# Colloids versus crystalloids for fluid resuscitation in critically ill patients (Review)

**Perel P, Roberts I**


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[Intervention Review]

# Colloids versus crystalloids for fluid resuscitation in critically ill patients

Pablo Perel[1], Ian Roberts[1]

[1]Cochrane Injuries Group, London School of Hygiene & Tropical Medicine, London, UK

Contact address: Pablo Perel, Cochrane Injuries Group, London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. pablo.perel@Lshtm.ac.uk.

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## ABSTRACT

### Background

Colloid solutions are widely used in fluid resuscitation of critically ill patients. There are several choices of colloid and there is ongoing debate about the relative effectiveness of colloids compared to crystalloid fluids.

### Objectives

To assess the effects of colloids compared to crystalloids for fluid resuscitation in critically ill patients.

### Search methods

We searched the Cochrane Injuries Group Specialised Register, CENTRAL (*The Cochrane Library* 2008, Issue 3), MEDLINE, EMBASE, ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED), ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S), and The Controlled Trials metaRegister (www.controlled-trials.com). Reference lists of relevant studies and review articles were searched for further trials. The searches were last updated in September 2008.

### Selection criteria

Randomised controlled trials (RCTs) of colloids compared to crystalloids, in patients requiring volume replacement. We excluded cross-over trials and trials in pregnant women and neonates.

### Data collection and analysis

Two authors independently extracted data and rated quality of allocation concealment. We analysed trials with a 'double-intervention', such as those comparing colloid in hypertonic crystalloid to isotonic crystalloid, separately. We stratified the analysis according to colloid type and quality of allocation concealment.

### Main results

We identified 65 eligible trials; 56 of these presented mortality data.

### Colloids compared to crystalloids

***Albumin or plasma protein fraction*** - 23 trials reported data on mortality, including a total of 7754 patients. The pooled relative risk (RR) from these trials was 1.01 (95% confidence interval (95% CI) 0.92 to 1.10). When we excluded the trial with poor quality

allocation concealment, pooled RR was 1.00 (95% CI 0.91 to 1.09). ***Hydroxyethyl starch*** - 17 trials compared hydroxyethyl starch with crystalloids, n = 1172 patients. The pooled RR was 1.18 (95% CI 0.96 to 1.44). ***Modified gelatin*** - 11 trials compared modified gelatin with crystalloid, n = 506 patients. The pooled RR was 0.91 (95% CI 0.49 to 1.72). (When the trials by Boldt et al were removed from the three preceding analyses, the results were unchanged.)

***Dextran*** - nine trials compared dextran with a crystalloid, n = 834 patients. The pooled RR was 1.24 (95% CI 0.94 to 1.65).

**Colloids in hypertonic crystalloid compared to isotonic crystalloid**

Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised participants. Pooled RR was 0.88 (95% CI 0.74 to 1.05).

**Authors' conclusions**

There is no evidence from RCTs that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. As colloids are not associated with an improvement in survival, and as they are more expensive than crystalloids, it is hard to see how their continued use in these patients can be justified outside the context of RCTs.

## PLAIN LANGUAGE SUMMARY

**Are colloids more effective than crystalloids in reducing mortality in people who are critically ill or injured**

Trauma, burns or surgery can cause people to lose large amounts of blood. Fluid replacement, giving fluids intravenously (into a vein) to replace lost blood, is used to try to maintain blood pressure and reduce the risk of dying. Blood products, non-blood products or combinations are used, including colloid or crystalloid solutions. Colloids are increasingly used but they are more expensive than crystalloids. The review of trials found no evidence that colloids reduce the risk of dying compared with crystalloids.

## BACKGROUND

Fluid resuscitation for hypovolaemia is a mainstay of the medical management of critically ill patients, whether as a result of trauma, burns, major surgery or sepsis. Although recent studies (Bickell 1994) have suggested that the timing of volume replacement deserves careful consideration, when it comes to selecting the resuscitation fluid, clinicians are faced with a range of options. At one level the choice is between a colloid or crystalloid solution. Colloids are widely used, having been recommended in a number of resuscitation guidelines and intensive care management algorithms (Armstrong 1994; Vermeulen 1995).

The US Hospital Consortium Guidelines recommend that colloids are used in haemorrhagic shock prior to the availability of blood products, and in non-haemorrhagic shock following an initial crystalloid infusion. A 1995 survey of US academic health centres, however, found that the use of colloids far exceeded even the Hospital Consortium recommendations (Yim 1995). Surveys of burn care in the US (Fakhry 1995) and in Australia (Victorian DUAC 1991) found that the use of colloids for resuscitation varied without a set pattern.

The choice of fluid has considerable cost implications. Volume replacement with colloids is considerably more expensive than with crystalloids. Clinical studies have shown that colloids and crystalloids have different effects on a range of important physiological parameters. Because of these differences, all-cause mortality is arguably the most clinically relevant outcome measure in randomised trials comparing the two fluid types.

### Why it is important to do this review

Although there have been previous meta-analyses of mortality in randomised trials comparing colloids and crystalloids (Bisonni 1991; Velanovich 1989), neither of these satisfy the criteria that have been proposed for scientific overviews (Oxman 1994), and they predate most of the trials that have been conducted using synthetic colloids, and hypertonic crystalloid solutions. The purpose of this systematic review is to identify and synthesise all available unconfounded evidence of the effect on mortality in critically ill patients of colloids compared to crystalloids for volume replacement.

## OBJECTIVES

To assess the effects on mortality of using colloids compared to crystalloids, during fluid resuscitation in critically ill patients.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Controlled trials in which participants were randomised to treatment groups (colloid or control) on the basis of random allocation. As the comparison between fluid type was in terms of effects on mortality, we excluded randomised cross-over trials.

#### Types of participants

Critically ill patients (excluding neonates) who required volume replacement. We included patients who were critically ill as a result of trauma, burns, were undergoing surgery, or had other critical conditions such as complications of sepsis.
We excluded pre-operative elective surgical patients.

#### Types of interventions

We considered the following colloids: Dextran 70, hydroxyethyl starches, modified gelatins, albumin or plasma protein fraction.
There is overlap between albumin given for volume replacement and albumin given as a nutritional supplement, and many patients with a critical illness have low serum albumin. Where the trial was of total parenteral nutrition with or without albumin, we excluded it. We included trials where the albumin was given as part of volume replacement guided by colloid osmotic pressure or albumin levels.
The control group received crystalloid (isotonic or hypertonic) for fluid replacement. We included trials in which both groups received blood.
We excluded trials of fluids used for other purposes. For example, we excluded trials of pre-loading in preparation for elective surgery, and trials in patients undergoing fluid loading before cardiopulmonary bypass.

#### Types of outcome measures

The principal outcome measure was mortality from all causes, assessed at the end of the follow-up period scheduled for each trial.

### Search methods for identification of studies

The searches were not restricted by date, language or publication status.

#### Electronic searches

We searched the following electronic databases:

- Cochrane Injuries Group Specialised Register (searched 30 Sept 2008)
- CENTRAL (*The Cochrane Library* 2008, Issue 3)
- MEDLINE (1966 to September 2008)
- PubMed (searched 30 September, last three months)
- EMBASE (1980 to September 2008)
- ISI Web of Knowledge (1970 to September 2008)
- National Research Register (2006, Issue 4)
- Controlled Trials metaRegister (www.controlled-trials.com) (searched 30 Sept 2008)

The search strategy can be found in Appendix 1.

#### Searching other resources

We checked the reference lists of all identified trials and review articles, and contacted the trialists to identify any studies that may have been missed.

### Data collection and analysis

#### Selection of studies

We independently examined titles, abstracts, and keywords of citations from electronic databases for eligibility. We obtained the full text of all relevant records and independently assessed whether each met the pre-defined inclusion criteria. We resolved disagreement by discussion.

#### Assessment of risk of bias in included studies

We scored allocation concealment as described by Higgins 2008, assigning 'No' to poorest quality and 'Yes' to best quality (the presence of solutions in identical containers was only taken to mean adequate concealment if the fluid containers were used sequentially).

