiogram

- Day 1 – normal LVEF, notable for estimated PASP 45. Normal RVSF. Mildly dilated RV.
- Day 10 – limited echo with estimated RVSP 65
Case 2

73-year-old man with controlled asthma, HL, BPH. Good functional capacity and active.

- 4 days prior to admit was seen in urgent care for 7 days of cough, fever, fatigue
- 2/27 – presents to ED with SpO2 82%. Placed on HFNC, intubated within 24 hrs
- At the time of admission, RF for COVID-19 were not identified. He was not tested for COVID-19.
4 days prior to admission

Day of admission
Hospital Course

- Cefepime, Vancomycin
- Paralyzed, prone x 4 days
- Day 7 compassionate use remdesivir was added
- Weaned off vasopressors by day 7
- Day 11 worsening acute kidney injury
- Day 11 worsening shock and LVEF (normal troponin)
- CRRT started day 14
- Comatose on day 24, failing SBT, remains on HD. MRI, CT, LP negative
- Goals changed to comfort-care and patient expired
Lab Trends

- **Lymph # Auto**
  - Graph showing trends with generalized normal high and low areas.

- **CPK**
  - Graph showing trends with generalized normal upper limit.

- **POC Flo2 A**
  - Graph showing percentage trends.

- **POC P/F Ratio**
  - Graph showing ratio trends.
Bronchoscopy & Laboratory Results

- Day 1 Bronchoscopy with lavage - 32% Ly, 34% PMN
- Procalcitonin 0.97
- Day 9 Bronch due to suspected VAP – negative cultures. PMN 63%
Echocardiogram Results

- Day 1 – normal transthoracic echocardiogram
- Day 4 – limited TTE remains normal
- Day 9 – LVEF 30% with global dysfunction
Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Waleed Alhazzani MD, FRCP, MSc
Associate Professor of Medicine
McMaster University
COI Disclosures

• Chair of GUIDE Group, and
• Member of the GRADE Working Group

The views expressed in this presentation are those of the author and do not necessarily represent the opinion of the Centers for Disease Control and Prevention.
<table>
<thead>
<tr>
<th>Morten Hylander</th>
<th>Hannah Wunsch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Møller</td>
<td>Maurizio Cecconi</td>
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<td>Andrew Rhodes</td>
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</table>
COVID-19

Systematic reviews
ARDS, MERS, SARS, shock

Summarize the evidence

Assess quality

New evidence

Recommendation

Panel Discussion

PICO question

Expert Identified evidence

Dissemination

Expeditied Review & Publication
Strong Recommendation for the Intervention

Desirable consequences

Undesirable consequences
Desirable consequences

Undesirable consequences
Weak Recommendation for the Intervention
# Patients

## For Patients

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
<th>Weak Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Most</strong> individuals in this situation would want the recommended course of action, and only a <strong>small</strong> proportion would not</td>
<td>The <strong>majority</strong> of individuals in this situation would want the suggested course of action, but <strong>many</strong> would not</td>
</tr>
<tr>
<td>For Clinicians</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td><strong>Clinicians</strong></td>
<td><strong>Most individuals should receive</strong> the recommended course of action.</td>
</tr>
<tr>
<td></td>
<td>Formal decision aids <strong>are not likely to be needed</strong> to help individuals make decisions consistent with their values and preferences</td>
</tr>
</tbody>
</table>
### Policymakers

<table>
<thead>
<tr>
<th>For Policymakers</th>
<th>Strong Recommendation</th>
<th>Weak Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Can be adapted as policy in most situations, including for use as performance indicators</td>
<td>Policies will likely be variable</td>
</tr>
</tbody>
</table>
Infection control

- Aerosol generating procedure vs not
- Negative pressure room vs regular room
- Surgical masks vs respirator masks
# Aerosol Generating Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Studies</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation</td>
<td>4</td>
<td>OR 6.6 (2.3, 18.9)</td>
</tr>
<tr>
<td>Manipulation of BiPAP mask</td>
<td>1</td>
<td>OR 6.2 (2.2, 18.1)</td>
</tr>
<tr>
<td>CPR</td>
<td>1</td>
<td>OR 4.5 (1.5, 13.8)</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>1</td>
<td>OR 4.2 (1.5, 11.5)</td>
</tr>
<tr>
<td>Non-Invasive Ventilation</td>
<td>2</td>
<td>OR 3.1 (1.4, 6.8)</td>
</tr>
<tr>
<td>Manual Ventilation</td>
<td>1</td>
<td>OR 2.8 (1.3, 6.4)</td>
</tr>
</tbody>
</table>

Infection Control

• For healthcare workers performing aerosol generating procedures on patients with COVID-19 in the ICU, we recommend using fitted respirator masks (N95 respirators, FFP2, or equivalent), as compared to surgical/medical masks, in addition to other personal protective equipment.

