**International Guidelines for Management of Sepsis and Septic Shock**

**Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2021**

**Appendix 4. Ventilation**

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# In adults with sepsis-induced ARDS, should we use plateau pressure less than 30 cm H2O (vs. greater than 30 cm H2O)

## Evidence profile: plateau pressure less than 30 cm H2O

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **plateau pressures less than 30 cm H20** | **higher plateau pressures** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious a | not serious | not serious | none | 173/516 (33.5%) | 208/513 (40.5%) | **RR 0.83** (0.70 to 0.97) | **69 fewer per 1,000** (from 122 fewer to 12 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality - Hospital Mortality** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | not serious | none | 146/458 (31.9%) | 186/455 (40.9%) | **RR 0.78** (0.66 to 0.93) | **90 fewer per 1,000** (from 139 fewer to 29 fewer) | ⨁⨁⨁⨁ HIGH | CRITICAL |
| **Mortality - 60-day mortality** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious b | none | 27/58 (46.6%) | 22/58 (37.9%) | **RR 1.23** (0.80 to 1.89) | **87 more per 1,000** (from 76 fewer to 338 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Barotrauma** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | not serious | serious b | none | 19/516 (3.7%) | 19/513 (3.7%) | **RR 1.00** (0.54 to 1.84) | **0 fewer per 1,000** (from 17 fewer to 31 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Ventilator Free Days** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | serious c | not serious | not serious | none | 490 | 487 | - | MD **1.8 higher** (0.35 higher to 3.25 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Duration of Mechanical Ventilation** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious d | none | 84 | 84 | - | MD **0.54 lower** (1.64 lower to 0.56 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. I2=60%; heterogeneity in pooled MA. Difference in mortality endpoints between studies (hospital mortality vs. 60-day mortality data)

b. Wide CI do not differentiate harm or benefit

c. I2=57%

d. Wide CI do not exclude harm or benefit

## EtD. Summary of Judgements plateau pressure less than 30 cm H2O

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | **Strong recommendation for the intervention** |
| ○ | ○ | ○ | ○ | **●** |

# In adults with sepsis-induced ARDS, should we use low tidal volume ventilation?

## Evidence profile: low tidal volume ventilation

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **low tidal-volume ventilation** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality** | | | | | | | | | | | | |
| 6 | randomised trials | not serious | not serious | not serious a | not serious b | none | 218/655 (33.3%) | 277/642 (43.1%) | **RR 0.78** (0.62 to 0.97) | **95 fewer per 1,000** (from 164 fewer to 13 fewer) | ⨁⨁⨁⨁ HIGH | CRITICAL |
| **Mortality - 28-day mortality** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious a | serious b | none | 11/29 (37.9%) | 17/24 (70.8%) | **RR 0.54** (0.31 to 0.91) | **326 fewer per 1,000** (from 489 fewer to 64 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality - 60-day mortality** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious a | serious c | none | 27/58 (46.6%) | 22/58 (37.9%) | **RR 1.23** (0.80 to 1.89) | **87 more per 1,000** (from 76 fewer to 338 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality - Hospital Mortality** | | | | | | | | | | | | |
| 5 | randomised trials | not serious | not serious d | not serious a | not serious b | none | 191/597 (32.0%) | 255/584 (43.7%) | **RR 0.73** (0.63 to 0.85) | **118 fewer per 1,000** (from 162 fewer to 65 fewer) | ⨁⨁⨁⨁ HIGH | CRITICAL |
| **Barotrauma** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious a | serious c | none | 15/537 (2.8%) | 26/542 (4.8%) | **RR 0.65** (0.34 to 1.24) | **17 fewer per 1,000** (from 32 fewer to 12 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Days on Mechanical Ventilation** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious a | serious c | none | 84 | 84 | - | MD **0.54 lower** (1.64 lower to 0.56 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Ventilator-Free Days** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious e | not serious a | serious c | none | 540 | 532 | - | MD **2.23 higher** (1.01 lower to 5.47 higher) | ⨁⨁◯◯ LOW | CRITICAL |
| **ICU LOS** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious a | serious c | none | 58 | 58 | - | MD **3.8 higher** (5.12 lower to 12.72 higher) | ⨁⨁⨁◯ MODERATE | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Patients included mixed ARDS, but majority (60% of more) were due to sepsis or sepsis-induced ARDS

b. Significant difference; small sample of patients

c. Crosses line of no effects; small sample of patients

d. I2=0% for hospital mortality across 5 studies. There was variability between protocols in managing control group and intervention (open lung strategy utilization, definition of low-tidal volume). This did not effect the overall heterogeneity in estimates.

