Surviving Sepsis Campaign Update and Priorities - June 2020

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Disclosures

> No financial conflicts to disclose
> Surviving Sepsis Campaign Adult Guidelines co-chair and Steering Committee member
1st edition of SSC Guidelines for sepsis in children

Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children

Pediatric Critical Care Medicine: Feb 2020; Vol 21(2). e52-e106
Children’s sepsis guideline panel

> 49 panelists
> 12 professional societies represented
> 3 methodologists and 3 public members
> 6 subgroups: recognition and management of infection, hemodynamics and resuscitation, ventilation, endocrine and metabolic therapies, adjunctive therapies and research priorities
Incorporating evidence from adults

Very low quality direct evidence

Quality of indirect evidence without considering indirectness

Low or Very low quality

Moderate or High quality

Assess degree of "indirectness"
- Is it clinically & biologically plausible to extrapolate from indirect population?
- Does indirect population have similar response (direction, magnitude) to intervention?

No serious "indirectness"

Use indirect evidence and do not rate down for indirectness

Serious "indirectness"

Use indirect evidence and rate down for indirectness by one level

Very serious "indirectness"

Rate down quality of evidence by two levels

Quality of evidence higher than Very low?
- Yes
- No

Do not use indirect evidence
SCREENING, DIAGNOSIS, AND SYSTEMATIC MANAGEMENT OF SEPSIS

1) In children who present as acutely unwell, we suggest implementing systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence).

Remarks: Systematic screening needs to be tailored to the type of patients, resources, and procedures within each institution. Evaluation for the effectiveness and sustainability of screening should be incorporated as part of this process.

2) We were unable to issue a recommendation about using blood lactate values to stratify children with suspected septic shock or other sepsis-associated organ dysfunction into low-vs high-risk of having septic shock or sepsis.

3) We recommend implementing a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction (BPS).

4) We recommend obtaining blood cultures before initiating antimicrobial therapy in situations where this does not substantially delay antimicrobial administration (BPS).
ANTIMICROBIAL THERAPY

5) In children with septic shock, we recommend starting antimicrobial therapy as soon as possible, within 1 hr of recognition (strong recommendation, very low quality of evidence).

6) In children with sepsis-associated organ dysfunction but without shock, we suggest starting antimicrobial therapy as soon as possible after appropriate evaluation, within 3 hr of recognition (weak recommendation, very low quality of evidence).

7) We recommend empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens (BPS).

8) Once the pathogen(s) and sensitivities are available, we recommend narrowing empiric antimicrobial therapy coverage (BPS).

9) If no pathogen is identified, we recommend narrowing or stopping empiric antimicrobial therapy according to clinical presentation, site of infection, host risk factors, and adequacy of clinical improvement in discussion with infectious disease and/or microbiological expert advice (BPS).

10) In children without immune compromise and without high risk for multidrug-resistant pathogens, we suggest against the routine use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy (weak recommendation, very low quality of evidence).
FLUID THERAPY

17) In healthcare systems with availability of intensive care, we suggest administering up to 40–60mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, low quality of evidence).

18) In healthcare systems with no availability of intensive care and in the absence of hypotension, we recommend against bolus fluid administration while starting maintenance fluids (strong recommendation, high quality of evidence).

19) In healthcare systems with no availability of intensive care, if hypotension is present, we suggest administering up to 40mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop (weak recommendation, low quality of evidence).

Remarks: Clinical markers of cardiac output may include heart rate, blood pressure, capillary refill time, level of consciousness, and urine output. In all settings, the need for fluid administration should be guided by frequent reassessment of clinical markers of cardiac output, serial blood lactate measurement, and advanced monitoring, when available. Signs of fluid overload that should limit further fluid bolus therapy may include clinical signs of pulmonary edema or new or worsening hepatomegaly.

20) We suggest using crystalloids, rather than albumin, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, moderate quality of evidence).

Remarks: Although there is no difference in outcomes, this recommendation takes into consideration cost and other barriers of administering albumin compared with crystalloids.

