# Appendix Table 5. EtD for initial vasopressor choice recommendation

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| --- | --- |
| Question | |
| **Should norepinephrine vs. other vasopressor be used for patients who remain hypotensive despite fluid resuscitation?** | |
| **Population:** | Patients with ALF or ACLF who remain hypotensive despite fluid resuscitation |
| **Intervention:** | norepinephrine |
| **Comparison:** | other vasopressor |
| **Main outcomes:** | Mortality - norepinephrine vs. dopamine; Mortality - norepinephrine vs. epinephrine; |
| **Setting:** | acute and chronic liver failure |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** |  |

Assessment

|  |  |  |
| --- | --- | --- |
| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know |  |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | | **Outcomes** | **№ of participants (studies) Follow up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with other vasopressor** | **Risk difference with norepinephrine** | | Mortality - norepinephrine vs. dopamine | 1718 (11 RCTs) | ⨁⨁⨁◯ MODERATEa | **RR 0.89** (0.81 to 0.98) | Study population | | | 508 per 1,000 | **56 fewer per 1,000** (97 fewer to 10 fewer) | | Mortality - norepinephrine vs. epinephrine | 540 (4 RCTs) | ⨁⨁◯◯ LOWa,b | **RR 0.96** (0.77 to 1.21) | Study population | | | 357 per 1,000 | **14 fewer per 1,000** (82 fewer to 75 more) |  1. Trials conducted in septic shock, not limited to patients with acute or chronic liver failure. 2. The confidence interval is wide and the total number of events low. |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know | | **Outcomes** | **№ of participants (studies) Follow up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with other vasopressor** | **Risk difference with norepinephrine** | | Mortality - norepinephrine vs. dopamine | 1718 (11 RCTs) | ⨁⨁⨁◯ MODERATEa | **RR 0.89** (0.81 to 0.98) | Study population | | | 508 per 1,000 | **56 fewer per 1,000** (97 fewer to 10 fewer) | | Mortality - norepinephrine vs. epinephrine | 540 (4 RCTs) | ⨁⨁◯◯ LOWa,b | **RR 0.96** (0.77 to 1.21) | Study population | | | 357 per 1,000 | **14 fewer per 1,000** (82 fewer to 75 more) |  1. Trials conducted in septic shock, not limited to patients with acute or chronic liver failure. 2. The confidence interval is wide and the total number of events low. |  |
| Certainty of evidence What is the overall certainty of the evidence of effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ● Moderate ○ High ○ No included studies | | **Outcomes** | **№ of participants (studies) Follow up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with other vasopressor** | **Risk difference with norepinephrine** | | Mortality - norepinephrine vs. dopamine | 1718 (11 RCTs) | ⨁⨁⨁◯ MODERATEa | **RR 0.89** (0.81 to 0.98) | Study population | | | 508 per 1,000 | **56 fewer per 1,000** (97 fewer to 10 fewer) | | Mortality - norepinephrine vs. epinephrine | 540 (4 RCTs) | ⨁⨁◯◯ LOWa,b | **RR 0.96** (0.77 to 1.21) | Study population | | | 357 per 1,000 | **14 fewer per 1,000** (82 fewer to 75 more) |  1. Trials conducted in septic shock, not limited to patients with acute or chronic liver failure. 2. The confidence interval is wide and the total number of events low. |  |
| Values Is there important uncertainty about or variability in how much people value the main outcomes? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability |  |  |
| Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ 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 How large are the resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know |  |  |
| Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ○ Moderate ○ High ● No included studies |  |  |
| Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ 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 What would be the impact on health equity? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know |  |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know |  |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know |  |  |

Summary of judgements

|  | **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** |
| ○ | ○ | ○ | ○ | **●** |

| Norepinephrine compared to other vasopressor for patients who remain hypotensive despite fluid resuscitation  **Bibliography: Avni T, Lador A, Lev S et al. Vasopressors for the treatment of septic shock: systematic review and meta-analysis. PLoS One. 2015; 10(8): e129305.** | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **quality assessment** | | | | | | | **Summary of findings** | | | | |
| **№ of participants (studies) Follow-up** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication bias** | **Overall quality of evidence** | **Study event rates (%)** | | **Relative effect (95% CI)** | **Anticipated absolute effects** | |
| **With other vasopressor** | **With norepinephrine** | **Risk with other vasopressor** | **Risk difference with norepinephrine** |
| **Mortality - norepinephrine vs. dopamine** | | | | | | | | | | | |
| 1718 (11 RCTs) | not serious | not serious | serious a | not serious | none | ⨁⨁⨁◯ MODERATE | 450/886 (50.8%) | 376/832 (45.2%) | **RR 0.89** (0.81 to 0.98) | 508 per 1,000 | **56 fewer per 1,000** (from 97 fewer to 10 fewer) |
| **Mortality - norepinephrine vs. epinephrine** | | | | | | | | | | | |
| 540 (4 RCTs) | not serious | not serious | serious a | serious b | none | ⨁⨁◯◯ LOW | 94/263 (35.7%) | 95/277 (34.3%) | **RR 0.96** (0.77 to 1.21) | 357 per 1,000 | **14 fewer per 1,000** (from 82 fewer to 75 more) |

**CI:** Confidence interval; **RR:** Risk ratio

#### Explanations

a. Trials conducted in septic shock, not limited to patients with acute or chronic liver failure.

b. The confidence interval is wide and the total number of events low.