e. I2 = 59%; heterogeneity between studies in terms of intervention/control protocols

## EtD. Summary of Judgements low tidal volume ventilation

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | **Small** | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | **Large savings** | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | No included studies |
| **Equity** | Reduced | Probably reduced | Probably no impact | **Probably increased** | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | **Strong recommendation for the intervention** |
| ○ | ○ | ○ | ○ | **●** |

# In adults with sepsis-induced ARDS, should a high PEEP strategy be used?

## Evidence profile: high PEEP strategy

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **high PEEP strategy** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Hospital Mortality** | | | | | | | | | | | | |
| 8 | randomised trials | not serious | not serious | not serious a | serious b | none | 751/1782 (42.1%) | 784/1806 (43.4%) | **RR 0.93** (0.81 to 1.06) | **30 fewer per 1,000** (from 82 fewer to 26 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **28-day Mortality** | | | | | | | | | | | | |
| 7 | randomised trials | not serious | not serious | not serious a | serious b | none | 554/1468 (37.7%) | 583/1500 (38.9%) | **RR 0.88** (0.72 to 1.07) | **47 fewer per 1,000** (from 109 fewer to 27 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **ICU Mortality** | | | | | | | | | | | | |
| 6 | randomised trials | not serious | not serious | not serious a | serious b | none | 503/1141 (44.1%) | 531/1169 (45.4%) | **RR 0.86** (0.69 to 1.06) | **64 fewer per 1,000** (from 141 fewer to 27 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Barotrauma** | | | | | | | | | | | | |
| 9 | randomised trials | not serious | not serious | not serious a | serious b | none | 177/1814 (9.8%) | 126/1834 (6.9%) | **RR 1.14** (0.69 to 1.89) | **10 more per 1,000** (from 21 fewer to 61 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Ventilator-free days at day 28** | | | | | | | | | | | | |
| 5 | randomised trials | not serious | serious c | not serious | serious d | none | 1269 | 1265 | - | MD **1.51 higher** (1.07 lower to 4.09 higher) | ⨁⨁◯◯ LOW | CRITICAL |
| **Days of Mechanical Ventilation** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | serious c | not serious a | serious b | none | 505 | 535 | - | MD **2.29 higher** (2.22 lower to 6.8 higher) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Included all ARDS patients. High PEEP>10 in all studies. Elected not to downgrade as majority of ARDS patients in each study were due to pneumonia, sepsis, or septic shock (approximately 60-70%)

b. Wide range of outcomes (CI)

c. Heterogeneity in outcomes between high PEEP and low PEEP

d. Large Confidence interval; large range of IQR reported in individual studies.

## EtD. Summary of Judgements high PEEP strategy

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | **Varies** | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | **Varies** | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# In adults with sepsis-induced ARDS, should we use recruitment maneuvers?