- Yes = trials deemed to have taken adequate measures to conceal allocation (that is, central randomisation; serially numbered, opaque, sealed envelopes; or other description that contained elements convincing of concealment).
- Unclear = trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories.

- No = trials in which concealment was inadequate (such as alternation or reference to case record numbers or to dates of birth).

We collected but did not score information on blinding and loss to follow up.

### Data synthesis

As a result of comments on the previous version of this review, we have stratified trials by type of fluid rather than type of original injury.
We calculated relative risks (RRs) and 95% confidence intervals (95% CI) for each study using a fixed-effect model. We then inspected each comparison visually for evidence of heterogeneity and performed a $Chi^2$ test. If there was no evidence of heterogeneity (visually or with a P value < 0.1) the trials were pooled within each type of fluid, but not combined between type of fluid.

### Sensitivity analysis

We then excluded trials with allocation concealment judged as inadequate and repeated the calculations.
The editorial group is aware that a clinical trial by Prof. Joachim Boldt has been found to have been fabricated (Boldt 2009). As the editors who revealed this fabrication point out (Reinhart 2011; Shafer 2011), this casts some doubt on the veracity of other studies by the same author. All Cochrane Injuries Group reviews which include studies by this author have therefore been edited to show the results with this author's trials included and excluded. Readers can now judge the potential impact of trials by this author on the conclusions of the review.

# RESULTS

## Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.
We identified 65 trials meeting the inclusion criteria for study design, participants and interventions. We were able to obtain mortality data for 56 of these. We have reported details of the included trials in the 'Characteristics of included studies' table.
Reasons for exclusion of trials were: the use of a cross-over design, testing a resuscitation algorithm, giving the control group oral fluids, the intervention being directed to the maintenance of serum albumin levels, for haemodilution, for fluid loading and for the reduction of intracranial pressure (see 'Characteristics of excluded studies' table).

Of the 56 trials with data on deaths, the quality of allocation concealment was adequate in seven trials and unclear in most of the others.
There were 60 comparisons of colloids and crystalloids (add-on colloid), nine comparisons of colloid in hypertonic crystalloid with isotonic crystalloid, and three comparisons of colloid with hypertonic crystalloid.

## Risk of bias in included studies

In general, the design of studies was not well reported. This is reflected in the number of unclear scores given for allocation concealment. We also collected information on blinding and loss to follow up. Blinding was not well reported and loss to follow up was generally small. The characteristics for each trial are listed in the 'Characteristics of included studies' table.

## Effects of interventions

### Colloids compared to crystalloids

#### Albumin or plasma protein fraction

Twenty-three trials reported data on mortality, including a total of 7754 patients. The pooled relative risk (RR) was 1.01 (95% confidence interval (95% CI) 0.92 to 1.10). When trials by Boldt were removed, the results were unchanged (RR 1.01 (95% CI 0.92 to 1.10)). When we excluded the trial with poor quality allocation concealment (Lucas 1978), pooled RR was 1.00 (95% CI 0.91 to 1.09).

#### Hydroxyethyl starch

Seventeen trials compared hydroxyethyl starch with crystalloids, including a total of 1172 randomised patients. The pooled RR was 1.18 (95% CI 0.96 to 1.44). When trials by Boldt were removed, the results were unchanged.

#### Modified gelatin

Eleven trials compared modified gelatin with crystalloid, including a total of 506 randomised patients. The pooled RR was 0.91 (95% CI 0.49 to 1.72). When trials by Boldt were removed, the results were unchanged.

#### Dextran

Nine trials compared dextran with a crystalloid, including a total of 834 randomised patients. The pooled RR was 1.24 (95% CI 0.94 to 1.65).

### Colloids in hypertonic crystalloid compared to isotonic crystalloid

One trial compared albumin and hypertonic saline with isotonic crystalloid. The RR of death was 0.50 (95% CI 0.06 to 4.33). Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised patients. The pooled RR was 0.88 (95% CI 0.74 to 1.05).

### Colloids in isotonic crystalloid compared to hypertonic crystalloid

Three trials compared colloids in isotonic crystalloid with hypertonic crystalloid. In two of these, where the colloid was either gelatin or starch, there were no deaths in either group. In the remaining trial, with 38 patients, there was a RR of death of 7.00 (0.39 to 126.93) for use of colloid, based on three deaths in the treatment group and none in the control group.

#### Sensitivity analysis

All three trials by Prof. Boldt (Boldt 1986; Boldt 1993; Boldt 2001) were of low methodological quality and were excluded as part of the sensitivity analysis in the original review.

## DISCUSSION

This systematic review synthesises the evidence from RCTs comparing colloid and crystalloid fluid resuscitation across a wide variety of clinical conditions. The review has been updated and extensively revised to take into account the comments made since it was first published. In particular, several commentators pointed out that it is inappropriate to combine effect estimates from studies of different colloids. For example, it was argued that large molecular weight colloids such as hydroxyethyl starch may be better retained in the vascular compartment than albumin and gelatins, and would therefore be more likely to show a favourable effect on mortality (Gosling 1998). In response to these concerns, the review has been stratified by type of colloid. However, the pooled relative risks fail to show a mortality benefit for resuscitation with any type of colloid.

There was a trend towards a favourable effect on mortality for colloids in hypertonic crystalloid, compared to isotonic crystalloids. Nevertheless, the results are compatible with the play of chance.

Common to all meta-analyses, this systematic review may have included studies whose interventions and patient characteristics are sufficiently incomparable that the calculation of a summary effect measure may be questioned. The resuscitation regimen differed between trials. Some trials randomised participants to an initial quantity of colloid or crystalloid, and then proceeded with some form of standard resuscitation for all participants. Other trials resuscitated with the allocated fluid to pre-determined end-points, either resuscitation end-points, or in the case of trauma, until corrective surgery. In addition, the type of colloid or crystalloid, the concentration, and the protocol to determine the quantity of fluid varied. Despite these differences, all participants were in need of volume replacement, and we believe that this variation in the intervention would have an impact on the size of the effect, rather than on its direction.

As regards the effects of albumin versus crystalloid, most of the information (as indicated by the weighting in the meta-analysis) was provided by the SAFE trial (SAFE 2004). The SAFE trial used central randomisation with a minimisation algorithm to ensure balance on known potential confounders. Blinding was assured through the use of specially designed masking cartons and specially designed and manufactured administration sets. The trial authors report that the effectiveness of the blinding was confirmed in a formal study before the trial was initiated. In brief, this was a well-conducted, high-quality trial. There were 726 deaths (20.9%) in the albumin-treated group and 729 deaths (21.1%) in the saline-treated group (RR of death 0.99; 95% CI 0.91 to 1.09). Although even this large trial was unable to confirm or refute the possibility of a modest benefit or harm from albumin, it has provided some reassurance that any hazard from albumin, if indeed there is any, is unlikely to be as extreme as was suggested by the results from the previously published (now here updated) meta-analysis of much smaller trials. The pooled RR for death with albumin in this updated meta-analysis is now 1.02 (95% CI 0.93 to 1.11). It is important to note that the effect estimate from the SAFE trial is entirely consistent with the results of previous trials of albumin in hypovolaemia and there is no significant heterogeneity ($I^2$ = 0%, P = 0.46).

The results of this updated meta-analysis have important policy implications. There is still no evidence that colloids are superior to crystalloids as a treatment for intravascular volume resuscitation in critically ill patients. Importantly, the SAFE trial also provided no evidence of any other clinical advantages from using albumin. It also debunked the belief, from pathophysiological inference, that very large volumes of crystalloid must be administered to reach the same resuscitation end-points as can be achieved using much smaller volumes of colloid. In the SAFE trial, the ratio of albumin administered to saline administered was approximately 1:1.4. Colloids, in particular albumin, are considerably more expensive than crystalloids, and albumin is a blood product and so carries at least a theoretical infectious disease risk. The economic opportunity cost of ongoing colloid use, particularly albumin use, is likely to be considerable and for this reason its ongoing use in this context is unjustified.

## AUTHORS' CONCLUSIONS

### Implications for practice

There is no evidence from RCTs that resuscitation with colloids, instead of crystalloids, reduces the risk of death in patients with trauma, burns or following surgery. As colloids are not associated with an improvement in survival, and further, colloids are considerably more expensive than crystalloids, it is hard to see how their continued use outside the context of RCTs in subsets of patients of particular concern, can be justified.