21) We suggest using balanced/buffered crystalloids, rather than 0.9% saline, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence).
Initial Resuscitation Algorithm for Children

Systematic Screening for Sepsis in Children

Within 1 hour of initial recognition of septic shock

Within 3 hours of initial suspicion of sepsis

Shock develops

Expedited diagnostic evaluation

Diagnostic evaluation supports sepsis-associated organ dysfunction

1. Obtain IV/IO access.
2. Collect blood culture.
3. Start empiric broad-spectrum antibiotics.
4. Measure lactate.
5. Administer fluid bolus(es) if shock is present.*
6. Start vasoactive agents if shock persists.*

Respiratory support
Assess for Pediatric Acute Respiratory Distress Syndrome

Infectious source control
Continuous reassessment
Advanced hemodynamic monitoring if shock persists

Fluid and vasoactive treatment*

*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients
Fluid and Vasoactive-Inotrope Management Algorithm For Children

**Healthcare Systems WITH Intensive Care**

- **Abnormal Perfusion with or without Hypotension**
  - If signs of fluid overload are absent, administer fluid bolus, 10-20 mL/kg.
  - Repeat assessment of hemodynamic response to fluid and consider fluid boluses, 10-20 mL/kg, until shock resolves or signs of fluid overload develop.
  - Assess cardiac function.
  - Consider epinephrine if there is myocardial dysfunction or epinephrine/norepinephrine if shock persists after 40-60 mL/kg (or sooner if signs of fluid overload develop).

**Healthcare Systems WITHOUT Intensive Care**

- **Abnormal perfusion WITHOUT hypotension**
  - Do NOT give fluid bolus unless there are signs of dehydration with ongoing fluid losses (e.g., diarrhea).
  - Start maintenance fluids.
  - Monitor hemodynamics closely.
  - Consider vasoactive-inotropic support (if available).

- **Abnormal perfusion WITH hypotension**
  - If signs of fluid overload are absent, administer fluid bolus, 10-20 mL/kg.
  - Assess hemodynamic response to fluid and repeat fluid boluses, 10-20 mL/kg, until hypotension resolves or signs of fluid overload develop.
  - Assess cardiac function (if available)
  - Consider epinephrine/norepinephrine if hypotension persists after 40 mL/kg or sooner if signs of fluid overload develop.

**Fluid in mL/kg should be dosed as ideal body weight.**

**Shock resolved, perfusion improved**

- Do not give more fluid boluses.
- Consider maintenance fluids.
- Monitor for signs/symptoms of recurrent shock.

*Hypotension in healthcare systems WITHOUT intensive care is defined as either:

- SBP < 50 mm Hg in children aged < 12 months
- SBP < 60 mm Hg in children aged 1 to 5 years
- SBP < 70 mm Hg in children aged > 5 years

OR

Presence of all 3 World Health Organization criteria: cold extremities, prolonged capillary refill > 3 seconds, weak/fast pulse

https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients
SSC COVID-19 Guidelines

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

Waleed Alhazzani,1, 2 Morten Hylander Møller,3, 4 Yaseen M. Arabi,5 Mark Loeb,2, 3 Michelle Ng Gong,6 Eddy Fan,7 Simon Oczkowski,1, 2 Mitchell M. Levy,8, 9 Lennie Derde,10, 11 Amy Dzierba,12, 13 Bin Du,13 Michael Aboodi14, Hannah Wunsch,14, 15 Maurizio Cecconi,16, 17 Younsuck Koh,18, 19 Daniel S. Chertow,9 Kathryn Maitland,19, 20 Fayez Alshamsi,21, 22 Emilie Belley-Cote,22, 23 Massimiliano Greco,16, 17 Matthew Laundy,23, 24 Jill S. Morgan,24, 25 Jozef Kesecioglu,26, 27 Allison McGeer,28, 29 Leonard Mermel,30, 31 Manoj J. Mammen,32, 33 Paul E. Alexander,34, 35 Amy Arrington,36, 37 John E. Centofanti,38, 39 Giuseppe Citerio,40, 41 Bandar Baw,41, 42 Ziad A. Memish,43, 44 Naomi Hammond,45, 46 Frederick G. Hayden,45, 46 Laura Evans,37, 47 Andrew Rhodes,38

Summary of recommendations on the initial management of hypoxic COVID-19 patients

COVID-19 with hypoxia

Yes

Indication for endotracheal intubation?

No

Tolerating supplemental oxygen?

No

Tolerating HFNC

Not tolerating HFNC or HFNC is not available

Indication for endotracheal intubation?

