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

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Colloids versus crystalloids for fluid resuscitation in critically ill patients

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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 (searched 16 March 2012), the Cochrane Central Register of Controlled Trials 2011, issue 3 (The Cochrane Library), MEDLINE (Ovid) 1946 to March 2012, EMBASE (Ovid) 1980 to March 2012, ISI Web of Science: Science Citation Index Expanded (1970 to March 2012), ISI Web of Science: Conference Proceedings Citation Index-Science (1990 to March 2012), PubMed (searched 16 March 2012), www.clinicaltrials.gov and www.controlled-trials.com. We also searched the bibliographies of relevant studies and review articles.

Selection criteria

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

Data collection and analysis

Two review 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 74 eligible trials; 66 of these presented mortality data.

Colloids compared to crystalloids

Albumin or plasma protein fraction - 24 trials reported data on mortality, including a total of 9920 patients. The pooled risk ratio (RR) from these trials was 1.01 (95% confidence interval (CI) 0.93 to 1.10). When we excluded the trial with poor-quality
allocation concealment, pooled RR was 1.00 (95% CI 0.92 to 1.09). **Hydroxyethyl starch** - 21 trials compared hydroxyethyl starch with crystalloids and included 1385 patients. The pooled RR was 1.10 (95% CI 0.91 to 1.32). **Modified gelatin** - 11 trials compared modified gelatin with crystalloid and included 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 and included 834 patients. The pooled RR was 1.24 (95% CI 0.94 to 1.65).

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

Nine trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1985 randomised participants. Pooled RR was 0.91 (95% CI 0.71 to 1.06).

**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. This 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 some 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. However, a 1995 survey of US academic health centres 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 and pregnant women) who required volume replacement. We included patients who were critically ill as a result of trauma, burns, undergoing surgery, or had other critical conditions such as complications of sepsis. We excluded preoperative 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

We did not restrict the search for trials by date, language or publication status.

Electronic searches

We searched the following electronic databases:
- Cochrane Injuries Group Specialised Register (searched 16 March 2012);
- the Cochrane Central Register of Controlled Trials 2011, issue 3 (The Cochrane Library);
- MEDLINE (Ovid) 1946 to March, Week 1, 2012;
- EMBASE (Ovid) 1980 to March 2012;
- ISI Web of Science: Science Citation Index Expanded (1970 to March 2012);
- ISI Web of Science: Conference Proceedings Citation Index-Science (1990 to March 2012);
- PubMed (searched 16 March 2012);

All search strategies are listed in full in Appendix 1.

Searching other resources

We searched the reference lists of all relevant papers and published review articles. We also contacted known trialists to identify any further studies that we may have missed. We searched the online trials registers www.clinicaltrials.gov and www.controlledtrials.com for published and unpublished studies.

Data collection and analysis

The Injuries Group Trials Search Coordinator ran the electronic database searches, collated the results and removed duplicates before passing the list of citations to the lead review author (PP) for screening.

Selection of studies

Two review authors independently examined the list of citations for eligibility. We obtained full-text copies 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 2011, assigning 'high risk of bias' to poorest quality and 'low risk of bias' to best quality (the presence of solutions in identical containers was only taken to mean adequate concealment if the fluid containers were used sequentially).
• Low risk of bias = trials deemed to have taken adequate measures to conceal allocation (i.e. 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.
• High risk of bias = 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 risk ratios (RRs) and 95% confidence intervals (CI) for each study using a fixed-effect model. We then inspected each comparison visually for evidence of heterogeneity and performed a Chi² 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 Professor 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 that 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.

Effects of interventions

Colloids compared to crystalloids

Albumin or plasma protein fraction
Twenty-four trials reported data on mortality, including a total of 9920 patients. The pooled RR was 1.01 (95% CI 0.93 to 1.10). When trials by Boldt were removed, the results were unchanged (RR 1.01; 95% CI 0.93 to 1.10). When we excluded the trial with poor-quality allocation concealment (Lucas 1978), pooled RR was 1.00 (95% CI 0.92 to 1.09).

Hydroxyethyl starch
Twenty-one trials compared hydroxyethyl starch with crystalloids, including a total of 1385 randomised patients. The pooled RR was 1.10 (95% CI 0.91 to 1.32). 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.

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.

Results

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.
We identified 74 trials meeting the inclusion criteria for study design, participants and interventions. We were able to obtain mortality data for 66 of these. We have reported details of the included trials in the 'Characteristics of included studies' table.
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). One trial compared 6% hydroxyethyl starch 130/0.4 and hypertonic saline with Ringer’s lactate. The RR of death was 0.25 (95% CI 0.03 to 2.15).

Nine trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1879 randomised patients. The pooled RR was 0.91 (95% CI 0.79 to 1.06).

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 (95% CI 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

When all trials authored by Professor Boldt (Boldt 1986; Boldt 1993; Boldt 2001; Lang 2001; Lang 2003) were excluded conclusions remain unchanged.

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 RRs 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 (Saline versus Albumin Fluid Evaluation) 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 (I² = 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. Col-
loids, 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.

A U T H O R S’ C O N C L U S I O N S

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.

A C K N O W L E D G E M E N T S
We acknowledge the contribution of Phil Alderson, Frances Bunn, Paul Chinnock, Gillian Schierhout and Mia Pearson who were authors of earlier versions of this review.

We would like to acknowledge the Intensive Care National Audit and Research Network in London (UK), for assistance with identification of trials for this review.

We thank Dr. Frank M. Brunkhorst for providing the Supplementary Appendix to the paper Brunkhorst 2008.

R E F E R E N C E S

References to studies included in this review

Boldt 1986 {published data only}

Boldt 1993 {published data only}

Boldt 2001 {published data only}

Boutros 1979 {published data only}

Bowser-Wallace 1986 {published data only}

Brunkhorst 2008 {published and unpublished data}

Bulger 2011 {published data only}

Chavez-Negrete 1991 {published data only}

Cifra 2003 {published data only}

Cooper 2006 {published data only}
Cooper AB, Cohn SM, Zhang HS, Hanna K, Stewart TE, Slutsky AS. Five percent albumin for adult burn shock resuscitation: lack of effect on daily multiple organ dysfunction score. Transfusion 2006; Vol. 46, issue 1:80–9.
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Dawidson 1991 [published data only]

Dehne 2001 [published data only]

Du 2011 [published data only]

Dubin 2010 [published data only]

Ernest 1999 [published data only]

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Evans 2003 [published data only]

Fries 2004 [published data only]

Gallagher 1985 [published data only]

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James MF, Michell WL, Joubert IA, Nicol AJ, Navsaria PH, Gillespie RS. Resuscitation with hydroxyethyl starch improves renal function and lactate clearance in penetrating trauma in a randomized controlled study: the FIRST trial (Fluids in Resuscitation of Severe Trauma). British Journal of Anaesthesia 2011; Vol. 107, issue 5:693–702.