### Implications for research

Future trials may need to concentrate on specific subgroups of patients to identify people who may benefit from colloids rather than crystalloids.

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* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

**Boldt 1986**

| | |
|---|---|
| Methods | Randomised controlled trial, using sealed opaque envelopes.<br>Information on allocation concealment was obtained on contact with the authors.<br>Blinding and loss to follow up not mentioned. |
| Participants | 55 patients undergoing elective aorta-coronary bypass surgery.<br>Exclusion criteria were ejection fraction < 50% and LVEDP > 15 mmHg |
| Interventions | 1. 300ml 20% human albumin solution (n = 15).<br>2. 500ml 3% hydroxyethyl starch (n = 13).<br>3. 500ml 3.5% gelatin (n = 14).<br>4. No colloid (n = 13). |
| Outcomes | Haemodynamic variables were measured.<br>Deaths not reported. |
| Notes | Follow up until discharge from intensive care. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Boldt 1993**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment by sealed opaque envelopes (information from author).<br>Blinding and loss to follow up not mentioned. |
| Participants | 75 males undergoing elective aortocoronary bypass grafting, who had a pulmonary capillary wedge pressure of less than 5 mmHg after induction of anaesthesia |
| Interventions | 1. 5% albumin (n = 15).<br>2. 6% HES, mean molecular weight 450,000 (n = 15).<br>3. 6% HES, mean molecular weight 200,000 (n = 15).<br>4. 3.5% gelatin (n = 15).<br>5. No colloid (n = 15).<br>Fluid used through operation and on intensive care post-op. |
| Outcomes | Deaths not reported, author confirmed there were no deaths. |
| Notes | Follow up to 1 day. |

**Boldt 1993** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Boldt 2001**

| | |
|---|---|
| Methods | Randomised controlled trial, using a closed-envelope system. |
| Participants | 100 patients undergoing major abdominal surgery. |
| Interventions | 1. Ringer's lactate (n = 25).<br>2. 6% HES, mean molecular weight 200kDa, degree of substitution 0.5 (n = 25).<br>3. 6% HES, mean molecular weight 130kDa, degree of substitution 0.4 (n = 25).<br>4. 4% modified fluid gelatin, molecular weight 35kDA (n = 25). |
| Outcomes | Deaths.<br>Orthostatic problems.<br>Haemodynamics and laboratory data.<br>Fluid input and output.<br>Costs. |
| Notes | Follow-up period unclear. |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Boutros 1979**

| | |
|---|---|
| Methods | Randomised controlled trial ("randomly divided").<br>Method of allocation concealment not described.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 24 people undergoing major operative procedures on the abdominal aorta |
| Interventions | 1. Albumin in 5% dextrose (n = 7).<br>2. 5% dextrose and Ringer's lactate (n = 8).<br>3. 5% dextrose in 0.45% saline (n = 9).<br>Allocated fluids were used on admission to ICU, following surgery, guided by PAWP. Whole blood also given if clinically needed |
| Outcomes | Deaths reported. |

**Boutros 1979** (*Continued*)

| | |
|---|---|
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Bowser-Wallace 1986**

| | |
|---|---|
| Methods | Quasi-randomised controlled trial (allocation by alternation).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Admitted for burns of 30% or more.<br>Age range 5 months to 21 years.<br>Excluded if already given more than half calculated daily requirement before reaching hospital |
| Interventions | 1. 2ml/kg/%burn Ringer's lactate over 24 hrs, then 0.5ml plasmanate/kg/%burn over 24 hrs plus 5% dextrose (n = 19).<br>2. 2ml/kg/%burn hypertonic lactated saline over 24 hrs, then 0.6ml/kg/%burn hypertonic lactated saline over 24 hrs plus oral Haldane's solution (n = 19).<br>IV fluids stopped at 48 hrs (n = 19). |
| Outcomes | Deaths reported.<br>Fluid and electrolytes given, weight, haematocrit. |
| Notes | Follow up to 5 days. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | Inadequate. |

**Brunkhorst 2008**

| | |
|---|---|
| Methods | Multicenter, randomised control study. Blinding not mentioned. Use of a two-by-two factorial, open label study design |
| Participants | Critically ill patients with severe sepsis or septic shock of at least 18 years of age. Excluded if onset of symptoms commenced more than 24 hours before admission to the ICU, if the symptoms commenced more than 12 hours after onset in the ICU or if patient had received more than 1000 ml of HES in the 24 hours before randomisation |

**Brunkhorst 2008** (*Continued*)

| | |
|---|---|
| Interventions | 1. 10% Pentastarch/HES (200/0.5) (n = 262)<br>2. Modified Ringer's Lactate (n = 275) |
| Outcomes | Deaths reported at 28 and 90 days. 90 day mortality rate was cited as it marked the end of the follow-up period |
| Notes | |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Chavez-Negrete 1991**

| | |
|---|---|
| Methods | Randomised controlled trial (allocation by "random numbers").<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Adults admitted to an emergency room with acute gastrointestinal haemorrhage, systolic blood pressure 90 mmHg or less for up to 1 hr and normal electrocardiograph.<br>Excluded if pregnant or had renal, cardiac or neurological disease |
| Interventions | 1. Initial infusion of 250ml 7.5% saline/6% Dextran 60 given IV (16 patients) or intraosseous (n = 10).<br>2. Initial IV infusion of 250ml Ringer's lactate (n = 23).<br>Resuscitation continued with red cells, 0.9% saline and Dextran 40 according to clinical judgement |
| Outcomes | Death.<br>Haemodynamic variables. |
| Notes | Follow up to 24 hours. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear. |

**Cifra 2003**

| | |
|---|---|
| Methods | Quasi-randomised controlled trial (allocation by alternation).<br>Allocation concealment not reported.<br>Blinding not reported.<br>No loss to follow up. |
| Participants | 27 children with dengue shock syndrome.<br>Exclusion criteria included: Other severe infection, protein-deficient abnormalities, bleeding diathesis, patients who have been given multiple plasma substitutes |
| Interventions | 1. 6% Haes-Steril (n = 11).<br>2. Ringer's Lactate (n = 16).<br>One patient from group 1 and three from group 2 were excluded because they needed inotropic support and multiple plasma substitute |
| Outcomes | Duration of control of shock.<br>Recurrence of shock.<br>Length of ICU stay.<br>Death not reported as an outcome but they reported that 4 patients died |
| Notes | Length of follow up not reported but all outcomes were in-hospital |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Not used |

**Dawidson 1991**

| | |
|---|---|
| Methods | Randomised controlled trial (allocation by drawing a card from a deck).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Adults undergoing elective abdominal aortic surgery.<br>No exclusions mentioned. |
| Interventions | 1. 3% Dextran 70 in Ringer's lactate (n = 10).<br>2. IV Ringer's lactate (n = 10).<br>Fluid used during and for 24 hrs after operation, guided by haemodynamic variables |
| Outcomes | Death.<br>Volume transfused, weight change, haemodynamic variables. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|

**Dawidson 1991** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment? | No | Inadequate |

**Dehne 2001**

| | |
|---|---|
| Methods | Randomised controlled trial; allocation by sealed envelope assignment |
| Participants | 60 male patients (of American Society of Anesthesiologists physical status 1 or 2) scheduled for middle ear surgery |
| Interventions | 1. Lactated Ringer's solution (n = 15).<br>2. 6% HES: molecular weight 200kD, degree of substitution 0.5 (n = 15).<br>3. 6% HES: molecular weight 200kD, degree of substitution 0.60-0.66 (n = 15).<br>4. 6% HES: molecular weight 450kD, degree of substitution 0.7 (n = 15). |
| Outcomes | Deaths not stated but 'all' patients discharged 10-14 days after surgery; therefore no deaths.<br>Central venous pressure.<br>Urine output.<br>Blood osmolality.<br>Urine osmolality. |
| Notes | Follow up two days. |