## Evidence profile: recruitment maneuvers

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **recruitment maneuvers** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality at 28-days** | | | | | | | | | | | | |
| 8 | randomised trials | not serious | not serious | not serious | serious a | none | 490/1256 (39.0%) | 509/1290 (39.5%) | **RR 0.90** (0.74 to 1.09) | **39 fewer per 1,000** (from 103 fewer to 36 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality at 28-days - Traditional Recruitment Maneuver** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | serious b | none | 184/658 (28.0%) | 232/688 (33.7%) | **RR 0.79** (0.64 to 0.96) | **71 fewer per 1,000** (from 121 fewer to 13 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality at 28-days - Incremental PEEP Recruitment** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | serious b | none | 306/598 (51.2%) | 277/602 (46.0%) | **RR 1.12** (1.00 to 1.25) | **55 more per 1,000** (from 0 fewer to 115 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Hospital Mortality** | | | | | | | | | | | | |
| 8 | randomised trials | not serious | not serious | not serious | serious a | none | 588/1255 (46.9%) | 623/1289 (48.3%) | **RR 0.90** (0.78 to 1.04) | **48 fewer per 1,000** (from 106 fewer to 19 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Hospital Mortality - Traditional Recruitment Maneuver** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | serious b | none | 238/658 (36.2%) | 288/687 (41.9%) | **RR 0.85** (0.75 to 0.97) | **63 fewer per 1,000** (from 105 fewer to 13 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Hospital Mortality - Incremental PEEP Recruitment** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | serious a | none | 350/597 (58.6%) | 335/602 (55.6%) | **RR 1.06** (0.97 to 1.17) | **33 more per 1,000** (from 17 fewer to 95 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **P/F Ratio after 24 hours** | | | | | | | | | | | | |
| 6 | randomised trials | not serious | serious c | not serious | not serious | none | 682 | 718 | - | MD **49.67 higher** (27.75 higher to 71.59 higher) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| **Barotrauma** | | | | | | | | | | | | |
| 5 | randomised trials | not serious | serious | not serious | serious a | none | 67/691 (9.7%) | 71/716 (9.9%) | **RR 0.79** (0.46 to 1.37) | **21 fewer per 1,000** (from 54 fewer to 37 more) | ⨁⨁◯◯ LOW | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Wide confidence interval; CI crosses line of no effect.

b. Only 4 RCTs included with N=1200. Did not grade down for indirectness although treatment incorporated various interventions along with recruitment (PEEP strategy, target Vt)

c. I2 = 87%

## EtD. Summary of Judgements recruitment maneuvers

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# In adults with sepsis-induced ARDS, should we use prone ventilation?

## Evidence profile: prone ventilation

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **prone ventilation** | **supine ventilation** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality** | | | | | | | | | | | | |
| 6 | randomised trials | not serious a | serious b | not serious | serious c | none | 335/1067 (31.4%) | 363/1012 (35.9%) | **RR 0.83** (0.66 to 1.05) | **61 fewer per 1,000** (from 122 fewer to 18 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Mortality - Lung Protective Ventilation group** | | | | | | | | | | | | |
| 3 | randomised trials | not serious a | serious d | not serious | serious c | none | 98/426 (23.0%) | 142/422 (33.6%) | **RR 0.69** (0.43 to 1.11) | **104 fewer per 1,000** (from 192 fewer to 37 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Mortality - Non-Lung protective ventilation** | | | | | | | | | | | | |
| 3 | randomised trials | not serious a | not serious | not serious | serious c | none | 237/641 (37.0%) | 221/590 (37.5%) | **RR 0.96** (0.80 to 1.16) | **15 fewer per 1,000** (from 75 fewer to 60 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality >12 hours prone** | | | | | | | | | | | | |
| 4 | randomised trials | not serious a | serious e | not serious | not serious | none | 131/502 (26.1%) | 177/482 (36.7%) | **RR 0.71** (0.52 to 0.97) | **106 fewer per 1,000** (from 176 fewer to 11 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality <12 hours prone** | | | | | | | | | | | | |
| 2 | randomised trials | not serious a | not serious | not serious | serious c | none | 204/565 (36.1%) | 186/530 (35.1%) | **RR 1.04** (0.89 to 1.21) | **14 more per 1,000** (from 39 fewer to 74 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality - Moderate to severe ARDS** | | | | | | | | | | | | |
| 4 | randomised trials | not serious a | serious e | not serious | not serious | none | 131/502 (26.1%) | 177/482 (36.7%) | **RR 0.71** (0.52 to 0.97) | **106 fewer per 1,000** (from 176 fewer to 11 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Mortality - All ARDS** | | | | | | | | | | | | |
| 2 | randomised trials | not serious a | not serious | not serious | serious c | none | 204/565 (36.1%) | 186/530 (35.1%) | **RR 1.04** (0.89 to 1.21) | **14 more per 1,000** (from 39 fewer to 74 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **P/F Ratio on Day 4** | | | | | | | | | | | | |
| 4 | randomised trials | not serious a | serious f | not serious | not serious | none | 588 | 590 | - | MD **24.39 higher** (11.64 higher to 37.14 higher) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| **Barotrauma** | | | | | | | | | | | | |
| 4 | randomised trials | not serious a | not serious | not serious | serious c | none | 44/747 (5.9%) | 46/685 (6.7%) | **RR 0.88** (0.59 to 1.31) | **8 fewer per 1,000** (from 28 fewer to 21 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Unplanned CVC Removal** | | | | | | | | | | | | |
| 2 | randomised trials | not serious a | very serious g | not serious | very serious c | none | 60/314 (19.1%) | 40/321 (12.5%) | **RR 1.72** (0.43 to 6.84) | **90 more per 1,000** (from 71 fewer to 728 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Pressure Sores** | | | | | | | | | | | | |
| 2 | randomised trials | not serious a | not serious | not serious | not serious | none | 244/561 (43.5%) | 185/526 (35.2%) | **RR 1.22** (1.05 to 1.41) | **77 more per 1,000** (from 18 more to 144 more) | ⨁⨁⨁⨁ HIGH | CRITICAL |
| **Airway Complications - Unplanned extubation** | | | | | | | | | | | | |
| 6 | randomised trials | not serious a | serious h | not serious | serious c | none | 112/1061 (10.6%) | 97/1006 (9.6%) | **RR 1.14** (0.78 to 1.67) | **13 more per 1,000** (from 21 fewer to 65 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Airway Complications - ETT Obstruction** | | | | | | | | | | | | |
| 3 | randomised trials | not serious a | serious i | not serious | not serious | none | 130/816 (15.9%) | 76/778 (9.8%) | **RR 1.78** (1.22 to 2.59) | **76 more per 1,000** (from 21 more to 155 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. All studies had lack of blinding of participants and personnel. However, ROB was not graded down as outcomes were objective and unlikely to be altered due to blinding.