Jelenko 1978 [published data only]

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**Karanko 1987** *(published data only)*  

**Lang 2001** *(published data only)*  

**Lang 2003** *(published data only)*  

**Ley 1990** *(published data only)*  

**Lowe 1977** *(published data only)*  

**Lowe 1979** *(published data only)*  


**Lu 2012** *(published data only)*  

**Lucas 1978** *(published data only)*  


**Maitland 2005** *(published data only)*  

**Maitland 2011** *(published data only)*  

**Mattos 1991** *(published data only)*  


**Mazher 1998** *(published data only)*  

**McIntyre 2008** *(published data only)*  

**McNulty 1993** *(published data only)*  

**Metildi 1984** *(published data only)*  

**Modig 1983** *(published data only)*  
Modig J. Advantages of dextran 70 over Ringer acetate solution in shock treatment and in prevention of adult respiratory distress syndrome. A randomized study in man...
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**Moretti 2003** [published data only]


**Nagy 1993** [published data only]


**Ngo 2001** [published data only]


**Nielsen 1985** [published data only]


**Pockaj 1994** [published data only]


**Prien 1990** [published data only]


**Rackow 1983** [published data only]


**Rocha e Silva 1994** [published data only (unpublished sought but not used)]


**SAFE 2004** [published data only]


**Shah 1977** [published data only]


**Shires 1983** [published data only]


**Sirieux 1999** [published data only]


**Skillman 1975** [published data only]


**Tollofsrud 1995** [published data only]


**Tollofsrud 1998** [published data only]


**Upadhay 2004** [published data only]


**Vassar 1990** [published data only]


**Vassar 1991** [published data only]

Holcroft JW, Vassar MJ, Turner JE, Derlet RW, Kramer GC. 3% NaCl and 7.5% NaCl/dextran 70 in the resuscitation


Vassar 1993a [published data only]

Vassar 1993b [published data only]

Verheij 2006 [published data only]

Virgilio 1979 [published data only]

Wahba 1996 [published data only]

Wills 2005 [published data only]

Woittez 1997 [published and unpublished data]

Wu 2001 [published data only]

Younes 1992 [published data only]

Younes 1994 [published data only]

Zetterstrom 1981a [published data only]

Zetterstrom 1981b [published data only]

Zhu 2011 [published data only]

References to studies excluded from this review

Artru 1989 [published data only]

Bocanegra 1966 [published data only]

Boldt 1996 [published data only]

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Bueno R 2004 [published data only]

Breheme 1993 [published data only]

Bueno R 2004 [published data only]

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Golub 1994 [published data only]

Goslinga 1992 [published data only]

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Niemi 2008 [published data only]

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Oliviera 2002 [published data only]

Paton-Gay 2007 [published data only]

Paul 2003 [published data only]

Steinberg 1989 [published data only]

Tiryakioğlu 2008 [published data only]

Tseng 2008 [published data only]

Valetova 2007 [published data only]

van der Heijden 2009 [published data only]

Vercueil 2006 [published data only]

Wilkes 2001 [published data only]

Woods 1993 [published data only]

References to ongoing studies

CHEST Trial [unpublished data only]

RASP trial [published data only]
Lactated Ringer Versus Albumin in Early Sepsis Therapy (RASP). Ongoing study May 2012.

The 6S trial [published data only]

Additional references

Armstrong 1994

Bickell 1994

Bisonni 1991
Boldt 2009

Fakhry 1995

Gosling 1998

Higgins 2011

Oxman 1994

Reinhart 2011

Shafer 2011

Velanovich 1989

Vermeulen 1995

Victorian DUAC 1991

Yim 1995

References to other published versions of this review

Schierhout 1998

*Indicates the major publication for the study
CHARACTERISTICS OF STUDIES

Characteristics of included studies  [ordered by study ID]

**Boldt 1986**

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

**Risk of bias**

| Bias | Authors' judgement | Support for judgement |
| Allocation concealment (selection bias) | Unclear risk | Unclear |

**Boldt 1993**

| Methods | RCT, allocation concealment by sealed opaque envelopes (information from author)  
Blinding and loss to follow-up not mentioned |
| Participants | 75 males undergoing elective aortocoronary bypass grafting, who had a pulmonary capillary WP < 5 mmHg after induction of anaesthesia |
| Interventions | 1. 5% Albumin (n = 15)  
2. 6% HES, mean molecular weight 450,000 (n = 15)  
3. 6% HES, mean molecular weight 200,000 (n = 15)  
4. 3.5% Gelatin (n = 15)  
5. No colloid (n = 15)  
Fluid used through operation and on intensive care postoperatively |
| Outcomes | Deaths not reported, author confirmed there were no deaths |
| Notes | Follow-up to 1 day |
### Risk of bias

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<td>Unclear risk</td>
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### Boldt 2001

**Methods**
- RCT, using a closed-envelope system

**Participants**
- 100 patients undergoing major abdominal surgery

**Interventions**
1. Ringer’s lactate (n = 25)
2. 6% HES, mean molecular weight 200 kDa, degree of substitution 0.5 (n = 25)
3. 6% HES, mean molecular weight 130 kDa, degree of substitution 0.4 (n = 25)
4. 4% Modified fluid gelatin, molecular weight 35 kDa (n = 25)

**Outcomes**
- Deaths
- Orthostatic problems
- Haemodynamics and laboratory data
- Fluid input and output
- Costs

**Notes**
- Follow-up period unclear

### Risk of bias

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### Boutros 1979

**Methods**
- RCT (“randomly divided”), method of allocation concealment not described
- Blinding not mentioned
- No loss to follow-up