***Risk of bias***

| **Item** | **Authors' judgement** | **Description** |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Eleftheriadis 1995**

| | |
|---|---|
| Methods | Patients "randomizedly distributed".<br>Blinding not mentioned.<br>Unable to assess loss to follow up. |
| Participants | Participants were undergoing coronary artery bypass surgery. |
| Interventions | 1. 6% hydroxyethyl starch.<br>2. 3.5% gelatin.<br>3. Ringer's lactate.<br>Allocated fluid was used in the post-operative period only guided by mean arterial pressure |
| Outcomes | Deaths were not reported.<br>Haemodynamic variables. |
| Notes | Follow up period unspecified. |

**Eleftheriadis 1995** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Ernest 1999**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment not described.<br>No blinding.<br>No loss to follow up mentioned. |
| Participants | Patients with a clinical diagnosis of sepsis. |
| Interventions | 1. 5% albumin (n = 9).<br>2. 0.9% saline (n = 9).<br>Volume of infusion guided by PAWP. |
| Outcomes | Haemodynamic variables and volume measurements.<br>Deaths not reported. |
| Notes | Follow up to immediately after infusion. |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Evans 1996**

| | |
|---|---|
| Methods | Quasi-randomised trial (allocation by day of the week).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Aged 16 or more, admitted with trauma to an emergency centre within 2 hours after injury, only crystalloid as a pre-hospital infusion.<br>Excluded if had underlying illness likely to affect clotting |
| Interventions | 1. IV haemaccel (n = 11).<br>2. IV Ringer's lactate (n = 14).<br>Fluid was used until vital signs were stable. |
| Outcomes | Deaths from author.<br>Clotting variables. |

**Evans 1996** (*Continued*)

| | |
|---|---|
| Notes | Follow up period unspecified. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | Inadequate |

**Evans 2003**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment not reported.<br>Blinding methods not reported.<br>Loss to follow up not reported. |
| Participants | 55 patients undergoing primary unilateral total hip replacement.<br>Exclusion criteria were pre-existing defect in platelet function or on aspirin that could not be stopped for 2 weeks prior to the operation |
| Interventions | 1. 4.5% Albumin (n = 13).<br>2. Gelofusine (n = 14).<br>3. Haemaccel (n = 14).<br>4. 0.9% Saline (n = 14). |
| Outcomes | Haemostatic parameters.<br>Death not reported. |
| Notes | Length of follow up not reported but all outcomes were in-hospital |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Fries 2004**

| | |
|---|---|
| Methods | Randomised controlled trial. (Patients "randomly" received crystalloid or colloids.)<br>Method of allocation concealment not reported.<br>Blinding not reported.<br>Loss to follow up not reported. |
| Participants | 60 patients undergoing knee replacement surgery.<br>Exclusion criteria were contraindication for regional anaesthesia, known allergies or haemostatic disorders |

**Fries 2004** (*Continued*)

| | |
|---|---|
| Interventions | 1. HES (n = 20).<br>2. Modified gelatin (n = 20).<br>3. Ringer's solution (n = 20).<br>Groups 1 and 2 also received a basis of Ringer's solution infusion |
| Outcomes | Coagulation parameters.<br>Death not reported. |
| Notes | Length of follow up not reported but all outcomes were in-hospital measures |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Gallagher 1985**

| | |
|---|---|
| Methods | Randomised controlled trial. Method of allocation concealment not described. Author contacted - allocation concealment by computerised system - patient details were entered before treatment assignment was revealed.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Patients after coronary artery bypass graft surgery.<br>Exclusions: patients with significant left main coronary artery stenosis, poor left ventricular function or poor pulmonary function |
| Interventions | 1. IV 5% albumin (n = 5).<br>2. IV 6% hydroxyethyl starch (n = 5).<br>3. IV Ringer's lactate (n = 5).<br>Fluid used from admission to intensive care post op, guided by PAWP. RBC given if needed.<br>Five patients received 5% albumin. Five patients received lactated Ringer's |
| Outcomes | Deaths were not reported. Author contacted and confirmed that there were no deaths in any group.<br>Haemodynamic data. |
| Notes | Follow up to 1 day. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Goodwin 1983**

| | |
|---|---|
| Methods | Randomised controlled trial - assigned by "random numbers table".<br>Method of allocation concealment unclear.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 79 previously healthy young adults admitted with burns.<br>No exclusion criteria reported. |
| Interventions | 1. 2.5% albumin in Ringer's lactate (n = 40).<br>2. Ringer's lactate (n = 39).<br>Fluids on day 1 guided by haemodynamic variable. On day 2, given at 0.3-0.5ml/kg/%burn, then 5% dextrose |
| Outcomes | Deaths reported.<br>Lung water in some.<br>Infections. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Grundmann 1982**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Method of allocation concealment unclear.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 20 people undergoing partial gastrectomy.<br>The average age was 50 years (range 19-84).<br>No exclusion criteria reported. |
| Interventions | 1. Colloid group received human albumin solution (n = 14).<br>2. Details of crystalloid were not reported (n = 6).<br>Allocated fluid was continued for 4 days after operation. |
| Outcomes | Deaths reported.<br>Volumes of fluid given.<br>Haemodynamic variables. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

**Grundmann 1982** (*Continued*)

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Guo 2003**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment not reported.<br>Blinding not reported.<br>No loss to follow up reported. |
| Participants | 42 patients undergoing elective cytoreductive surgery for ovarian cancer.<br>Exclusion criteria included: preoperative anaemia, allergic response to HES or perioperative administration of cardiovascular agents.<br>2 patients randomised but excluded because of use of cardiovascular agents |
| Interventions | 1. Ringer's Lactate (n = 20).<br>2. 6% HES (n = 20). |
| Outcomes | Splanchnic perfusion.<br>Death not reported but in results authors mentioned that "all patients were discharged." |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Hall 1978**

| | |
|---|---|
| Methods | Quasi-randomised controlled trial (participants were stratified by age, extent of burn and aetiology, and then allocated by alternation).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Burns covering more than 10% of the body surface (for children), and more than 15% of the body surface (for adults).<br>No exclusions mentioned. |
| Interventions | 1. 120ml/%burn IV 6% Dextran 70 in 0.9% saline over 48 hrs plus oral water or IV 5% dextrose for 'metabolic requirements' (n = 86).<br>2. 4ml/kg/%burn IV Ringer's lactate over 24 hrs, then 10% of initial body weight of fluid over 24 hrs plus oral water (n = 86). |

**Hall 1978** (*Continued*)

| | | |
|---|---|---|
| Outcomes | Death.<br>Fluid given, haemodynamic variables. | |
| Notes | Follow up to discharge from hospital. | |
| ***Risk of bias*** | | |
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | No | Inadequate |

**Hartmann 1993**

| | | |
|---|---|---|
| Methods | Randomised controlled trial (method of allocation unclear).<br>Blinding not mentioned.<br>No loss to follow up. | |
| Participants | Adults undergoing major abdominal surgery.<br>Exclusions: cardiorespiratory dysfunction, uraemia, diabetes, taking steroids, anticoagulants or diuretics | |
| Interventions | 1. IV Dextran 70 in saline (concentration not given) with 2.5% dextrose (n = 15).<br>2. IV saline (concentration not given) with 2.5% dextrose (n = 14).<br>Both groups given red cells, plasma, Dextran 70 and crystalloids during the operation as decided by the clinician. Post-operative fluids according to the trial group guided by tissue oxygen tension to the end of resuscitation | |
| Outcomes | Death not reported.<br>Fluid given, haemodynamic variables. | |
| Notes | Follow up to 7 days. | |
| ***Risk of bias*** | | |
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Jelenko 1978**

| | | |
|---|---|---|
| Methods | Randomised controlled trial, method of allocation concealment unclear.<br>Blinding not mentioned.<br>No loss to follow up. | |
| Participants | 19 people with burns covering more than 20% of body surface. | |