b. Heterogeneity between studies, I2=70%

c. Wide CI - outcomes crosses line of no effect

d. I2 = 74%

e. I2=62%

f. I2=43%

g. I2=91%

h. I2-35%

i. I2=31%

## EtD. Summary of judgements prone ventilation

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | **Small** | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | **Strong recommendation for the intervention** |
| ○ | ○ | ○ | ○ | **●** |

# In adults with sepsis-induced respiratory failure, should we use Non-invasive ventilation?

## Evidence profile: Non-invasive ventilation

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **non-invasive ventilation** | **IPPV** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **ICU Mortality** | | | | | | | | | | | | |
| 3 | randomised trials | not serious a | serious b | serious c | serious d | none | 26/74 (35.1%) | 30/73 (41.1%) | **RR 0.84** (0.44 to 1.62) | **66 fewer per 1,000** (from 230 fewer to 255 more) | ⨁◯◯◯ VERY LOW |  |
| **NIV Failure (Intubation Rates)** | | | | | | | | | | | | |
| 3 | randomised trials | serious a | not serious | serious c | serious e | none | 37/74 (50.0%) | 73/73 (100.0%) | **RR 0.58** (0.25 to 1.35) | **420 fewer per 1,000** (from 750 fewer to 350 more) | ⨁◯◯◯ VERY LOW |  |
| **ICU LOS** | | | | | | | | | | | | |
| 2 | randomised trials | serious a | not serious | serious c | not serious | none | 56 | 48 | - | MD **13.65 lower** (17.43 lower to 9.87 lower) | ⨁⨁◯◯ LOW |  |
| **P/F Ratio after 60 minutes** | | | | | | | | | | | | |
| 2 | randomised trials | serious a | not serious | serious c | serious e | none | 54 | 59 | - | MD **21.49 higher** (7.82 lower to 50.81 higher) | ⨁◯◯◯ VERY LOW |  |
| **P/F Ratio after 24 hours** | | | | | | | | | | | | |
| 1 | randomised trials | serious a | not serious | not serious f | serious e | none | 34 | 31 | - | MD **9 higher** (28.44 lower to 46.44 higher) | ⨁⨁◯◯ LOW |  |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Blinding did not occur in all studies

b. I2=58%; point estimate from each study favours different modality

c. Causes of acute hypoxemic respiratory failure (ARF) varied in studies. Pneumonia/sepsis accounted for 30-72% of patients between studies.

d. Wide CIs do not exclude harm

e. Wide CIs do not distinguish which modality more effective

f. Single study excluded patients with COPD; causes of ARDS due to pneumonia/infection account for 73% and 52% of patients between NIV and IPPV groups respectively