**Participants**
- 24 people undergoing major operative procedures on the abdominal aorta

**Interventions**
1. Albumin in 5% dextrose (n = 7)
2. 5% Dextrose and Ringer’s lactate (n = 8)
3. 5% Dextrose in 0.45% saline (n = 9)

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)

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### Bowser-Wallace 1986

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

#### Risk of bias

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<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>

### Brunkhorst 2008

| Methods | Multicentre, RCT  
Blinding not mentioned  
Use of a 2 x 2 factorial, open label study design |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Critically ill patients with severe sepsis or septic shock of at least 18 years of age. Excluded if onset of symptoms commenced &gt; 24 hours before admission to the ICU, if the symptoms commenced &gt; 12 hours after onset in the ICU or if patient had received more than 1000 mL of HES in the 24 hours before randomisation</td>
</tr>
</tbody>
</table>
### Brunkhorst 2008

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deaths reported at 28 and 90 days. 90-day mortality rate was cited as it marked the end of the follow-up period</td>
<td></td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Bulger 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-blind RCT</td>
<td>15 years or older with hypovolaemic shock (&lt; 70 mmHg SBP or SBP 71 mmHg to &lt; 90 mmHg and HR &lt; 108 bpm)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 7.5% saline per 6% dextran (n = 220) 2. 0.9% saline (n = 376)</td>
<td>Primary outcome: 28-day survival Secondary outcomes: fluid and blood requirements, ARDS, MODS and nosocomial infections</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>All care providers, investigators and patients remained blinded to the treatment assignment</td>
</tr>
</tbody>
</table>

### Chavez-Negrete 1991

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT, allocation by “random numbers” Blinding not mentioned No loss to follow-up</td>
<td>Adults admitted to an emergency department with acute GI haemorrhage, SBP ≤ 90 mmHg for up to 1 hour and normal ECG Excluded if pregnant or had renal, cardiac or neurological disease</td>
</tr>
</tbody>
</table>
### Chavez-Negrete 1991  (Continued)

| Interventions | 1. Initial infusion of 250 mL 7.5% saline/6% dextran 60 given IV (16 patients) or intraosseous (n = 10)  
2. Initial IV infusion of 250 mL Ringer’s lactate (n = 23)  
Resuscitation continued with red cells, 0.9% saline and dextran 40 according to clinical judgement |
| Outcomes | Death  
Haemodynamic variables |
| Notes | Follow-up to 24 hours |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Cifra 2003

| Methods | Quasi-RCT (allocation by alternation), allocation concealment not reported  
Blinding not reported  
No loss to follow-up |
| Participants | 27 children with dengue shock syndrome  
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)  
2. Ringer's lactate (n = 16)  
1 patient from group 1 and 3 patients from group 2 were excluded because they needed inotropic support and multiple plasma substitute |
| Outcomes | Duration of control of shock  
Recurrence of shock  
Length of ICU stay  
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

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not used</td>
</tr>
</tbody>
</table>
### Cooper 2006

<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>Multicentre unblinded controlled trial with stratified block randomisation by centre and mortality prediction at enrolment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>Patients with cutaneous thermal burns of at least 20% TBSA within 12 hours of injury</td>
</tr>
</tbody>
</table>
| **Interventions** | 1. Ringer lactate and 5% albumin (n = 19)  
2. Ringer lactate (n = 23) |
| **Outcomes** | Primary outcome was MODS  
Mortality was reported |
| **Notes** | The trial was suspended due to slow enrolment |

**Risk of bias**

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Support for judgement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Patients were allocated to study groups with stratified randomisation with a computer-generated randomisation list and sequentially numbered sealed, opaque envelopes</td>
</tr>
</tbody>
</table>

### Dawidson 1991

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

**Risk of bias**

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Support for judgement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>
#### Dehne 2001

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT, allocation by sealed envelope assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>60 male patients (of ASA physical status 1 or 2) scheduled for middle ear surgery</td>
</tr>
</tbody>
</table>
| Interventions    | 1. Ringer’s lactate solution (n = 15)  
2. 6% HES: molecular weight 200 kDa, degree of substitution 0.5 (n = 15)  
3. 6% HES: molecular weight 200 kDa, degree of substitution 0.60 to 0.66 (n = 15)  
4. 6% HES: molecular weight 450 kDa, degree of substitution 0.7 (n = 15) |
| Outcomes         | Deaths not stated but ‘all’ patients discharged 10 to 14 days after surgery; therefore no deaths  
Central venous pressure  
Urine output  
Blood osmolality  
Urine osmolality |
| Notes            | Follow-up 2 days |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

#### Du 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Participants had confirmed diagnosis of severe acute pancreatitis. Patients were included within 72 hours after the onset of symptoms</td>
</tr>
</tbody>
</table>
| Interventions    | 1. 6% HES 130/0.4 (n = 20)  
2. Ringer’s lactate (n = 21) |
| Outcomes         | Primary outcome was intra-abdominal pressure. They also reported in-hospital mortality, organ complications, inflammatory markers and fluid requirement |
| Notes            | Patients were excluded if they died within 72 hours after admission |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
### Dubin 2010

<table>
<thead>
<tr>
<th>Method</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Patients with severe sepsis</td>
</tr>
</tbody>
</table>
| Interventions | 1. 6% HES 130/0.4 (n = 12)  
2. Normal saline (n = 13) |
| Outcomes | Sublingual microcirculation |
| Notes | Data on mortality are not clear from the report |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>sealed enveloped were used</td>
</tr>
</tbody>
</table>

### Eleftheriadis 1995

| Method | Patients “randomizedly distributed”  
Blinding not mentioned  
Unable to assess loss to follow-up |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Participants were undergoing coronary artery bypass surgery</td>
</tr>
</tbody>
</table>
| Interventions | 1. 6% HES  
2. 3.5% Gelatin  
3. Ringer’s lactate  
Allocated fluid was used in the postoperative period only guided by mean arterial pressure |
| Outcomes | Deaths were not reported  
Haemodynamic variables |
| Notes | Follow-up period unspecified |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
### Ernest 1999

| Methods | RCT, allocation concealment not described  
No blinding  
No loss to follow-up mentioned |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Patients with a clinical diagnosis of sepsis</td>
</tr>
</tbody>
</table>
| Interventions | 1. 5% Albumin (n = 9)  
2. 0.9% Saline (n = 9)  
Volume of infusion guided by PAWP |
| Outcomes | Haemodynamic variables and volume measurements  
Deaths not reported |
| Notes | Follow-up to immediately after infusion |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Evans 1996