**Jelenko 1978** (*Continued*)

| | |
|---|---|
| Interventions | 1. 12.5% albumin in hypertonic saline (240MeQ Na+, 120 MeQ chloride, 120 MeQ lactate), (n = 7).<br>2. Hypertonic saline (240MeQ Na+, 120 MeQ chloride, 120 MeQ lactate). (n = 5).<br>3. Ringer's lactate (n = 7).<br>Allocated fluid was used, guided by haemodynamic variables, to the end of resuscitation |
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Follow up to end of resuscitation. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Karanko 1987**

| | |
|---|---|
| Methods | Randomised controlled trial. Description of allocation procedure unclear.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 32 adult men scheduled for coronary artery bypass surgery.<br>Exclusions: left ventricular ejection fraction under 40%, abnormal lung function |
| Interventions | 1. Colloid group received 6% dextran 70 (n = 14).<br>2. Ringer's lactate (n = 18).<br>Allocated fluid was used to the end of resuscitation. |
| Outcomes | Deaths reported.<br>Haemodynamic variables.<br>Lung water. |
| Notes | Follow up 2 weeks. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Lang 2001**

| | |
|---|---|
| Methods | Randomised controlled trial, using a closed-envelope system. |
| Participants | 42 patients scheduled for elective major abdominal surgery. |
| Interventions | 1. Lactated Ringer's (n = 21).<br>2. 6% HES, molecular weight 139kD, degree of substitution 0.4 (n = 21). |
| Outcomes | Deaths.<br>Haemodynamics and laboratory data.<br>Tissue oxygenation.<br>Volume input and output. |
| Notes | Follow up period unclear. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Lang 2003**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment not clearly reported ("Closed envelope system").<br>Blinding method not reported ("...treatment in the ICU was performed by physicians who were blinded to the study") |
| Participants | 36 patients undergoing elective major abdominal surgery.<br>Exclusion criteria included:myocardial failure, renal insufficiency, severe pulmonary disease, liver dysfunction, diabetes mellitus, steroid therapy, pre-existing viral or bacterial infection and known allergic reactions to starch preparations |
| Interventions | 1. 6% HES (n = 18).<br>2. Ringer's Lactate (n = 18).<br>Additional crystalloid solutions were supplied to equalize insensible fluid loss or as a solvent for drugs in group 1 |
| Outcomes | Pro- and anti-inflammatory cytokines.<br>All patients survived. |
| Notes | Length of follow up not reported but all outcomes were in-hospital measures |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Ley 1990**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Method of allocation concealment unclear.<br>Assessment of chest x-ray blinded.<br>No loss to follow up. |
| Participants | 21 people undergoing coronary artery bypass grafting or valve surgery |
| Interventions | 1. 6% hetastarch up to 1.5L then 5% plasma protein fraction (n = 11).<br>2. 0.9% saline (n = 10).<br>Allocated fluid was used for post-operative fluid resuscitation |
| Outcomes | Deaths were not reported.<br>Pulmonary and peripheral oedema.<br>Haemodynamic variables. |
| Notes | Follow up to discharge. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Lowe 1977**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation by sealed envelopes.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants with serious trauma. |
| Interventions | 1. 25% albumin in Ringer's lactate (n = 77).<br>2. Ringer's lactate (n = 94).<br>Allocated fluid was used throughout the pre- and intra-operative period |
| Outcomes | Deaths reported. |
| Notes | Follow up to 5 days post-operatively. Data on the 30 participants with chest injuries who were left out of the Lowe 1977 report, but included in Moss 1981, have been included in the meta-analysis |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Lucas 1978**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Randomisation was based on the last digit of each patient's case number |
| Participants | 52 seriously injured patients. |
| Interventions | 1. Standard resuscitation regimen ('balanced electrolyte', blood, fresh frozen plasma) plus salt poor albumin, maximum 150g during surgery and 150g per day for the next 5 days (n = 27).<br>2. Standard resuscitation regimen as above (n = 25). |
| Outcomes | Deaths reported in some patients. |
| Notes | In the final report of 94 randomised patients deaths were not reported. However, in this preliminary report of 52 injured patients deaths were reported |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | Inadequate |

**Maitland 2005**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Open label.<br>Random allocation was assigned by the use of sealed cards.<br>No loss to follow up. |
| Participants | 159 children with severe malaria and metabolic acidosis.<br>Exclusion criteria included pulmonary oedema, oedematous malnutrition or papilledema |
| Interventions | Severe acidosis<br>1. 4.5% Albumin (n = 23).<br>2. 0.9% Saline (n = 26).<br>Moderate acidosis<br>1. 4.5% Albumin (n = 33).<br>2. 0.9% Saline (n = 35).<br>3. Control (n = 33). |
| Outcomes | Reduction in base deficit.<br>Neurological sequelae.<br>Death reported. |
| Notes | Length of follow up not reported but all outcomes were in-hospital measures |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|

| | | |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Mattox 1991**

| | |
|---|---|
| Methods | Quasi-randomised, allocation by alternation.<br>Double-blind.<br>2 patients excluded from the analysis as code of fluid lost. |
| Participants | Participants were pre-hospital trauma victims attended to by emergency personnel within an hour of injury, who had systolic blood pressure of 90 mmHg or less and were 16 years or older. 72% of participants had sustained penetrating trauma |
| Interventions | 1. 250 mL Dextran-70 in 7.5% NaCl (n = 211).<br>2. 250 mL Ringer's lactate, saline or plasmalyte (n = 211).<br>Allocated fluid was for initial pre-hospital resuscitation only |
| Outcomes | Deaths reported. |
| Notes | Follow up to hospital discharge or transfer. |

***Risk of bias***

| **Item** | **Authors' judgement** | **Description** |
|---|---|---|
| Allocation concealment? | No | Inadequate |

**Mazher 1998**

| | |
|---|---|
| Methods | Patients 'randomized'.<br>Blinding of care givers by use of pharmacy prepared solutions.<br>No loss to follow up. |
| Participants | Patients undergoing elective coronary artery surgery.<br>Exclusions: age over 75, ejection fraction under 35%, creatinine over 135umol/L, ACE inhibitors |
| Interventions | 1. 5mL/kg polygeline (n = 10).<br>2. 5mL/kg 7.2% saline (n = 10).<br>Allocated fluid given post-op over one hour. All patients subsequently receive polygeline and red blood cells |
| Outcomes | Haemodynamic variables.<br>Death. |
| Notes | Follow up to discharge from intensive care. |

***Risk of bias***

**Mazher 1998** (*Continued*)

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**McNulty 1993**

| | |
|---|---|
| Methods | Randomised controlled trial. Method of allocation concealment not described.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Patients following elective cardiopulmonary bypass. |
| Interventions | 1. 5% albumin and cell-saved blood (n = 14).<br>2. Plasmalyte and cell-saved blood (n = 14).<br>Allocated fluid used as part of fluid volume replacement. |
| Outcomes | Deaths not reported.<br>Study was designed to look at the effect of protein infusion on the accuracy of a haematocrit measuring device |
| Notes | Length of follow up unspecified. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Metildi 1984**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were admissions to an intensive care and a trauma unit with adult respiratory distress syndrome and established pulmonary failure. Included both trauma and non-trauma patients |
| Interventions | 1. 5% salt-poor albumin (n = 20).<br>2. Ringer's lactate (n = 26).<br>Allocated fluid was used throughout resuscitation, and if an operation was required the allocated fluid was used for volume replacement before and during the operation |
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Follow up to discharge. |

**Metildi 1984** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Modig 1983**

| | |
|---|---|
| Methods | Quasi-randomised controlled trial, allocation by admission date.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were trauma admissions to an emergency department with a systolic blood pressure of less than 70mmHg. Age range was 20-58 years |
| Interventions | 1. Dextran-70 in Ringer's lactate (n = 12).<br>2. Ringer's lactate (n = 11).<br>Allocated fluids were given as the initial resuscitation fluid on admission to the emergency department, and continued as needed until after the 6th day when major reconstructive surgery was undertaken |
| Outcomes | Deaths reported.<br>Development of respiratory distress syndrome. |
| Notes | Follow up to definitive reconstructive surgery. |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | No | Inadequate |