*FFP3 respirators are more commonly used in many parts of the world.
Infection Control

1. Usual care for non-ventilated COVID-19 patients, or
2. Performing **non-AGP** on MV (closed circuit) patients with COVID-19

We **suggest** using surgical/medical masks, as compared to respirator masks, in addition to other personal protective equipment.
Laboratory Confirmed Influenza Infection

<table>
<thead>
<tr>
<th>Study</th>
<th>N95 Events</th>
<th>N95 Total</th>
<th>Face Mask Events</th>
<th>Face Mask Total</th>
<th>Odds Ratio</th>
<th>OR</th>
<th>95%-CI</th>
<th>Weight (fixed)</th>
<th>Weight (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loeb 2009</td>
<td>48</td>
<td>221</td>
<td>50</td>
<td>225</td>
<td>0.97</td>
<td>0.62</td>
<td>1.52</td>
<td>30.9%</td>
<td>30.9%</td>
</tr>
<tr>
<td>Macintyre 2011</td>
<td>2</td>
<td>475</td>
<td>3</td>
<td>246</td>
<td>0.34</td>
<td>0.06</td>
<td>2.06</td>
<td>1.9%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Macintyre 2013</td>
<td>3</td>
<td>665</td>
<td>1</td>
<td>347</td>
<td>1.57</td>
<td>0.16</td>
<td>15.13</td>
<td>1.2%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Radonovich 2019</td>
<td>92</td>
<td>1112</td>
<td>85</td>
<td>1181</td>
<td>1.16</td>
<td>0.86</td>
<td>1.58</td>
<td>66.0%</td>
<td>66.0%</td>
</tr>
<tr>
<td>Fixed effect model</td>
<td>2473</td>
<td>1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects model</td>
<td>2473</td>
<td>1999</td>
<td></td>
<td></td>
<td>1.08</td>
<td>0.84</td>
<td>1.38</td>
<td>100.0%</td>
<td>--</td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2 = 0\%$, $r^2 = 0$, $p = 0.55$
## Laboratory Confirmed Respiratory Infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Total</th>
<th>Odds Ratio</th>
<th>OR</th>
<th>95%-CI</th>
<th>Weight (fixed)</th>
<th>Weight (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loeb 2009</td>
<td>70</td>
<td>221</td>
<td></td>
<td>1.03</td>
<td>[0.69; 1.53]</td>
<td>16.2%</td>
<td>16.2%</td>
</tr>
<tr>
<td>MacIntyre 2011</td>
<td>7</td>
<td>475</td>
<td></td>
<td>0.51</td>
<td>[0.18; 1.47]</td>
<td>2.3%</td>
<td>2.3%</td>
</tr>
<tr>
<td>MacIntyre 2013</td>
<td>18</td>
<td>665</td>
<td></td>
<td>0.78</td>
<td>[0.37; 1.63]</td>
<td>4.7%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Radonovich 2019</td>
<td>300</td>
<td>1112</td>
<td></td>
<td>0.95</td>
<td>[0.79; 1.14]</td>
<td>76.8%</td>
<td>76.8%</td>
</tr>
<tr>
<td><strong>Fixed effect model</strong></td>
<td><strong>2473</strong></td>
<td><strong>1999</strong></td>
<td></td>
<td><strong>0.94</strong></td>
<td><strong>[0.80; 1.11]</strong></td>
<td><strong>100.0%</strong></td>
<td>--</td>
</tr>
<tr>
<td><strong>Random effects model</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.94</strong></td>
<td><strong>[0.80; 1.11]</strong></td>
<td>--</td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.63$
influenza-like illness
Oxygen Targets

Mortality vs. SPO₂

- 90%
- 92%
- 96%
we recommend that SPO$_2$ be maintained no higher than 96%
we suggest starting supplemental oxygen if the SPO$_2$ < 92%
Oxygen Targets

we recommend starting oxygen if SPO$_2$ < 90%
SPO$_2$ and Mortality

Hypoxemia

• For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we suggest using HFNC over conventional oxygen therapy.
Hypoxemia