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

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>
### Evans 2003

| Methods | RCT, allocation concealment not reported  
|         | Blinding methods not reported  
|         | Loss to follow-up not reported  
| Participants | 55 patients undergoing primary unilateral total hip replacement  
|             | Exclusion criteria: 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)  
|                | 2. Gelofusine (n = 14)  
|                | 3. Haemaccel (n = 14)  
|                | 4. 0.9% Saline (n = 14)  
| Outcomes | Haemostatic parameters  
|           | Death not reported  
| Notes | Length of follow-up not reported but all outcomes were in-hospital  

#### Risk of bias

| Bias | Authors’ judgement | Support for judgement  
|------|---------------------|----------------------  
| Allocation concealment (selection bias) | Unclear risk | Unclear |

### Fries 2004

| Methods | RCT, patients “randomly” received crystalloid or colloids  
|         | Method of allocation concealment not reported  
|         | Blinding not reported  
|         | Loss to follow-up not reported  
| Participants | 60 patients undergoing knee replacement surgery  
|             | Exclusion criteria: contraindication for regional anaesthesia, known allergies or haemostatic disorders  
| Interventions | 1. HES (n = 20)  
|               | 2. Modified gelatin (n = 20)  
|               | 3. Ringer’s solution (n = 20)  
|               | Groups 1 and 2 also received a basis of Ringer’s solution infusion  
| Outcomes | Coagulation parameters  
|          | Death not reported  
| Notes | Length of follow-up not reported but all outcomes were in-hospital measures  

#### Risk of bias

| Bias | Authors’ judgement | Support for judgement  
|------|---------------------|----------------------  
| Allocation concealment (selection bias) | Unclear risk | Unclear |
### Gallagher 1985

**Methods**
- RCT, method of allocation concealment not described. Author contacted - allocation concealment by computerised system - patient details were entered before treatment assignment was revealed
- Blinding not mentioned
- No loss to follow-up

**Participants**
- Patients after coronary artery bypass graft surgery
- Exclusion criteria: patients with significant left main coronary artery stenosis, poor left ventricular function or poor pulmonary function

**Interventions**
1. IV 5% albumin (n = 5)
2. IV 6% HES (n = 5)
3. IV Ringer’s lactate (n = 5)
- Fluid used from admission to ICU post operation, guided by PAWP. RBC given if needed

**Outcomes**
- Deaths were not reported. Author contacted and confirmed that there were no deaths in any group
- Haemodynamic data

**Notes**
- Follow-up to 1 day

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Goodwin 1983

**Methods**
- RCT, assigned by “random numbers table”, method of allocation concealment unclear
- Blinding not mentioned
- No loss to follow-up

**Participants**
- 79 previously healthy young adults admitted with burns
- No exclusion criteria reported

**Interventions**
1. 2.5% Albumin in Ringer’s lactate (n = 40)
2. Ringer’s lactate (n = 39)
- Fluids on day 1 guided by haemodynamic variable. On day 2, given at 0.3 to 0.5 mL/kg/ %burn, then 5% dextrose
### Goodwin 1983

(Continued)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Deaths reported</th>
<th>Pulmonary oedema</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infections</td>
<td></td>
</tr>
</tbody>
</table>

| Notes          | Follow-up to discharge from hospital |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Grundmann 1982

**Methods**

- RCT, method of allocation concealment unclear
- Blinding not mentioned
- No loss to follow-up

**Participants**

- 20 people undergoing partial gastrectomy
- The average age was 50 years (range 19 to 84 years)
- No exclusion criteria reported

**Interventions**

1. Colloid group received human albumin solution (n = 14)
2. Details of crystalloid were not reported (n = 6)

Allocated fluid was continued for 4 days after operation

**Outcomes**

- Deaths reported
- Volumes of fluid given
- Haemodynamic variables

| Notes          | Follow-up to discharge from hospital |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Guo 2003

**Methods**

- RCT, allocation concealment not reported
- Blinding not reported
- No loss to follow-up reported

**Participants**

- 42 patients undergoing elective cytoreductive surgery for ovarian cancer
- Exclusion criteria: preoperative anaemia, allergic response to HES or perioperative administration of cardiovascular agents
**Guo 2003 (Continued)**

<table>
<thead>
<tr>
<th>Interventions</th>
<th>2 patients randomised but excluded because of use of cardiovascular agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td>Splanchnic perfusion</td>
</tr>
<tr>
<td></td>
<td>Death not reported but in results authors mentioned that &quot;all patients were discharged&quot;</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Follow-up to discharge from hospital</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

**Hall 1978**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Quasi-RCT (participants were stratified by age, extent of burn and aetiology, and then allocated by alternation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blinding not mentioned</td>
</tr>
<tr>
<td></td>
<td>No loss to follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Burns covering &gt; 10% of the body surface (for children), and &gt; 15% of the body surface (for adults)</td>
</tr>
<tr>
<td></td>
<td>No exclusions mentioned</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>1. 120 mL/%burn IV 6% dextran 70 in 0.9% saline over 48 hours plus oral water or IV 5% dextrose for 'metabolic requirements' (n = 86)</td>
</tr>
<tr>
<td></td>
<td>2. 4 mL/kg/%burn IV Ringer's lactate over 24 hours, then 10% of initial body weight of fluid over 24 hours plus oral water (n = 86)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>Fluid given, haemodynamic variables</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Follow-up to discharge from hospital</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>
### Hartmann 1993

**Methods**
- RCT, method of allocation unclear
- Blinding not mentioned
- No loss to follow-up

**Participants**
- Adults undergoing major abdominal surgery
- Exclusion criteria: cardiorespiratory dysfunction, uraemia, diabetes, taking steroids, anti-coagulants or diuretics

**Interventions**
1. IV Dextran 70 in saline (concentration not given) with 2.5% dextrose (n = 15)
2. IV Saline (concentration not given) with 2.5% dextrose (n = 14)
Both groups given red cells, plasma, dextran 70 and crystalloids during the operation as decided by the clinician. Postoperative fluids according to the trial group guided by tissue oxygen tension to the end of resuscitation