**Moretti 2003**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment method not clearly reported ("Patients randomized...by using a closed-envelope technique").<br>Blinding method not clearly reported ("Researchers were unaware of the patient's randomization").<br>No loss to follow up. |
| Participants | 90 adult patients undergoing major elective general, gynaecological, orthopedic or urologic surgery with an anticipated blood loss > 500 ml.<br>Exclusion criteria included age < 16 years, coagulopathy, renal or hepatic dysfunction and congestive heart failure |
| Interventions | 1. Hetastarch-Normal Saline (n = 30).<br>2. Hetastarch-Balanced Salt (n = 30).<br>3. Ringer's Lactate (n = 30). |

| | |
|---|---|
| Outcomes | Postoperative nausea and vomiting.<br>Death not reported. |
| Notes | Follow up to discharge. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Nagy 1993**

| | |
|---|---|
| Methods | Randomised controlled trial, contact with author showed it was an open label study.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were adult admissions to a trauma unit, with measurable systolic blood pressure less than 90 mmHg |
| Interventions | 1. Pentastarch in 0.9% NaCl (n = 21).<br>2. Ringer's lactate (n = 20).<br>Allocated fluid was used throughout resuscitation with the exception that colloid patients received a maximum 4L of pentastarch, after which Ringer's lactate was given |
| Outcomes | Deaths were not reported.<br>Haemodynamic variables. |
| Notes | Follow up to discharge. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | Inadequate |

**Ngo 2001**

| | |
|---|---|
| Methods | Randomised controlled trial, opaque envelopes containing only treatment pack number |
| Participants | 230 children with dengue shock syndrome. |
| Interventions | 1. Dextran 70 (n = 55).<br>2. 3% gelatin (n = 56).<br>3. Lactated Ringer's (n = 55). |

**Ngo 2001** (*Continued*)

| | |
|---|---|
| | 4. 'Normal' saline (n = 56). |
| Outcomes | Initial pulse recovery time.<br>Occurrence of timing and subsequent episodes of shock.<br>Fall in haematocrit.<br>Volume of fluid administered till recovery.<br>Complications.<br>And noted that there were no deaths in any group |
| Notes | Follow up period unclear. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Nielsen 1985**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Method of allocation concealment not described.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 26 patients admitted for reconstructive surgery of the abdominal aorta |
| Interventions | 1. Whole blood, crystalloid plus 80g albumin on the day of the operation, and 20g per day for the next 3 days. Albumin given as 100mL 20% human albumin solution (n = 13).<br>2. Whole blood and crystalloid, type not specified (n = 13). |
| Outcomes | Deaths not reported.<br>Author when contacted confirmed that there were no deaths in either group |
| Notes | Length of follow up 4 days. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Pockaj 1994**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment unclear.<br>Blinding not mentioned.<br>Loss to follow up 18/54 in colloid group, 13/53 in saline group |
| Participants | Participants required fluid resuscitation as a result of vascular leak syndrome associated with Interleukin-2 therapy for metastatic cancer |
| Interventions | 1. 250 mL boluses of 5% albumin in saline (n = 36 reported).<br>2. 250 mL boluses of 0.9% normal saline (n = 40 reported).<br>Boluses guided by haemodynamic variables. Both groups also received 0.45% saline with 10mmol/L KCl |
| Outcomes | Deaths.<br>Toxic effects of chemotherapy.<br>Haemodynamic variables. |
| Notes | |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Prien 1990**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were undergoing modified Whipple's operation. |
| Interventions | 1. 10% hydroxyethyl starch in 0.9% saline plus plasma protein fraction if requirements > 20mL/kg (n = 6).<br>2. 20% human albumin solution (n = 6).<br>3. Ringer's lactate.<br>Allocated fluid was administered intra-operatively only. |
| Outcomes | Deaths.<br>Intestinal oedema formation. |
| Notes | Follow up period was unspecified. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Rackow 1983**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment unclear.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were aged 54 to 97, and had any one of the following pre-determined indicators of shock: systolic blood pressure of 90 mmHg or less, a cardiac index of less than 2.2 L./min.m2, a serum arterial lactate greater than 18mg/dl and WP less than 15mmHg |
| Interventions | 1. 6% hydroxyethyl starch (n = 9).<br>2. 5% albumin (n = 9).<br>3. 0.9% saline (n = 8).<br>Allocated fluid was given as needed until the end of resuscitation |
| Outcomes | Deaths reported.<br>Fluid balance. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Rocha e Silva 1994**

| | |
|---|---|
| Methods | Randomised controlled trial. |
| Participants | Participants were admissions to the emergency room, with a systolic blood pressure of 90 mmHg or less and were 16 years of age or older |
| Interventions | Colloid group received 6% dextran-70 in 7.5% NaCl; crystalloid group received Ringer's lactate. Allocated fluid was used for the first intravenous infusion only |
| Outcomes | Death was the main outcome measure, but the data are unpublished |
| Notes | Follow up to 30 days. By April 1994, 125 patients had been entered into the study |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**SAFE 2004**

| | |
|---|---|
| Methods | Randomised controlled trial. Randomisation by minimisation algorithm accessed through secure website |
| Participants | Patients aged 18 years and above admitted to closed multidisciplinary intensive care units in 16 tertiary hospitals in Australia over 19-month period |
| Interventions | 1. 4% albumin (Albumex, CSL) (n = 3499).<br>2. Normal saline (n = 3501). |
| Outcomes | Death.<br>Patients with new single or multiple-organ failure.<br>Mean number of days: in ICU, in hospital, on mechanical ventilation, on renal replacement therapy |
| Notes | Follow up to 28 days. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Shah 1977**

| | |
|---|---|
| Methods | Randomised controlled trial. Allocation by sealed envelope.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Patients with severe, multiple trauma and a systolic blood pressure of less than 90mmHg. All patients were adults and both sexes were included |
| Interventions | 1. 5% salt-poor albumin in Ringer's lactate (n = 9).<br>2. Ringer's lactate (n = 11).<br>Volume infused guided by physiological parameters. |
| Outcomes | Death reported.<br>Haemodynamic variables. |
| Notes | Length of follow up not stated. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Shires 1983**

| | |
|---|---|
| Methods | Patients 'assigned randomly'.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | People undergoing aortic reconstruction surgery.<br>No exclusion criteria mentioned. |
| Interventions | 1. Plasmanate (n = 9).<br>2. Ringer's lactate (n = 9).<br>Allocated fluid used guided by haemodynamic variables until the first postoperative morning. All patients then received 0.45% saline |
| Outcomes | Lung water.<br>Haemodynamic variables.<br>Death. |
| Notes | Follow up to two days post-op. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Sirieix 1999**

| | |
|---|---|
| Methods | Patients "randomly assigned". Blinding not described.<br>Two patients excluded after randomisation due to arrhythmias on giving the fluid (both in hypertonic saline group) |
| Participants | Patients undergoing mitral valve repair.<br>Exclusions: LVEF < 0.4, systolic PAP > 50mmHg, coagulation disorders, creatinine >150mmoL/L, electrolyte imbalance, diabetes, previous atrial fibrillation lasting > 1 year |
| Interventions | 1. 250mL 7.2% hypertonic saline, 6%HES (n = 8).<br>2. 250mL 7.2% hypertonic saline (n = 10).<br>3. 250mL 6% HES (n = 8).<br>Fluid given over 15mins, 1 hour after admission to post-op intensive care |
| Outcomes | Haemodynamic variables.<br>Deaths reported.<br>Side effects (2 had severe hypotension in group 2 and 1 in group 1; arrhythmias in 1 patient in group 1, 3 in group 2 and 1 in group 3) |
| Notes | Follow up to discharge from hospital (all within 10 days). |

***Risk of bias***

**Sirieix 1999** (*Continued*)

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Skillman 1975**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment unclear.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were undergoing elective abdominal reconstructive surgery |
| Interventions | 1. 25% salt-poor albumin 1g/kg and 5% albumin 1L (n = 7).<br>2. Ringer's lactate.<br>Allocated fluid was given intra-operatively. All patients received crystalloids only for pre-loading before surgery |
| Outcomes | Deaths were not reported. |
| Notes | |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Tollofsrud 1995**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation by sealed envelopes.<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were adult patients in need of volume replacement during and after coronary artery bypass surgery |
| Interventions | 1. Haemaccel (n = 10).<br>2. Dextran 70 (n = 10).<br>3. Albumin 40 (n = 10).<br>4. Ringer's lactate (n = 10).<br>Allocated fluid was used throughout resuscitation. |
| Outcomes | Deaths reported.<br>Fluid balance. |
| Notes | Follow up to 48 hours. |

