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

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| 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

|  |
| --- |
| 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 |  |  |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Large○ Moderate○ Small● Trivial○ Varies○ Don't know |  |  |
| 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 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.

 |  |
| 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 | Based on our experience and guesstimate. |  |
| 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 |
| ○  | ○  | ○  | **●**  | ○  |

| Albumin compared to crystalloids for ALF and ACLFBibliography: 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.