**Outcomes**
- Death not reported
- Fluid given, haemodynamic variables

**Notes**
- Follow-up to 7 days

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### James 2011

**Methods**
- RCT
- Double-blind

**Participants**
- Patients with blunt or penetrating trauma requiring more than 3 L volume resuscitation (blunt and penetrating trauma patients were randomised separately)

**Interventions**
1. HES 130/0.4, penetrating trauma (n = 36)
2. 0.9% Saline, penetrating trauma (n = 34)
3. HES 130/0.4, blunt trauma (n = 22)
4. 0.9% Saline, blunt trauma (n = 23)

**Outcomes**
- Primary outcomes were the volumes of first fluid needed in the first 24 hours, and normal GI function by day 5

**Notes**
- Although mortality at 30 days was a safety measure, the authors did not report data on mortality for each group

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>

---

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

Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
**Jelenko 1978**

| Methods | RCT, method of allocation concealment unclear  
|         | Blinding not mentioned  
|         | No loss to follow-up  |
| Participants | 19 people with burns covering more than 20% of body surface  |
| Interventions | 1. 12.5% Albumin in hypertonic saline (240 mEq/L sodium, 120 mEq/L chloride, 120 mEq/L lactate) (n = 7)  
|         | 2. Hypertonic saline (240 mEq/L sodium, 120 mEq/L chloride, 120 mEq/L lactate) (n = 5)  
|         | 3. Ringer's lactate (n = 7)  
|         | Allocated fluid was used, guided by haemodynamic variables, to the end of resuscitation  |
| Outcomes | Deaths reported  
|         | Haemodynamic variables  |
| Notes | Follow-up to end of resuscitation  |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

**Karanko 1987**

| Methods | RCT, description of allocation procedure unclear  
|         | Blinding not mentioned  
|         | No loss to follow-up  |
| Participants | 32 adult men scheduled for coronary artery bypass surgery  
|         | Exclusion criteria: LVEF < 40%, abnormal lung function  |
| Interventions | 1. 6% Dextran 70 (n = 14)  
|         | 2. Ringer's lactate (n = 18)  
|         | Allocated fluid was used to the end of resuscitation  |
| Outcomes | Deaths reported  
|         | Haemodynamic variables  
|         | Pulmonary oedema  |
### Notes

Follow-up 2 weeks

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Lang 2001

**Methods**

RCT, using a closed-envelope system

**Participants**

42 patients scheduled for elective major abdominal surgery

**Interventions**

1. Ringer’s lactate (n = 21)
2. 6% HES, molecular weight 139 kDa, degree of substitution 0.4 (n = 21)

**Outcomes**

Deaths
Haemodynamics and laboratory data
Tissue oxygenation
Volume input and output

**Notes**

Follow-up period unclear

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Lang 2003

**Methods**

RCT, allocation concealment not clearly reported (“closed envelope system”)
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
Exclusion criteria: 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)
2. Ringer’s lactate (n = 18)

Additional crystalloid solutions were supplied to equalise insensible fluid loss or as a solvent for drugs in group 1
### Lang 2003

| Outcomes | Pro- and anti-inflammatory cytokines  
| All patients survived |
| Notes | Length of follow-up not reported but all outcomes were in-hospital measures |

#### Risk of bias

| Bias | Authors' judgement | Support for judgement |
| Allocated concealment (selection bias) | Unclear risk | Unclear |

### Ley 1990

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

#### Risk of bias

| Bias | Authors' judgement | Support for judgement |
| Allocated concealment (selection bias) | Unclear risk | Unclear |

### Lowe 1977

| Methods | RCT, allocation by sealed envelopes  
| Blinding not mentioned  
| No loss to follow-up |
| Participants | Participants with serious trauma |
| Interventions | 1. 25% Albumin in Ringer's lactate (n = 77)  
| 2. Ringer's lactate (n = 94)  
| Allocated fluid was used throughout the pre- and intraoperative period |
### Lowe 1977 (Continued)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Deaths reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notes</td>
<td>Follow-up to 5 days postoperatively. 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</td>
</tr>
</tbody>
</table>

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Lu 2012

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>42 patients with septic shock</td>
</tr>
</tbody>
</table>
| Interventions | 1. Ringer’s lactate (n = 20)  
2. HES 130/0.4 (n = 22) |
| Outcomes | Mortality, fluid replacement, use of vasoactive drugs and inflammatory markers |
| Notes | - |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
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<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Lucas 1978

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT, randomisation was based on the last digit of each patient’s case number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>52 seriously injured patients</td>
</tr>
</tbody>
</table>
| Interventions | 1. Standard resuscitation regimen (‘balanced electrolyte’, blood, fresh frozen plasma) plus salt-poor albumin, maximum 150 g during surgery and 150 g/day for the next 5 days (n = 27)  
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

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>

### Maitland 2005

**Methods**

RCT, open label, random allocation was assigned by the use of sealed cards
No loss to follow-up

**Participants**

159 children with severe malaria and metabolic acidosis
Exclusion criteria: pulmonary oedema, oedematous malnutrition or papilloedema

**Interventions**

Severe acidosis
1. 4.5% Albumin (n = 23)
2. 0.9% Saline (n = 26)

Moderate acidosis
1. 4.5% Albumin (n = 33)
2. 0.9% Saline (n = 35)
3. Control (n = 33)

**Outcomes**

Reduction in base deficit
Neurological sequelae
Death reported

**Notes**

Length of follow-up not reported but all outcomes were in-hospital measures

### Risk of bias

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
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<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Maitland 2011

**Methods**

2 stratum multicentre open, RCT

**Participants**

Children aged between 60 days and 12 years, with severe febrile illness, randomly assigned within 2 strata (stratum A was children with severe febrile illness and impaired perfusion but without severe hypotension; stratum B was children with severe hypotension)

**Interventions**

Children were randomly allocated to rapid volume replacement over the course of 1 hour with either:
1. 20 mL 5% Human albumin solution per kg body weight (n = 1063)
2. 20 mL 0.9% Saline solution per kg body weight (n = 1063)
### Mattox 1991