Yes

DO IT:
Monitor closely short intervals

DO NOT:
Delay intubation if worsening

CONSIDER: a trial of NIPPV

DO IT:
Monitor closely short intervals

DO NOT:
Delay intubation if worsening

CONSIDER: HFNC

CONSIDER: if available

Video-laryngoscope

DO IT:
Endotracheal intubation

DO IT:
Expert in airway to intubate

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

DO IT:
Minimize staff in the room

DO IT:
Monitor closely for worsening

Target SpO2 92% to 96%

DO IT:
Appropriate infection control precautions

Note: N-95/FFP-2 are facial masks
HFNC = high-flow nasal cannula
NIPPV = noninvasive positive-pressure ventilation
PPE = personal protective equipment
SpO2 = peripheral capillary oxygen saturation
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.
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>№ of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Certainty of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality &gt;12 hours prone</td>
<td>1,002 (5 RCTs)</td>
<td>RR 0.71 (0.52 to 0.97)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Mortality &lt;12 hours prone</td>
<td>1,135 (3 RCTs)</td>
<td>RR 1.04 (0.89 to 1.21)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Mortality – Moderate to severe ARDS</td>
<td>1,002 (5 RCTs)</td>
<td>RR 0.71 (0.52 to 0.97)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Mortality - All ARDS</td>
<td>1,135 (3 RCTs)</td>
<td>RR 1.04 (0.89 to 1.21)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Accidental CVC Removal</td>
<td>635 (2 RCTs)</td>
<td>RR 1.72 (0.43 to 6.84)</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Pressure Sores</td>
<td>1087 (3 RCTs)</td>
<td>RR 1.22 (1.06 to 1.41)</td>
<td>HIGH</td>
</tr>
<tr>
<td>Airway Complications – Unplanned extubation</td>
<td>2067 (6 RCTs)</td>
<td>RR 1.14 (0.78 to 1.67)</td>
<td>LOW</td>
</tr>
<tr>
<td>Airway Complications – ETT Obstruction</td>
<td>1594 (3 RCTs)</td>
<td>RR 1.76 (1.24 to 2.50)</td>
<td>MODERATE</td>
</tr>
</tbody>
</table>
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 $P_{pl}$; 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>Weight</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu 2012</td>
<td>2</td>
<td>12</td>
<td>3.0%</td>
<td>0.33 [0.08, 1.31]</td>
<td></td>
</tr>
<tr>
<td>Meduri 2007</td>
<td>15</td>
<td>63</td>
<td>12.6%</td>
<td>0.56 [0.30, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Rezk 2013</td>
<td>0</td>
<td>18</td>
<td>0.7%</td>
<td>0.08 [0.00, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Steinberg 2006</td>
<td>26</td>
<td>89</td>
<td>19.7%</td>
<td>1.02 [0.65, 1.62]</td>
<td></td>
</tr>
<tr>
<td>Tongyo 2016</td>
<td>34</td>
<td>98</td>
<td>26.8%</td>
<td>0.86 [0.60, 1.23]</td>
<td></td>
</tr>
<tr>
<td>Villar 2020</td>
<td>33</td>
<td>139</td>
<td>26.0%</td>
<td>0.66 [0.45, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Zhao 2014</td>
<td>9</td>
<td>24</td>
<td>11.3%</td>
<td>0.84 [0.43, 1.61]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>443</td>
<td>408</td>
<td>100.0%</td>
<td>0.75 [0.59, 0.95]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 119, 151

Heterogeneity: Tau² = 0.02; Chi² = 7.69, df = 6 (P = 0.26); I² = 22%

Test for overall effect: Z = 2.36 (P = 0.02)
## 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>
<th>Risk Ratio M–H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td><strong>1.8.1 Timing of corticosteroid therapy &lt; 7 days</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liu 2012</td>
<td>2</td>
<td>12</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Meduri 2007</td>
<td>15</td>
<td>63</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>Rezk 2013</td>
<td>0</td>
<td>18</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Tongyoo 2016</td>
<td>34</td>
<td>98</td>
<td>40</td>
<td>99</td>
</tr>
<tr>
<td>Villar 2020</td>
<td>33</td>
<td>139</td>
<td>50</td>
<td>138</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>330</td>
<td>845</td>
<td>288</td>
<td>576</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>84</td>
<td>112</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Tau² = 0.03; Chi² = 5.42, df = 4 (P = 0.25); I² = 26%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 2.59 (P = 0.010)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**1.8.2 Timing of corticosteroid therapy > 7 days**

| Steinberg 2006    | 26              | 89      | 26     | 91      | 22.6%   | 1.02 [0.65, 1.62]               |                               |
| **Subtotal (95% CI)** | 89             | 91      |        |         | 22.6%   | 1.02 [0.65, 1.62]               |                               |
| **Total events**  | 26              | 26      |        |         |        |                                |                               |
| **Heterogeneity:** Not applicable | | | | | | |
| **Test for overall effect:** Z = 0.10 (P = 0.92) | | | | | | |