**Tollofsrud 1995** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Tollofsrud 1998**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation by sealed envelope. Described as double blind, no loss to follow up mentioned |
| Participants | Patients with three vessel coronary artery disease undergoing elective coronary artery surgery. Exclusions: LVEF < 0.4, ventricular aneurysm, significant arrhythmia, diabetes, renal failure, lung disease |
| Interventions | 1. 4mL/kg of 75mg/mL hypertonic saline in dextran 70 60mg/mL over 30 mins (n = 10).<br>2. Same volume and rate of isotonic saline (n = 10).<br>Fluid given just after surgery while still in operating theatre. Ringer's lactate for additional fluid |
| Outcomes | Fluid balance.<br>Haemodynamic variables.<br>Deaths not reported. |
| Notes | Follow up to 48 hours. |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Upadhyay 2004**

| | |
|---|---|
| Methods | Open label randomised trial.<br>Allocation by sealed envelope.<br>No loss to follow up mentioned. |
| Participants | 60 patients with septic shock aged 1 month to 12 years.<br>Exclusion criteria: age less than one month, multiorgan failure and immunodeficiency states |
| Interventions | 1. Normal saline (n = 31).<br>2. Polymer from degraded gelatin in saline (gelatin) (n = 29). |
| Outcomes | Haemodynamic data.<br>Death reported. |
| Notes | Length of follow up not reported but all outcomes were in-hospital measures |

**Upadhyay 2004** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Vassar 1990**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment unclear.<br>Double blind study (solutions prepared in identical containers).<br>No loss to follow up. |
| Participants | Participants were emergency department admissions with trauma and a systolic blood pressure below 80mmHg and were 18 years or older.<br>Pregnant women and people with preexisting cardiac, hepatic or renal disease were excluded |
| Interventions | 1. 6% dextran 70 in 7.5% saline (n = 23).<br>2. Ringer's lactate (n = 24).<br>Allocated fluids were given as the initial resuscitation in the emergency department. Additional isotonic crystalloids (Ringer's lactate) were given as needed |
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Follow up to hospital discharge. |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Vassar 1991**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation by randomised sequence of coded containers.<br>Double blind study.<br>No loss to follow up. |
| Participants | Participants were pre-hospital trauma cases undergoing helicopter transport to an emergency centre, with a systolic blood pressure of 100mmHg or less and were 18 years or older.<br>Exclusions: preexisting cardiac renal, hepatic or neurological disease. Peripheral oedema |
| Interventions | 1. 4.2% dextran 70 in 7.5% saline or 6% dextran 70 in 7.5% saline (n = 83).<br>2. Ringer's lactate (n = 83).<br>Fluids were given as the initial resuscitation fluid in the pre-hospital setting. Supplemental isotonic fluids were given at the discretion of the flight nurses |

**Vassar 1991** (*Continued*)

| | |
|---|---|
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Follow up to discharge. Allocation was to 4.2% dextran-70; to 6% dextran-70; or to crystalloid; for the calculation of the summary effect measure, the two dextran groups are combined |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Vassar 1993a**

| | |
|---|---|
| Methods | Randomised controlled blind trial, allocation concealed by random sequence of identical containers.<br>Double blind study.<br>36 people excluded post randomisation as deemed not to have met eligibility criteria.<br>No loss to follow up. |
| Participants | Participants, who were undergoing ambulance transport to an emergency centre, had systolic blood pressure 90 mmHg or less, and were 18 years or older.<br>Exclusions: asystolic, undergoing CPR, lack sinus complex on ECG, more than 2 hours after trauma, pregnant, preexisting seizures, bleeding disorder, hepatic, cardiac or renal disease |
| Interventions | 1. 6% dextran 70 in 7.5% saline (n = 89).<br>2. 7.5% saline (n = 85).<br>3. 0.9% saline (n = 84).<br>Participants received 250mL of the allocated fluid in the pre-hospital setting. Additional isotonic crystalloids were given as needed |
| Outcomes | Deaths reported.<br>Haemodynamic variables.<br>Trauma scores. |
| Notes | Follow up was to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Vassar 1993b**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealed by sequential use of coded identical containers.<br>Double blind study.<br>39/233 patients excluded as deemed not to meet eligibility criteria, unclear from which groups |
| Participants | Participants were pre-hospital trauma cases undergoing helicopter transport to an emergency centre, had a systolic blood pressure of 100mmHg or less and were 18 years or older.<br>Exclusions: asystolic, undergoing CPR, lack sinus complex on ECG, more than 2 hours after trauma, pregnant, preexisting seizures, bleeding disorder, hepatic, cardiac or renal disease |
| Interventions | 1. 12% dextran 70 in 7.5% saline (n = 49).<br>2. 6% dextran 70 in 7.5% saline (n = 50).<br>3. 7.5% saline (n = 50).<br>4. Ringer's lactate (n = 45).<br>Participants received 250mL of the allocated fluid in the pre-hospital setting. Additional isotonic crystalloids were given as needed |
| Outcomes | Deaths reported.<br>Haemodynamic variables.<br>Trauma scores and neurological outcome scores. |
| Notes | Follow up to hospital discharge. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Verheij 2006**

| | |
|---|---|
| Methods | Randomised controlled trial.<br>Allocation concealment by "the sealed envelope method".<br>Blinding method not reported.<br>No loss to follow up. |
| Participants | 67 patients with presumed hypovolemia after cardiac and major vascular surgery.<br>Exclusion criteria; age > 79 years and known anaphylactoid reaction to colloids |
| Interventions | 1. Saline (n = 16).<br>2. Gelatin (n = 16).<br>3. HES (n = 16).<br>4. Albumin (n = 16). |
| Outcomes | Haemodynamic data.<br>Death not reported. |
| Notes | Length of follow up not reported but all outcomes were in-hospital measures |

**Verheij 2006** (*Continued*)

| ***Risk of bias*** | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Virgilio 1979**

| | |
|---|---|
| Methods | Allocation "by random number".<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Participants were undergoing abdominal aortic surgery. |
| Interventions | 1. 5% albumin (n = 15).<br>2. Ringer's lactate (n = 14).<br>Allocated fluid was used during operation for maintenance of pre-defined physiological parameters, and the resuscitation was continued with the allocated fluid until the day following the operation. This was followed by 5% dextrose in half-normal saline, with potassium chloride as needed |
| Outcomes | Deaths reported. |
| Notes | Follow up two and a half weeks. |

| ***Risk of bias*** | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | Unclear |

**Wahba 1996**

| | |
|---|---|
| Methods | Patients "randomly allocated".<br>Blinding not mentioned.<br>Two patients excluded as they required reoperation for bleeding |
| Participants | 22 adult patients in need of volume replacement following coronary artery bypass surgery.<br>Exclusions: abnormal left ventricular function, platelet active medication or heparin |
| Interventions | 1. Haemaccel (n = 10).<br>2. Ringer's lactate (n = 10).<br>Allocated fluid was used from the time of admission to intensive care following operation, to the end of resuscitation |
| Outcomes | Deaths reported.<br>Pulmonary oedema. |

**Wahba 1996** (*Continued*)

| | |
|---|---|
| Notes | Follow up to discharge. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Wills 2005**

| | |
|---|---|
| Methods | Randomised controlled study.<br>Allocation concealed by specially prepared cardboard containers.<br>Method of blinding not mentioned.<br>No loss to follow up. |
| Participants | 512 children with Dengue shock syndrome aged 2 to 15 years. |
| Interventions | Children with immoderately severe shock were randomised to the three interventions:<br>1. Ringer's lactate (n = 128).<br>2. 6 percent dextran 70 (n = 126).<br>3. 6 percent hydroxyethyl starch 200/0.5 (n = 129).<br>Children with severe shock were randomized only to either of the two colloids interventions:<br>1. 6 percent dextran 70 (n = 67).<br>2. 6 percent hydroxyethyl starch 200/0.5 (n = 62). |
| Outcomes | Requirement for supplemental intervention with rescue colloid.<br>Time taken to achieve initial cardiovascular stability.<br>Time taken to achieve sustained cardiovascular stability.<br>Volume required.<br>Change in the Hematocrit.<br>Days in hospital.<br>One death reported but not specified in which group. |
| Notes | Length of follow up not clear. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | Adequate |