**Methods**
- Quasi-randomised, allocation by alternation
- Double-blind
- 2 patients excluded from the analysis as code of fluid lost

**Participants**
- Participants were pre-hospital trauma victims attended to by emergency personnel within 1 hour of injury, with SBP ≤ 90 mmHg, ≥ 16 years. 72% of participants had sustained penetrating trauma

**Interventions**
- 1. 250 mL Dextran 70 in 7.5% saline (n = 211)
- 2. 250 mL Ringer's lactate, saline or plasmalyte (n = 211)

**Outcomes**
- Deaths reported

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
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</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>

### Maitland 2011 (Continued)

**Outcomes**
- Mortality at 4 weeks after randomisation

**Notes**
- Children (n = 1044) assigned to no treatment were not included in the analysis

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Trial numbers kept inside opaque, sealed envelopes. Opened in numerical order by clinician</td>
</tr>
</tbody>
</table>

### Mazher 1998

**Methods**
- Patients “randomized”
- Blinding of carers by use of pharmacy-prepared solutions
- No loss to follow-up

**Participants**
- Patients undergoing elective coronary artery surgery
- Exclusion criteria: age > 75 years, ejection fraction < 35%, creatinine > 135 µmol/L, ACE inhibitors
### Mazher 1998  (Continued)

| Interventions | 1. 5 mL/kg Polygeline (n = 10)  
|               | 2. 5 mL/kg 7.2% Saline (n = 10)  
| Allocated fluid given postoperatively over 1 hour. All patients subsequently receive polygeline and RBCs |

| Outcomes | Haemodynamic variables  
| Death |

| Notes | Follow-up to discharge from ICU |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
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<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### McIntyre 2008

| Methods | A feasibility RCT |

| Participants | Patients with early septic shock defined with at least 2 systemic inflammatory response syndrome criteria, infectious source and persistent hypotension after > 1 L of crystalloid fluid |

| Interventions | 1. Normal saline (n = 19)  
|               | 2. Pentastarch (n = 21)  

| Outcomes | Primary outcomes were feasibility measures for the pilot RCT. ICU and 28-day mortality were also reported |

| Notes | - |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Only the designated research pharmacist at each institution was aware of the treatment allocation for individual patients. Study fluids were prepared and blinded ahead of time by the site research pharmacist</td>
</tr>
</tbody>
</table>
McNulty 1993

| Methods | RCT, method of allocation concealment not described  
|         | Blinding not mentioned  
|         | No loss to follow-up  
| Participants | Patients following elective cardiopulmonary bypass  
| Interventions | 1. 5% Albumin and cell-saved blood (n = 14)  
|         | 2. Plasmalyte and cell-saved blood (n = 14)  
|         | Allocated fluid used as part of fluid volume replacement  
| Outcomes | Deaths not reported  
|         | 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

<table>
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<tr>
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<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Metildi 1984

| Methods | RCT  
|         | Blinding not mentioned  
|         | No loss to follow-up  
| Participants | Participants were admissions to an ICU and a trauma unit with ARDS and established pulmonary failure. Included both trauma and non-trauma patients  
| Interventions | 1. 5% Salt-poor albumin (n = 20)  
|         | 2. Ringer's lactate (n = 26)  
|         | 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  
|         | Haemodynamic variables  
| Notes | Follow-up to discharge  

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
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<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
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</tbody>
</table>
### Modig 1983

| Methods | Quasi-RCT, allocation by admission date  
| Blinding not mentioned  
| No loss to follow-up |
| Participants | Participants were trauma admissions to an emergency department with SBP < 70 mmHg.  
| Age range 20 to 58 years |
| Interventions | 1. Dextran 70 in Ringer’s lactate (n = 12)  
| 2. Ringer’s lactate (n = 11)  
| 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  
| Development of ARDS |
| Notes | Follow-up to definitive reconstructive surgery |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>

### Moretti 2003

| Methods | RCT, allocation concealment method not clearly reported (“Patients randomized...by using a closed-envelope technique”)  
| Blinding method not clearly reported (“Researchers were unaware of the patient’s randomization”)  
| No loss to follow-up |
| Participants | 90 adult patients undergoing major elective general, gynaecological, orthopaedic or urological surgery with an anticipated blood loss > 500 mL  
| Exclusion criteria: age < 16 years, coagulopathy, renal or hepatic dysfunction and congestive heart failure |
| Interventions | 1. Hetastarch-normal saline (n = 30)  
| 2. Hetastarch-balanced salt (n = 30)  
| 3. Ringer’s lactate (n = 30) |
| Outcomes | Postoperative nausea and vomiting  
| Death not reported |
| Notes | Follow-up to discharge |

### Risk of bias
Moretti 2003  (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Nagy 1993

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT, contact with author showed it was an open-label study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blinding not mentioned</td>
</tr>
<tr>
<td></td>
<td>No loss to follow-up</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
<th>Participants were adult admissions to a trauma unit, with measureable SBP &lt; 90 mmHg</th>
</tr>
</thead>
</table>

| Interventions                     | 1. Pentastarch in 0.9% saline (n = 21) |
|                                  | 2. Ringer’s lactate (n = 20)           |
|                                  | Allocated fluid was used throughout resuscitation with the exception that colloid patients received a maximum 4 L of pentastarch, after which Ringer’s lactate was given |

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Deaths were not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Haemodynamic variables</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
<th>Follow-up to discharge</th>
</tr>
</thead>
</table>

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Inadequate</td>
</tr>
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</table>

Ngo 2001

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT, opaque envelopes containing only treatment pack number</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
<th>230 children with dengue shock syndrome</th>
</tr>
</thead>
</table>

| Interventions                     | 1. Dextran 70 (n = 55)                                      |
|                                  | 2. 3% Gelatin (n = 56)                                       |
|                                  | 3. Ringer’s lactate (n = 55)                                 |
|                                  | 4. ’Normal’ saline (n = 56)                                  |

| Outcomes                          | Initial pulse recovery time                                 |
|                                  | Occurrence of timing and subsequent episodes of shock     |
|                                  | Decrease in haematocrit                                   |
|                                  | Volume of fluid administered until recovery              |
|                                  | Complications                                             |
|                                  | No deaths in any group                                    |

Colloids versus crystalloids for fluid resuscitation in critically ill patients (Review)
### Ngo 2001 (Continued)

