# Appendix Table 2. EtD for HES vs. Crystalloids recommendation

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| Question |
| **Should synthetic colloids (HES) vs. crystalloids be used for patients with acute or chronic liver failure?** |
| **Population:** | patients with ALF or ACLF |
| **Intervention:** | synthetic colloids (HES) |
| **Comparison:** | crystalloids |
| **Main outcomes:** | Mortality; Renal replacement therapy; Transfusion; |
| **Setting:** | initial 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 |

| **Outcomes** | **№ of participants(studies)Follow up** | **Certainty of the evidence(GRADE)** | **Relative effect(95% CI)** | **Anticipated absolute effects\* (95% CI)** |
| --- | --- | --- | --- | --- |
| **Risk with colloids** | **Risk difference with crystalloids** |
| Mortality | 6644(12 RCTs) | ⨁⨁◯◯LOWa,b | **OR 0.99**(0.89 to 1.10) | Study population |
| 336 per 1,000 | **2 fewer per 1,000**(26 fewer to 22 more) |

1. Statistical heterogeneity is 53%. Clinical heterogeneity with different crystalloids and colloids.
2. Trials conducted in patients with sepsis. No trial dedicated to patients with acute and chronic liver failure.

 |  |
| 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 colloids** | **Risk difference with crystalloids** |
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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 colloids** | **Risk difference with crystalloids** |
| Mortality | 6644(12 RCTs) | ⨁⨁◯◯LOWa,b | **OR 0.99**(0.89 to 1.10) | 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 | This is based on our impressions and experience. |  |
| 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 |
| **●**  | ○  | ○  | ○  | ○  |

| Synthetic colloids (HES) compared to crystalloids for patients with acute or chronic liver failureBibliography: 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. |
| --- |
| **Certainty assessment**  | **Summary of findings**  |
| **№ of participants(studies)Follow-up** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication bias** | **Overall certainty of evidence** | **Study event rates (%)** | **Relative effect(95% CI)** | **Anticipated absolute effects** |
| **With crystalloids** | **With synthetic colloids (HES)** | **Risk with crystalloids** | **Risk difference with synthetic colloids (HES)** |
| **Mortality** |
| 6644(12 RCTs)  | not serious  | serious a | serious b | not serious  | none  | ⨁⨁◯◯LOW  | 1119/3326 (33.6%)  | 1124/3318 (33.9%)  | **OR 0.99**(0.89 to 1.10)  | 336 per 1,000  | **2 fewer per 1,000**(from 26 fewer to 22 more)  |
| **Renal replacement therapy** |
| 3893(8 RCTs)  | not serious  | not serious  | serious b | not serious  | none  | ⨁⨁⨁◯MODERATE  | 274/1943 (14.1%)  | 358/1950 (18.4%)  | **OR 1.39**(1.17 to 1.66)  | 141 per 1,000  | **45 more per 1,000**(from 20 more to 73 more)  |
| **Transfusion** |
| 744(8 RCTs)  | not serious  | not serious  | serious c | serious d | none  | ⨁⨁◯◯LOW  | 83/389 (21.3%)  | 76/355 (21.4%)  | **RR 1.10**(0.86 to 1.41)  | 213 per 1,000  | **21 more per 1,000**(from 30 fewer to 87 more)  |

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

#### Explanations

a. Statistical heterogeneity is 53%. Clinical heterogeneity with different crystalloids and colloids.

b. Trials conducted in patients with sepsis. No trial dedicated to patients with acute and chronic liver failure.

c. Trials conducted in peri-operative population. No trial dedicated to patients with acute and chronic liver failure.

d. Confidence interval includes significant benefit and significant harm.