**Woittiez 1997**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation concealment by sealed opaque envelopes.<br>No information on blinding or loss to follow up. |
| Participants | 60 patients who had developed hypoalbuminaemia (< 20g/l) after major surgery.<br>2 patients died after randomisation and before treatment started. They were excluded from the analysis |
| Interventions | 1. saline (500ml/24 hr) (n = 16).<br>2. albumin 20% (300 ml/24h) (n = 15).<br>3. HES 10% (500ml/24h) for 3 days (n = 27).<br>Aim was to restore colloid osmotic pressure. |
| Outcomes | Changes in fluid balance, serum albumin, COP and clinical signs of oedema were followed daily.<br>Death rates supplied by the author. |
| Notes | Length of follow up unspecified. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Wu 2001**

| | |
|---|---|
| Methods | Randomised controlled trial. No details given of randomisation method |
| Participants | 41 adolescent or adult patients in emergency room suffering from shock |
| Interventions | 1. 4% modified fluid gelatin: succinated gelatin 40g/L, sodium chloride 7g/L, sodium hydroxide 1. 36g/L (n = 18).<br>2. Lactated Ringer's (n = 16). |
| Outcomes | Death.<br>Haemodynamic variables. |
| Notes | Not intention-to-treat: five patients who received blood transfusion and two who had surgery within the first hour of resuscitation were dropped from the analysis.<br>Length of follow up not clear. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Younes 1992**

| | |
|---|---|
| Methods | Randomised "in a double blind fashion".<br>Blinding by use of similar bottles.<br>No loss to follow up. |
| Participants | Participants were emergency department admissions, who had a systolic blood pressure of less than 80mmHg and were 19 years and older.<br>Exclusions: pregnant, preexisting cardiac or metabolic disease |
| Interventions | 1. 6% dextran 70 in 7.5% saline (n = 35).<br>2. 7.5% saline (n = 35).<br>3. 0.9% saline (n = 35).<br>Allocated fluid was for initial bolus of 250mL, followed by isotonic crystalloids as needed |
| Outcomes | Deaths reported.<br>Fluid balance. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Younes 1994**

| | |
|---|---|
| Methods | Trial conducted in a "double blind randomised fashion".<br>Blinding by use of coded, identical containers. |
| Participants | Participants were trauma admissions to the emergency room requiring treatment for haemorrhagic hypovolaemia; all were over 15 years old.<br>Exclusions: pregnant, cardiac or renal failure, cardiac arrest on arrival |
| Interventions | 1. 6% dextran 70 in 7.5% saline (n = 101).<br>2. 0.9% saline (n = 111).<br>Allocated fluid was for the first intravenous infusion only. |
| Outcomes | Deaths reported.<br>Complications. |
| Notes | Follow up period was 30 days. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Younes 1998**

| | |
|---|---|
| Methods | Randomised controlled trial, allocation by sealed envelope. Blinding not mentioned, no apparent loss to follow up |
| Participants | Trauma patients with systolic blood pressure <90mmHg admitted to the emergency room, with no previous treatment |
| Interventions | 1. 10% pentastarch (n = 12).<br>2. 0.9% saline (n = 11).<br>Fluid given in 250mL boluses until systolic blood pressure > 100mmHg |
| Outcomes | Deaths reported.<br>No complications reported in either group. |
| Notes | Follow up to 24 hours. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Zetterstrom 1981a**

| | |
|---|---|
| Methods | The patients were randomly divided into two groups.<br>Allocation concealment was by sealed opaque envelopes (information supplied by author).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | Adult patients undergoing elective major abdominal surgery. |
| Interventions | 1. Standard volume replacement regimen (1L Dextran 70 then up to 4 units of RBC with electrolyte, then whole blood or RBC with plasma; post-op patients were given crystalloids and whole blood) plus 20% human albumin solution 100ml at end of operation, 200-300ml on same day, then 200ml on first post-op day, then 100ml for next 3 days (n = 15).<br>2. Standard volume replacement regimen as above (n = 15). |
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Length of follow up unspecified. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

**Zetterstrom 1981b**

| | |
|---|---|
| Methods | The patients were randomly divided into two groups.<br>Allocation concealment was by sealed opaque envelopes (information supplied by author).<br>Blinding not mentioned.<br>No loss to follow up. |
| Participants | 18 patients who had undergone elective abdominal aortic surgery.<br>No exclusions mentioned. |
| Interventions | 1. 5% human albumin solution (n = 9).<br>2. Ringer's lactate solution (n = 9).<br>Administration guided by pulmonary arterial occlusion pressure |
| Outcomes | Deaths reported.<br>Haemodynamic variables. |
| Notes | Follow up to discharge from hospital. |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | Unclear |

COP = colloid osmotic pressure
HES = hydroxyethylstarch
LVEDP = left ventricular end diastolic pressure
LVEF = left ventricular ejection fraction
PAP = pulmonary artery pressure
PAWP = pulmonary artery wedge pressure
RBC = red blood cells
WP = wedge pressure

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Artru 1989 | Intervention to control intracranial pressure not directed at fluid resuscitation |
| Bocanegra 1966 | This study contained two quasi-randomised comparisons of colloid with glucose and plasma/saline with saline. In both studies, the control solution was only given IV if the patient was in coma or shock. It was therefore not a reasonable comparison of colloid and crystalloid |
| Boldt 1996 | All groups received some colloid. |

(*Continued*)

| | |
|---|---|
| Boldt 2007 | Comparison was not between colloids and crystalloids, rather two different colloid solutions |
| Bothner 1998 | Participants were having minor elective surgery, therefore not considered to be critically ill |
| Breheme 1993 | Intervention directed at haemodilution, not at volume replacement |
| Bueno R 2004 | The participants had elective surgery. |
| Chin 2006 | Participants were undergoing elective surgery, therefore not considered to be critically ill |
| Golub 1994 | Albumin given solely as a nutritional supplement. |
| Goslinga 1992 | Intervention directed at haemodilution, not volume replacement |
| Green 2008 | Article is a review. |
| Greenhalgh 1995 | Intervention directed at the maintenance of serum albumin levels, not for volume replacement |
| Hauser 1980 | Cross-over trial. |
| Ko 2007 | Comparison of crystalloids and colloids as preloading solutions |
| Krasheninnikov 2007 | Not a randomised controlled trial. |
| Lagonidis 1995 | Intervention was pre-loading for coronary artery bypass surgery |
| Lobo 2008 | Experiment conducted on rabbits. |
| Marhofer 1999 | Trial of fluid for preloading before spinal anaesthesia. |
| Mittermayr 2007 | Patients were undergoing elective surgery. |
| Mittermayr 2008 | Outcome was the change in concentration of tissue-type plasminogen activator |
| Niemi 2008 | Solutions were used for pump priming. |
| Nilsson 1980 | Albumin given as a nutritional supplement. |
| Oliviera 2002 | The participants had sepsis. |
| Paton-Gay 2007 | The outcome was non-relevant to comparing crystalloids and colloids |
| Paul 2003 | The participants had elective surgery. |
| Rehm 2001 | Two colloids (albumin and hetastarch) compared. |
| Steinberg 1989 | Cross-over trial. |

(*Continued*)

| | |
|---|---|
| Tiryakioglu 2008 | Patients were undergoing elective surgery and not considered critically ill. Also, the solutions were used as priming solutions |
| Tseng 2008 | Crystalloid and colloid treatment was not randomised. |
| Valetova 2007 | Patients were randomised depending upon their treatment not prior to treatment |
| Vercueil 2006 | Article is a review. |
| Wilkes 2001 | One group received saline plus hetastarch; the other received 'balanced' fluid plus hetastarch. Thus, each group received both a colloid and a crystalloid. This conflicts with the purpose our review which compares patients who had one of these with patients who had the other |
| Woods 1993 | This quasi-randomised trial looked at albumin supplementation in post operative patients, with the aim of maintaining the serum albumin. Since the main aim of giving albumin was not to replace volume, the study was excluded |