# Appendix Table 3. EtD framework for Albumin vs. Crystalloids recommendation

|  |  |
| --- | --- |
| Question | |
| **Should albumin vs. crystalloids be used for acute liver failure?** | |
| **Population:** | ALF or ACLF |
| **Intervention:** | albumin |
| **Comparison:** | crystalloids |
| **Main outcomes:** | Mortality; Renal replacement therapy; |
| **Setting:** | resuscitation |

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 |  |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know |  |  |
| 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 saline** | **Risk difference with albumin** | | Mortality | 1229 (2 RCTs) | ⨁⨁◯◯ LOWa,b | **OR 0.81** (0.64 to 1.03) | Study population | | | 355 per 1,000 | **47 fewer per 1,000** (95 fewer to 7 more) |  1. Trials conducted in patients with sepsis. None specifically in patients with acute or liver failure. 2. Confidence interval includes significant benefit and harm. |  |
| 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 | Based on our experience and guesstimate. |  |
| 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 |
| ○ | ○ | ○ | **●** | ○ |

| Albumin compared to crystalloids for ALF and ACLF  Bibliography: Rochwerg B, Alhazzani W, Sindi A et al. Fluid resuscitation in sepsis: a systematic review and network meta-analysis. Ann Intern Med 2014 Sep 2; 161 (5) 347-555. | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 crystalloids** | **With albumin** | **Risk with crystalloids** | **Risk difference with albumin** |
| **Mortality** | | | | | | | | | | | |
| 1229 (2 RCTs) | not serious | not serious | serious a | serious b | none | ⨁⨁◯◯ LOW | 220/619 (35.5%) | 190/610 (31.1%) | **OR 0.81** (0.64 to 1.03) | 355 per 1,000 | **47 fewer per 1,000** (from 95 fewer to 7 more) |
| **Renal replacement therapy** | | | | | | | | | | | |
| 1218 (1 RCT) | not serious | not serious | serious | serious b | none | ⨁⨁◯◯ LOW | 112/615 (18.2%) | 113/603 (18.7%) | **OR 1.04** (0.78 to 1.38) | 182 per 1,000 | **6 more per 1,000** (from 34 fewer to 53 more) |

**CI:** Confidence interval; **OR:** Odds ratio

#### Explanations

a. Trials conducted in patients with sepsis. None specifically in patients with acute or liver failure.

b. Confidence interval includes significant benefit and harm.