**Notes**
- Follow-up period unclear

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
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</tr>
</thead>
<tbody>
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<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Nielsen 1985

**Methods**
- RCT, method of allocation concealment not described
- Blinding not mentioned
- No loss to follow-up

**Participants**
- 26 patients admitted for reconstructive surgery of the abdominal aorta

**Interventions**
1. Whole blood, crystalloid plus 80 g albumin on the day of the operation, and 20 g/day for the next 3 days. Albumin given as 100 mL 20% human albumin solution (n = 13)
2. Whole blood and crystalloid, type not specified (n = 13)

**Outcomes**
- Deaths not reported
- Author when contacted confirmed that there were no deaths in either group

**Notes**
- Length of follow-up 4 days

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Pockaj 1994

**Methods**
- RCT, allocation concealment unclear
- Blinding not mentioned
- 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 Bolus of 5% albumin in saline (n = 36 reported)
2. 250 mL Bolus of 0.9% normal saline (n = 40 reported)
- Boluses guided by haemodynamic variables. Both groups also received 0.45% saline with 10 mmol/L KCl
### Pockaj 1994  (Continued)

| Outcomes | Deaths  
| - | Toxic effects of chemotherapy  
| - | Haemodynamic variables  |

| Notes | - |

#### Risk of bias

| Bias | Authors' judgement | Support for judgement |
| Allocation concealment (selection bias) | Unclear risk | Unclear |

### Prien 1990

| Methods | RCT  
| - | Blinding not mentioned  
| - | No loss to follow-up  |

| Participants | Participants were undergoing modified Whipple’s operation |

| Interventions | 1. 10% HES in 0.9% saline plus plasma protein fraction if requirements > 20 mL/kg (n = 6)  
| - | 2. 20% human albumin solution (n = 6)  
| - | 3. Ringer’s lactate (n = 6)  
| - | Allocated fluid was administered intraoperatively only |

| Outcomes | Deaths  
| - | Intestinal oedema formation |

| Notes | Follow-up period was unspecified |

#### Risk of bias

| Bias | Authors' judgement | Support for judgement |
| Allocation concealment (selection bias) | Unclear risk | Unclear |

### Rackow 1983

| Methods | RCT, allocation concealment unclear  
| - | Blinding not mentioned  
| - | No loss to follow-up  |

| Participants | Participants were aged 54 to 97 years, and had any 1 of the following pre-determined indicators of shock: SBP ≤ 90 mmHg, cardiac index < 2.2 L/minute/m², serum arterial lactate > 18 mg/dL and WP < 15 mmHg |
### Rackow 1983
*(Continued)*

<table>
<thead>
<tr>
<th>Interventions</th>
<th>1.  6% HES (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.  5% Albumin (n = 9)</td>
</tr>
<tr>
<td></td>
<td>3.  0.9% Saline (n = 8)</td>
</tr>
<tr>
<td>Allocated fluid was given as needed until the end of resuscitation</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Deaths reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fluid balance</td>
</tr>
</tbody>
</table>

| Notes                          | Follow-up to discharge from hospital |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
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</tr>
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<tr>
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<td>Unclear</td>
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</tbody>
</table>

### Rocha e Silva 1994

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Participants were admissions to the emergency department, with SBP $\leq$ 90 mmHg and $\geq$ 16 years of age</td>
</tr>
</tbody>
</table>

| Interventions                | 1.  6% Dextran 70 in 7.5% saline |
|-------------------------------| 2.  Ringer’s lactate          |
| Allocated fluid was used for the first IV 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

<table>
<thead>
<tr>
<th>Bias</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### SAFE 2004

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT. Randomisation by minimisation algorithm accessed through secure website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Patients aged $\geq$ 18 years admitted to closed multidisciplinary ICUs in 16 tertiary hospitals in Australia over 19-month period</td>
</tr>
</tbody>
</table>

| Interventions                | 1.  4% Albumin (Albumex, CSL) (n = 3499) |
|-------------------------------| 2.  Normal saline (n = 3501)            |
| Outcomes | Death  
| Patients with new single- or multiple-organ failure  
| Mean number of days: in ICU, in hospital, on mechanical ventilation, on renal replacement therapy |
| Notes | Follow-up to 28 days |

### Risk of bias

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Shah 1977

**Methods** | RCT, allocation by sealed envelope  
| Blinding not mentioned  
| No loss to follow-up |

**Participants** | Patients with severe, multiple trauma and SBP < 90 mmHg. All patients were adults and both sexes were included |

**Interventions** | 1. 5% Salt-poor albumin in Ringer's lactate (n = 9)  
| 2. Ringer's lactate (n = 11)  
| Volume infused guided by physiological parameters |

**Outcomes** | Death reported  
| Haemodynamic variables |

**Notes** | Length of follow-up not stated |

### Shires 1983

**Methods** | Patients 'assigned randomly'  
| Blinding not mentioned  
| No loss to follow-up |

**Participants** | People undergoing aortic reconstruction surgery  
| No exclusion criteria mentioned |
### Shires 1983

*(Continued)*

| Interventions | 1. Plasmanate (n = 9)  
2. Ringer’s lactate (n = 9)  
Allocated fluid used guided by haemodynamic variables until the first postoperative morning. All patients then received 0.45% saline |
| Outcomes | Pulmonary oedema  
Haemodynamic variables  
Death |
| Notes | Follow-up to 2 days postoperative |

#### Risk of bias

<table>
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<tr>
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<th>Authors’ judgement</th>
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<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Sirieix 1999

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

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
### Skillman 1975

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

### Risk of bias

<table>
<thead>
<tr>
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<tbody>
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<td>Unclear</td>
</tr>
</tbody>
</table>

### Tollofsrud 1995

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

### Risk of bias

<table>
<thead>
<tr>
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<td>Unclear</td>
</tr>
</tbody>
</table>
### Tollofsrud 1998

| Methods | RCT, allocation by sealed envelope  
Described as double blind  
No loss to follow-up mentioned |
|---------|--------------------------------------------------------------------------------|
| Participants | Patients with 3 vessel coronary artery disease undergoing elective coronary artery surgery  
Exclusion criteria: LVEF < 0.4, ventricular aneurysm, significant arrhythmia, diabetes, renal failure, lung disease |
| Interventions | 1. 4 mL/kg of 75 mg/mL hypertonic saline in dextran 70 60 mg/mL over 30 minutes (n = 10)  
2. Same volume and rate of isotonic saline (n = 10)  
Fluid given just after surgery while still in operating theatre. Ringer's lactate for additional fluid |
| Outcomes | Fluid balance  
Haemodynamic variables  
Deaths not reported |
| Notes | Follow-up to 48 hours |