• For adults with COVID-19 and acute hypoxemic respiratory failure, we suggest using HFNC over NIPPV.
Hypoxemia

- For adults with COVID-19 and **acute hypoxemic respiratory failure**, if HFNC is not available and no emergent indication for endotracheal intubation; we **suggest** a trial of NIPPV with close monitoring and short interval assessment for worsening of respiratory failure.
We were not able to make a recommendation regarding the use of helmet NIPPV compared to mask NIPPV, it is an option, but we are not certain about its safety or efficacy for COVID-19 patients.
Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial

![Graph showing survival rates with Helmet NIV and Face mask NIV.](image)

No. at risk
- Face mask: 39, 20, 18, 18, 18, 18, 17
- Helmet: 44, 33, 31, 29, 29, 29, 29

Log-rank P = .02

**JAMA.** 2016 Jun 14;315(22):2435-41
Endotracheal Intubation

• For healthcare workers performing endotracheal intubation on patients with COVID-19, we recommend endotracheal intubation is performed by healthcare worker experienced with airway management, to minimize the number of attempts and risk of transmission.
Endotracheal Intubation

- For healthcare workers performing **endotracheal intubation** on patients with COVID-19, we **suggest** using video guided laryngoscopy, over direct laryngoscopy, if available.
COVID-19 with hypoxia

Indication for endotracheal intubation?

Yes

Tolerating supplemental oxygen?

No

Tolerating HFNC

Yes

Not tolerating HFNC or HFNC is not available

Indication for endotracheal intubation?

No

Consider: a trial of NIPPV

Yes

Do it: Monitor closely at short intervals

No

Do not: Delay intubation if worsening

Avoid intubation

Expert in airway to intubate

Use N-95/FFP-2 or equivalent and other PPE/infection control precautions

Minimize staff in the room

Consider: if available

Video- laryngoscope
Acute Respiratory Distress Syndrome
We **recommend** using low Vt (4-8 mL/kg) and Targeting Pplat <30 cmH$_2$O
We recommend using low Vt (4-8 mL/kg) and Targeting Pplat <30 cmH₂O

we suggest using a higher PEEP strategy
We recommend using low Vt (4-8 mL/kg) and Targeting Pplat <30 cmH₂O.

We suggest using a higher PEEP strategy.

we suggest using a conservative, over a liberal, fluid strategy.
Prone Ventilation

• For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest prone ventilation for 12 to 16 hours, over no prone ventilation.
Neuromuscular Blocking Agents (NMBA)?
NMBA

• For MV adults with COVID-19 and moderate to severe ARDS, we suggest using as needed intermittent boluses of NMBA, over a continuous NMBA infusion, to facilitate protective lung ventilation.
NMBA

• In case of persistent ventilator dyssynchrony, requirement of ongoing deep sedation, prone ventilation, or persistently high \( P_{plt} \); we suggest using a continuous NMBA infusion for up to 48 hours.
Corticosteroids
## Steroids in ARDS - Mortality Outcome

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Corticosteroids</th>
<th>Control</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Liu 2012</td>
<td>2</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Meduri 2007</td>
<td>15</td>
<td>63</td>
<td>12</td>
</tr>
<tr>
<td>Rezk 2013</td>
<td>0</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Steinberg 2006</td>
<td>26</td>
<td>89</td>
<td>26</td>
</tr>
<tr>
<td>Tongyoo 2016</td>
<td>34</td>
<td>98</td>
<td>40</td>
</tr>
<tr>
<td>Villar 2020</td>
<td>33</td>
<td>139</td>
<td>50</td>
</tr>
<tr>
<td>Zhao 2014</td>
<td>9</td>
<td>24</td>
<td>13</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>443</td>
<td>408</td>
</tr>
<tr>
<td>Total events</td>
<td>119</td>
<td>151</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.02$; $\text{Chi}^2 = 7.69$, df = 6 ($P = 0.26$); $I^2 = 22$