**Total (95% CI)**

| Total events      | 419             | 379     | 100.0% | 0.73 [0.55, 0.97] |

**Total events**

| 110              | 138              |

**Heterogeneity:** Tau² = 0.04; Chi² = 7.59, df = 5 (P = 0.18); I² = 34%

**Test for overall effect:** Z = 2.18 (P = 0.03)

**Test for subgroup differences:** Chi² = 2.34, df = 1 (P = 0.13), I² = 57.2%
### Steroids in ARDS- duration of MV

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Corticosteroids</th>
<th>Control</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meduri 2007</td>
<td>5.25 1.46</td>
<td>63</td>
<td>11.1 3.9 28 21.9% -5.85 [-7.34, -4.36]</td>
</tr>
<tr>
<td>Rezk 2013</td>
<td>10.6 4.4</td>
<td>18</td>
<td>20.3 1.9 9 20.1% -9.70 [-12.08, -7.32]</td>
</tr>
<tr>
<td>Tongyoo 2016</td>
<td>11.8 7.8</td>
<td>98</td>
<td>13.9 9 99 20.1% -2.10 [-4.45, 0.25]</td>
</tr>
<tr>
<td>Villar 2020</td>
<td>14.3 13.3</td>
<td>139</td>
<td>20.2 14 138 18.0% -5.90 [-9.12, -2.68]</td>
</tr>
<tr>
<td>Zhao 2014</td>
<td>10.5 4.6</td>
<td>24</td>
<td>11.6 4.6 29 19.8% -1.10 [-3.59, 1.39]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>342</td>
<td>303</td>
<td>100.0% -4.93 [-7.81, -2.06]</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 9.22$; $\chi^2 = 31.72$, df = 4 ($P < 0.00001$); $I^2 = 87$

Test for overall effect: $Z = 3.37$ ($P = 0.0008$)
Steroids in ARDS – ventilator free days

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Corticosteroids</th>
<th>Control</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Liu 2012</td>
<td>13.9</td>
<td>11.3</td>
<td>12</td>
</tr>
<tr>
<td>Meduri 2007</td>
<td>16.5</td>
<td>10.1</td>
<td>63</td>
</tr>
<tr>
<td>Steinberg 2006</td>
<td>11.2</td>
<td>9.4</td>
<td>89</td>
</tr>
<tr>
<td>Tongyoo 2016</td>
<td>12</td>
<td>9.7</td>
<td>98</td>
</tr>
<tr>
<td>Villar 2020</td>
<td>12.3</td>
<td>9.9</td>
<td>139</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>401</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.69; Chi² = 5.04, df = 4 (P = 0.28); I² = 21%
Test for overall effect: Z = 5.23 (P < 0.000001)

Favours controls  Favours corticosteroids
**Steroids for viral ARDS 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>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>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>1.40 [0.76, 2.57]</td>
<td></td>
</tr>
</tbody>
</table>