## EtD. Summary of judgements Non invasive ventilation

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | Large |  | Varies | **Don't know** |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | Varies | **Don't know** |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **Don't know** |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | **Conditional recommendation for either the intervention or the comparison** | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | ○ | **●** | ○ | ○ |

# In adults with sepsis-induced respiratory failure without ARDS, should we use low tidal volume?

## Evidence profile: low tidal volume

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **low tidal volume ventilation** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality** | | | | | | | | | | | | |
| 3 | randomised trials | not serious a | not serious | serious b | serious c | none | 193/562 (34.3%) | 182/567 (32.1%) | **RR 1.07** (0.91 to 1.26) | **22 more per 1,000** (from 29 fewer to 83 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Duration of Mechanical Ventilation (days)** | | | | | | | | | | | | |
| 3 | randomised trials | not serious d,e | serious f | serious b | serious c | none | 534 | 550 | - | MD **0.11 higher** (2.11 lower to 2.33 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Development of ARDS** | | | | | | | | | | | | |
| 2 | randomised trials | serious d | not serious g | serious b | not serious | none | 19/524 (3.6%) | 33/536 (6.2%) | **RR 0.59** (0.34 to 1.02) | **25 fewer per 1,000** (from 41 fewer to 1 more) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Intervention was not blinded in most studies; not lowered as mortality is objective outcome

b. Studies were performed in a wide variety of patients with respiratory failure. Sepsis accounted for less than the majority of patients included.

c. Wide confidence intervals cannot exclude harm or benefit

d. Intervention was not blinded in most studies.

e. Not downgraded as the point estimate is non-significant

f. Statistical heterogeneity with I2>80%. Point estimates of each study showed varying results.

g. I2=65%, non-significant. Point estimates of trials favour intervention (low-tidal volume)

## EtD. Summary of judgements low tidal volume

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# In adults with sepsis-induced hypoxemic failure, should we use HFNO vs. NIV?

## Evidence profile: HFNO therapy compared to NIV for sepsis-induced hypoxemic respiratory failure

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **HFNO therapy** | **NIV** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **ICU Mortality** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious a | none | 12/106 (11.3%) | 27/110 (24.5%) | **RR 0.46** (0.25 to 0.86) | **133 fewer per 1,000** (from 184 fewer to 34 fewer) | ⨁⨁◯◯ LOW | CRITICAL |
| **Mortality at Day 90** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious a | none | 13/106 (12.3%) | 31/110 (28.2%) | **RR 0.44** (0.24 to 0.79) | **158 fewer per 1,000** (from 214 fewer to 59 fewer) | ⨁⨁◯◯ LOW | CRITICAL |
| **Need for Intubation** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious a,b | none | 40/106 (37.7%) | 55/110 (50.0%) | **RR 0.75** (0.55 to 1.03) | **125 fewer per 1,000** (from 225 fewer to 15 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Ventilator Free Days at Day 28** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious a | none | 106 | 110 | - | MD **5 higher** (2.29 higher to 7.71 higher) | ⨁⨁◯◯ LOW | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Small sample size, single study, low event rate (3-5 events could change confidence in estimate)

b. Wide CI

## EtD. Summary of judgements HFNO therapy compared to NIV for sepsis-induced hypoxemic respiratory failure

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | **Conditional recommendation for either the intervention or the comparison** | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | ○ | **●** | ○ | ○ |