Test for overall effect: $Z = 2.36$ ($P = 0.02$)
Steroids in ARDS - DMV

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Corticosteroids</th>
<th>Control</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Meduri 2007</td>
<td>5.25</td>
<td>1.46</td>
<td>63</td>
<td>11.1</td>
</tr>
<tr>
<td>Rezk 2013</td>
<td>10.6</td>
<td>4.4</td>
<td>18</td>
<td>20.3</td>
</tr>
<tr>
<td>Tongyoo 2016</td>
<td>11.8</td>
<td>7.8</td>
<td>98</td>
<td>13.9</td>
</tr>
<tr>
<td>Villar 2020</td>
<td>14.3</td>
<td>13.3</td>
<td>139</td>
<td>20.2</td>
</tr>
<tr>
<td>Zhao 2014</td>
<td>10.5</td>
<td>4.6</td>
<td>24</td>
<td>11.6</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>342</td>
<td></td>
<td>303</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: $\text{Tau}^2 = 9.22; \text{Chi}^2 = 31.72, \text{df} = 4 (P < 0.00001); I^2 = 87\%$

Test for overall effect: $Z = 3.37 (P = 0.0008)$
Steroids for **Viral ARDS - Mortality**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brun-Buisson 2011</td>
<td>0.9517</td>
<td>0.3066</td>
<td>21.5%</td>
<td>2.59 [1.42, 4.72]</td>
<td></td>
</tr>
<tr>
<td>Cao 2016</td>
<td>0.6152</td>
<td>0.3849</td>
<td>19.1%</td>
<td>1.85 [0.87, 3.93]</td>
<td></td>
</tr>
<tr>
<td>Kim 2011</td>
<td>0.5878</td>
<td>0.4892</td>
<td>16.2%</td>
<td>1.80 [0.69, 4.70]</td>
<td></td>
</tr>
<tr>
<td>Li 2017</td>
<td>-0.4005</td>
<td>0.1919</td>
<td>24.6%</td>
<td>0.67 [0.46, 0.98]</td>
<td></td>
</tr>
<tr>
<td>Martin-Loeches 2011</td>
<td>0.0953</td>
<td>0.4023</td>
<td>18.6%</td>
<td>1.10 [0.50, 2.42]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)** 100.0% 1.40 [0.76, 2.57]

Heterogeneity: Tau² = 0.35; Chi² = 17.29, df = 4 (P = 0.002); I² = 77%
Test for overall effect: Z = 1.09 (P = 0.28)
Direct Evidence

Retrospective study
N=201
with COVID-19 pneumonia

Corticosteroids

• For mechanically ventilated adults with COVID-19 and ARDS, we suggest using systemic corticosteroids over not using corticosteroids.

• Remark: The majority of our panel support a weak recommendation (i.e. suggestion) to use steroids in the sickest patients with COVID-19 and ARDS. However, because of the very low quality evidence, some experts on the panel preferred not to issue a recommendation until higher quality direct-evidence is available.
Steroids for Viral Pneumonia - Mortality

All observational studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Influenza</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delaney 2016</td>
<td>0.6152</td>
<td>0.2561</td>
<td>8.8%</td>
<td>1.95 [1.12, 3.06]</td>
<td></td>
</tr>
<tr>
<td>Delgado-Rodriguez 2012</td>
<td>1.2149</td>
<td>0.4518</td>
<td>7.6%</td>
<td>3.37 [1.39, 8.17]</td>
<td></td>
</tr>
<tr>
<td>Jung 2011</td>
<td>1.1262</td>
<td>0.4107</td>
<td>7.8%</td>
<td>3.09 [1.36, 7.02]</td>
<td></td>
</tr>
<tr>
<td>Kim 2011</td>
<td>0.7885</td>
<td>0.3872</td>
<td>8.0%</td>
<td>2.20 [1.03, 4.70]</td>
<td></td>
</tr>
<tr>
<td>Liem 2009</td>
<td>1.4134</td>
<td>0.6543</td>
<td>6.2%</td>
<td>4.11 [1.14, 14.82]</td>
<td></td>
</tr>
<tr>
<td>Uoi 2011</td>
<td>1.1939</td>
<td>0.9628</td>
<td>4.0%</td>
<td>3.30 [0.50, 21.78]</td>
<td></td>
</tr>
<tr>
<td>Tsi 2020</td>
<td>1.6134</td>
<td>0.3786</td>
<td>8.0%</td>
<td>5.02 [2.39, 10.54]</td>
<td></td>
</tr>
<tr>
<td>XI 2010</td>
<td>1.3002</td>
<td>0.6685</td>
<td>6.1%</td>
<td>3.67 [0.99, 13.66]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>56.2% [2.76, 3.69]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.00; Ch^2 = 6.13, df = 7 (P = 0.52); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 6.81 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.1.2 Corona/SARS/MERS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfaraj 2019</td>
<td>1.3455</td>
<td>0.3457</td>
<td>8.2%</td>
<td>3.84 [1.95, 7.56]</td>
<td></td>
</tr>
<tr>
<td>Alghamdi 2016</td>
<td>1.0716</td>
<td>1.5877</td>
<td>2.3%</td>
<td>2.92 [0.13, 65.59]</td>
<td></td>
</tr>
<tr>
<td>Arabi 2017</td>
<td>-0.4943</td>
<td>0.1904</td>
<td>9.1%</td>
<td>0.61 [0.42, 0.89]</td>
<td></td>
</tr>
<tr>
<td>Angkong 2005</td>
<td>3.0601</td>
<td>1.4122</td>
<td>2.7%</td>
<td>20.70 [1.30, 329.63]</td>
<td></td>
</tr>
<tr>
<td>Chen 2006</td>
<td>-2.4889</td>
<td>1.2617</td>
<td>3.2%</td>
<td>0.08 [0.01, 0.98]</td>
<td></td>
</tr>
<tr>
<td>Yam 2007 HC</td>
<td>-0.5657</td>
<td>0.5657</td>
<td>6.0%</td>
<td>1.00 [0.33, 3.03]</td>
<td></td>
</tr>
<tr>
<td>Yam 2007 MP</td>
<td>-1.3853</td>
<td>0.8495</td>
<td>6.2%</td>
<td>0.25 [0.07, 0.89]</td>
<td></td>
</tr>
<tr>
<td>Yam 2007 F</td>
<td>-1.772</td>
<td>0.885</td>
<td>4.8%</td>
<td>0.17 [0.03, 0.96]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>43.3% [0.83, 2.17]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 1.24; Ch^2 = 38.32, df = 7 (P &lt; 0.00001), I^2 = 82%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.37 (P = 0.71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 1.76 [1.03, 3.03]

Heterogeneity: Tau^2 = 0.80; Ch^2 = 75.61, df = 15 (P < 0.00001), I^2 = 80%
| Test for overall effect: Z = 2.06 (P = 0.04) |
| Test for subgroup differences: Ch^2 = 5.48, df = 1 (P = 0.02), I^2 = 81.8% |
Corticosteroids

• For mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), we suggest against the routine use of systemic corticosteroids.
<table>
<thead>
<tr>
<th>COVID-19 with mild ARDS</th>
<th>COVID-19 with Mod to Severe ARDS</th>
<th>Rescue/Adjunctive therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Do:</strong> Vt 4-8 ml/kg and P\textsubscript{plat} &lt; 30 cm H\textsubscript{2}O</td>
<td><strong>CONSIDER:</strong> Higher PEEP</td>
<td><strong>CONSIDER:</strong> if proning, high P\textsubscript{plt}, asynchrony</td>
</tr>
<tr>
<td><strong>Do:</strong> Investigate for bacterial infection</td>
<td><strong>CONSIDER:</strong> NMBA boluses to facilitate ventilation targets</td>
<td><strong>CONSIDER:</strong> Prone ventilation 12-16 h</td>
</tr>
<tr>
<td><strong>Do:</strong> Target SPO2 92% - 96%</td>
<td><strong>CONSIDER:</strong> if PEEP responsive Traditional Recruitment maneuvers</td>
<td><strong>CONSIDER:</strong> STOP if no quick response</td>
</tr>
<tr>
<td><strong>CONSIDER:</strong> Conservative fluid strategy</td>
<td><strong>CONSIDER:</strong> Prone ventilation 12-16 h</td>
<td><strong>CONSIDER:</strong> A trial of inhaled Nitric Oxide</td>
</tr>
<tr>
<td><strong>CONSIDER:</strong> Empiric antibiotics</td>
<td><strong>CONSIDER:</strong> if proning, high P\textsubscript{plt}, asynchrony NMBA infusion for 24 h</td>
<td><strong>CONSIDER:</strong> follow local criteria for ECMO V-V ECMO or referral to ECMO center</td>
</tr>
<tr>
<td>Uncertain: Systemic corticosteroids</td>
<td><strong>CONSIDER:</strong> Don’t do: Staircase Recruitment maneuvers</td>
<td></td>
</tr>
<tr>
<td><strong>CONSIDER:</strong> Short course of systemic corticosteroids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Antibiotics

• For mechanically ventilated patients with COVID-19 and respiratory failure, we suggest using empiric antimicrobials/antibacterial agents, compared to no antimicrobials.

• Remark: if the treating team initiates empiric antimicrobials, they should assess for de-escalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient’s clinical status.
Therapy

For critically ill adults with COVID-19, we **suggest against** the routine use of standard intravenous immunoglobulins.

For critically ill adults with COVID-19, we **suggest against** the routine use of convalescent plasma.

For critically ill adults with COVID-19, we **suggest against** the routine use of lopinavir/ritonavir.
Therapy

- Insufficient evidence to support recommendations for:
  - Antivirals
  - Hydroxychloroquine
  - Immunomodulators
Hemodynamic Support

• For the **acute resuscitation** of adults with **COVID-19 and shock**, we **suggest** using a conservative, over a liberal fluid strategy

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Certainty of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause Mortality</td>
<td>637 (9 RCTs)</td>
<td>RR 0.87 (0.69–1.10)</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>637 (9 RCTs)</td>
<td>RR 0.91 (0.78–1.05)</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>
Hemodynamic Support

- For adults with **COVID-19 and refractory shock**, we **suggest** using low-dose corticosteroid therapy (“shock-reversal”), over no corticosteroid therapy.

- Remark: typical corticosteroid regimen in septic shock is intravenous hydrocortisone 200 mg per day either as an infusion or intermittent doses.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Certainty of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term Mortality (&lt;90 days)</td>
<td>7297 (22 RCTs)</td>
<td>RR 0.96 (0.91–1.02)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Long-term Mortality (&gt;90 days)</td>
<td>5667 (5 RCTs)</td>
<td>RR 0.96 (0.90–1.02)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>5908 (10 RCTs)</td>
<td>RR 0.98 (0.90–1.08)</td>
<td>LOW</td>
</tr>
</tbody>
</table>
Special Thank You

• Guidelines panelists
• Methodologists
• SCCM and ESICM
• Colleagues around the world caring for patients
CDC COVID-19 Resources

- Coronavirus Disease 2019 Website
  https://www.cdc.gov/COVID19

- Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease

- Information for Clinicians on Therapeutic Options for COVID-19 Patients

- Healthcare Professionals: Frequently Asked Questions and Answers

- Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 in Healthcare Settings

- What Healthcare Personnel Should Know about Caring for Patients with Confirmed or Possible COVID-19 Infection

- Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Patients Under Investigation for COVID-19

- Rapid Guidelines for Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with COVID-19
To Ask a Question

- **Using the Webinar System**
  - Click on the Q&A button in the Zoom webinar system.
  - Type your question in the Q&A box.
  - Submit your question.
  - You may also email your question to coca@cdc.gov.

- For media questions, please contact CDC Media Relations at 404-639-3286 or email media@cdc.gov.

- **For more Clinical Care information on COVID-19**
  - Call COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
  - Refer patients to state and local health departments for COVID-19 COVID19 testing and test results.
    - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19 OR to get COVID-19 test results.
Today’s COCA Call Will Be Available On-Demand

**When:** Soon after the live call

**What:** Video recording

**Where:**
On the COCA Call webpage at
https://emergency.cdc.gov/coca/calls/2020/callinfo_040220.asp
COCA Products & Services

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As-needed messages that provide specific, immediate action clinicians should take. Contains comprehensive CDC guidance so clinicians can easily follow recommended actions.
COCA Products & Services

COCA Digest
CDC Clinician Outreach and Communication Activity

Monthly newsletter providing updates on emergency preparedness and response topics, emerging public health threat literature, resources for health professionals, and additional information important during public health emergencies and disasters.

Informs clinicians of new CDC resources and guidance related to emergency preparedness and response. This email is sent as soon as possible after CDC publishes new content.

Coca's primary method of sharing information about urgent public health incidents with public information officers; federal, state, territorial, and local public health practitioners; clinicians; and public health laboratories.

COCA Now
CDC Clinician Outreach and Communication Activity

HAN
HEALTH ALERT NETWORK
Join COCA’s Mailing List

- Receive information about:
  - Upcoming COCA Calls
  - Health Alert Network (HAN) messages
  - CDC emergency response activations
  - Emerging public health threats
  - Emergency preparedness and response conferences and training opportunities

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