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

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><strong>1.1.1 Influenza</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deleney 2016</td>
<td>0.6152</td>
<td>0.2561</td>
<td>8.8%</td>
<td>1.05 [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>0.4187</td>
<td>7.8%</td>
<td>3.09 [1.36, 7.02]</td>
<td></td>
</tr>
<tr>
<td>Kim 2011</td>
<td>0.7985</td>
<td>0.2872</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>4.31 [1.14, 14.82]</td>
<td></td>
</tr>
<tr>
<td>Linko 2011</td>
<td>1.3399</td>
<td>0.9628</td>
<td>4.4%</td>
<td>3.30 [1.90, 21.78]</td>
<td></td>
</tr>
<tr>
<td>Tsai 2020</td>
<td>1.6134</td>
<td>0.3786</td>
<td>8.0%</td>
<td>5.04 [2.39, 10.54]</td>
<td></td>
</tr>
<tr>
<td>Xi 2010</td>
<td>1.2002</td>
<td>0.6685</td>
<td>6.1%</td>
<td>3.67 [1.93, 13.60]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>56.7%</strong> [2.76, 3.69]</td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td><strong>Tau² = 0.00; Chi² = 6.13, df = 7 (p = 0.52); I² = 0%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong></td>
<td><strong>Z = 6.81 (p &lt; 0.000001)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **1.1.2 Corona/SARS/MERS** |                |     |        |                               |                               |
| Alfaraj 2019       | 1.3455         | 0.3547 | 8.2%  | 3.84 [1.95, 7.56]             |                               |
| Alghamdi 2015      | 1.0716         | 1.5877 | 2.2%  | 2.92 [0.13, 65.59]            |                               |
| Arabi 2017         | -0.4943        | 0.1904 | 9.1%  | 0.61 [0.42, 0.89]             |                               |
| Alqayouq 2005      | 3.0301         | 1.4122 | 2.7%  | 20.70 [1.30, 329.64]          |                               |
| Chen 2006          | -2.4859        | 1.2617 | 3.2%  | 0.08 [0.01, 0.92]             |                               |
| Yam 2007 HC        | 0              | 0.5657 | 6.8%  | 1.00 [0.33, 3.03]             |                               |
| Yam 2007 MP        | -1.3853        | 0.6425 | 6.2%  | 0.25 [0.07, 0.89]             |                               |
| Yam 2007 P         | -1.7772        | 0.8885 | 4.8%  | 0.17 [0.03, 0.96]             |                               |
| **Subtotal (95% CI)** |               |     |        | **43.3%** [0.32, 2.17]        |                               |
| **Heterogeneity** | **Tau² = 1.24; Chi² = 38.12, df = 7 (p = 0.000001); I² = 82%** |   |        |                               |                               |
| **Test for overall effect:** | **Z = 0.27 (p = 0.71)** |   |        |                               |                               |

| **Total (95% CI)** | **100.0%** | **1.76 [1.03, 3.03]** |
| **Heterogeneity** | **Tau² = 0.80; Chi² = 75.61, df = 15 (p = 0.000001); I² = 80%** |   |        |                               |
| **Test for overall effect:** | **Z = 2.06 (p = 0.04)** |   |        |                               |
| **Test for subgroup differences:** | **Chi² = 5.48, df = 1 (p = 0.02); I² = 81.8%** |   |        |                               |
Corticosteroids

> For mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), we suggest against the routine use of systemic corticosteroids
## Summary of recommendations on the management of patients with COVID-19 and ARDS

### COVID-19 with mild ARDS

- **DO:**
  - VT 4-8 ml/kg and $P_{\text{plat}} < 30$ cm H$_2$O
  - Investigate for bacterial infection
  - Target SpO2 92% - 96%

- **CONSIDER:**
  - Conservative fluid strategy
  - Empiric antibiotics

- **UNCERTAIN:**
  - Systemic corticosteroids

### COVID-19 with mod to severe ARDS

- **DO:**
  - Prone ventilation 12-16 h
  - Staircase recruitment maneuvers

- **CONSIDER:**
  - Higher PEEP
  - NMBA boluses to facilitate ventilation targets
  - Traditional recruitment maneuvers
  - If PEEP responsive, NMBA infusion for 24 h
  - If prone ventilation, high $P_{\text{pl}}$ asynchrony
  - A trial of inhaled nitric oxide
  - Follow local criteria for ECMO

- **DON'T DO:**
  - Staircase recruitment maneuvers

### Rescue/adjunctive therapy

- **CONSIDER:**
  - Antivirals, chloroquine, anti-IL6
  - If prone ventilation, high $P_{\text{pl}}$, asynchrony: NMBA infusion for 24 h

- **DON'T DO:**
  - Staircase recruitment maneuvers

### Definitions
- **Mod** = moderate
- **ARDS** = adult respiratory distress syndrome
- **VT** = tidal volume
- **$P_{\text{plat}}$** = plateau pressure
- **SpO2** = peripheral capillary oxygen saturation
- **PEEP** = positive end-expiratory pressure
- **NMBA** = neuromuscular blocking agents
- **ECMO** = extracorporeal membrane oxygenation

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SSC adult sepsis guideline

> Update in progress
> Recommendations formulated
> Voting complete
> Anticipated publication early 2021
Thank You!