# 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

|  |
| --- |
| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know |  |  |
| Desirable EffectsHow 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 EffectsHow 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** |
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 |  |
| Certainty of evidenceWhat 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 |
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 |  |
| ValuesIs 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 effectsDoes 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 requiredHow 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 resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low○ Low○ Moderate○ High● No included studies |  |  |
| Cost effectivenessDoes 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 |  |  |
| EquityWhat 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 |  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know |  |  |
| FeasibilityIs 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.