# In adults with sepsis-induced hypoxemic failure, should we use conservative oxygen targets vs. control?

## Evidence profile: Conservative oxygen targets compared to control for sepsis-induced hypoxemic respiratory failure

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **conservative oxygen targets** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mortality** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious a | serious b | serious c | none | 112/398 (28.1%) | 121/389 (31.1%) | **RR 0.95** (0.64 to 1.43) | **16 fewer per 1,000** (from 112 fewer to 134 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Mortality - Mortality at day 90** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | serious b | serious c | none | 60/182 (33.0%) | 47/171 (27.5%) | **RR 1.20** (0.87 to 1.65) | **55 more per 1,000** (from 36 fewer to 179 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Mortality - Hospital Mortality** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | serious b | serious d | none | 52/216 (24.1%) | 74/218 (33.9%) | **RR 0.71** (0.53 to 0.96) | **98 fewer per 1,000** (from 160 fewer to 14 fewer) | ⨁⨁◯◯ LOW | CRITICAL |
| **ICU LOS** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | serious b | serious e | none | 398 | 390 | - | MD **0.4 higher** (0.52 lower to 1.32 higher) | ⨁⨁◯◯ LOW | IMPORTANT |
| **Ventilator Free Days** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious f | serious b | serious e | none | 398 | 390 | - | MD **0.68 lower** (3.56 lower to 2.2 higher) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| **Mortality (full ICU Rox)** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious g | serious b | serious c | none | 231/747 (30.9%) | 242/749 (32.3%) | **RR 0.92** (0.67 to 1.25) | **26 fewer per 1,000** (from 107 fewer to 81 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Mortality - Mortality at Day 90 (full ICU Rox)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | serious b | serious c | none | 179/531 (33.7%) | 168/531 (31.6%) | **RR 1.07** (0.90 to 1.27) | **22 more per 1,000** (from 32 fewer to 85 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **ICU LOS (full ICU Rox)** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | serious b | serious e | none | 752 | 750 | - | MD **0.06 higher** (0.81 lower to 0.92 higher) | ⨁⨁◯◯ LOW | IMPORTANT |
| **Ventilator Free Days (full ICU Rox)** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | serious f | serious b | serious e | none | 752 | 750 | - | MD **0.22 higher** (1.16 lower to 1.61 higher) | ⨁◯◯◯ VERY LOW | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. I2=65%; point estimates vary between studies between harm and benefit.

b. Small subset of sepsis patients in included studies

c. Wide CI do not exclude harm or benefit

d. Single study with small sample size

e. CI does not discriminate harm from benefit

f. I2 = 61%; heterogeneity between study outcomes

g. I2=62%

## EtD. Summary of judgements Conservative oxygen targets compared to control for sepsis-induced hypoxemic respiratory failure

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

# In adults with sepsis-induced ARDS, should we use ECMO?

## Evidence profile: ECMO compared to usual care for sepsis-induced ARDS

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **ECMO** | **usual care** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **60-day Mortality** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious a | not serious | very serious b | none | 73/214 (34.1%) | 101/215 (47.0%) | **RR 0.73** (0.57 to 0.92) | **127 fewer per 1,000** (from 202 fewer to 38 fewer) | ⨁⨁◯◯ LOW | CRITICAL |
| **30-day Mortality** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious a | not serious | very serious b | none | 61/214 (28.5%) | 90/215 (41.9%) | **RR 0.68** (0.52 to 0.89) | **134 fewer per 1,000** (from 201 fewer to 46 fewer) | ⨁⨁◯◯ LOW | CRITICAL |
| **Death or severe disability at 6 months** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b,d | none | 33/90 (36.7%) | 46/90 (51.1%) | **RR 0.72** (0.51 to 1.01) | **143 fewer per 1,000** (from 250 fewer to 5 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Stroke** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b,d | none | 3/124 (2.4%) | 8/125 (6.4%) | **RR 0.38** (0.10 to 1.39) | **40 fewer per 1,000** (from 58 fewer to 25 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Hemorrhagic Stroke** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b,d | none | 3/124 (2.4%) | 5/125 (4.0%) | **RR 0.60** (0.15 to 2.48) | **16 fewer per 1,000** (from 34 fewer to 59 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Bleeding - leading to transfusion** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b | none | 57/124 (46.0%) | 35/125 (28.0%) | **RR 1.64** (1.17 to 2.31) | **179 more per 1,000** (from 48 more to 367 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Bleeding - Massive transfusion** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b,d | none | 3/124 (2.4%) | 1/125 (0.8%) | **RR 3.02** (0.32 to 28.68) | **16 more per 1,000** (from 5 fewer to 221 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Days free from mechanical ventilation** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious c | not serious | very serious b,d | none | 124 | 125 | - | MD **9 lower** (18.05 lower to 0.05 higher) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Combes study stopped early for no benefit; Peek trial with smaller sample size showed small effect

b. Small total sample

c. Only 1 study reporting data with small sample - unable to compare consistency across studies.

d. CI cross line of no effect

## EtD. Summary of judgements ECMO compared to usual care for sepsis-induced ARDS

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | **Varies** | Don't know |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | **Large costs** | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | **Probably reduced** | Probably no impact | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |
| **Feasibility** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |

**Type of recommendation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |