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

|  |  |
| --- | --- |
| 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

|  |  |  |
| --- | --- | --- |
| 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 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 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 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. |  |
| 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 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. |  |
| 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 | This is based on our impressions and experience. |  |
| 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 |
| **●** | ○ | ○ | ○ | ○ |

| Synthetic colloids (HES) compared to crystalloids for patients with acute or chronic liver failure  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. | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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.