#### Risk of bias

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<td>Unclear</td>
</tr>
</tbody>
</table>

### Upadhyay 2004

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

#### Risk of bias

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
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<td>Unclear</td>
</tr>
<tr>
<td><strong>Vassar 1990</strong></td>
<td></td>
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</tr>
</tbody>
</table>
| **Methods** | RCT, allocation concealment unclear  
Double-blind study (solutions prepared in identical containers)  
No loss to follow-up |
| **Participants** | Participants were emergency department admissions with trauma and SBP < 80 mmHg and ≥ 18 years of age  
Exclusion criteria: pregnant women and people with pre-existing cardiac, hepatic or renal disease |
| **Interventions** | 1. 6% Dextran 70 in 7.5% saline (n = 23)  
2. Ringer's lactate (n = 24)  
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  
Haemodynamic variables |
| **Notes** | Follow-up to hospital discharge |

**Risk of bias**

<table>
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<tr>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Vassar 1991</strong></th>
<th></th>
</tr>
</thead>
</table>
| **Methods** | RCT, allocation by randomised sequence of coded containers  
Double-blind study  
No loss to follow-up |
| **Participants** | Participants were pre-hospital trauma cases undergoing helicopter transport to an emergency centre, with SBP ≤ 100 mmHg and ≥ 18 years  
Exclusion criteria: pre-existing 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)  
2. Ringer's lactate (n = 83)  
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 |
| **Outcomes** | Deaths reported  
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 2 dextran groups were combined |
### Risk of bias

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Vassar 1993a

**Methods**
- RCT, allocation concealed by random sequence of identical containers
- Double-blind study
- 36 people excluded post randomisation as deemed not to have met eligibility criteria
- No loss to follow-up

**Participants**
- Participants, who were undergoing ambulance transport to an emergency centre, SBP $\leq 90$ mmHg, $\geq 18$ years
- Exclusion criteria: asystolic; undergoing CPR; lack sinus complex on ECG; $> 2$ hours after trauma; pregnant; pre-existing seizures; bleeding disorder; hepatic, cardiac or renal disease

**Interventions**
- 1. 6% Dextran 70 in 7.5% saline ($n = 89$)
- 2. 7.5% Saline ($n = 85$)
- 3. 0.9% Saline ($n = 84$)
- Participants received 250 mL of the allocated fluid in the pre-hospital setting. Additional isotonic crystalloids were given as needed

**Outcomes**
- Deaths reported
- Haemodynamic variables
- Trauma scores

**Notes**
- Follow-up was to discharge from hospital

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

### Vassar 1993b

**Methods**
- RCT, allocation concealed by sequential use of coded identical containers
- Double-blind study
- 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, SBP $\leq 100$ mmHg, $\geq 18$ years
- Exclusion criteria: asystolic; undergoing CPR; lack sinus complex on ECG; $> 2$ hours after trauma; pregnant; pre-existing seizures; bleeding disorder; hepatic, cardiac or renal disease
### Interventions
1. 12% Dextran 70 in 7.5% saline (n = 49)
2. 6% Dextran 70 in 7.5% saline (n = 50)
3. 7.5% Saline (n = 50)
4. Ringer's lactate (n = 45)
Participants received 250 mL of the allocated fluid in the pre-hospital setting. Additional isotonic crystalloids were given as needed.

### Outcomes
- Deaths reported
- Haemodynamic variables
- Trauma scores and neurological outcome scores

### Notes
Follow-up to hospital discharge

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Low risk</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

## Verheij 2006

### Methods
- RCT, allocation concealment by “the sealed envelope method”
- Blinding method not reported
- No loss to follow-up

### Participants
- 67 patients with presumed hypovolaemia after cardiac and major vascular surgery
- Exclusion criteria: age > 79 years and known anaphylactoid reaction to colloids

### Interventions
1. Saline (n = 16)
2. Gelatin (n = 16)
3. HES (n = 16)
4. Albumin (n = 16)

### Outcomes
- Haemodynamic data
- Death not reported

### Notes
- Length of follow-up not reported but all outcomes were in-hospital measures

### Risk of bias

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
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<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
**Virgilio 1979**

| Methods | Allocation “by random number”  
| Blinding not mentioned  
| No loss to follow-up |

| Participants | Participants were undergoing abdominal aortic surgery |

| Interventions | 1. 5% Albumin (n = 15)  
| 2. Ringer’s lactate (n = 14)  
| 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 2.5 weeks |

**Risk of bias**

| Bias | Authors’ judgement | Support for judgement |
| Allocation concealment (selection bias) | Unclear risk | Unclear |

**Wahba 1996**

| Methods | Patients “randomly allocated”  
| Blinding not mentioned  
| 2 patients excluded as they required reoperation for bleeding |

| Participants | 22 adults in need of volume replacement following coronary artery bypass surgery  
| Exclusion criteria: abnormal left ventricular function, platelet active medication or heparin |

| Interventions | 1. Haemaccel (n = 10)  
| 2. Ringer’s lactate (n = 10)  
| Allocated fluid was used from the time of admission to ICU following operation, to the end of resuscitation |

| Outcomes | Deaths reported  
| Pulmonary oedema |

| Notes | Follow-up to discharge |

**Risk of bias**

| Bias | Authors’ judgement | Support for judgement |
| Allocation concealment (selection bias) | Unclear risk | Unclear |
### Wills 2005

**Methods**
- RCT, allocation concealed by specially prepared cardboard containers
- Method of blinding not mentioned
- 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 3 interventions:
  1. Ringer's lactate (n = 128)
  2. 6% Dextran 70 (n = 126)
  3. 6% HES 200/0.5 (n = 129)
- Children with severe shock were randomised only to either of the 2 colloids interventions:
  1. 6% Dextran 70 (n = 67)
  2. 6% HES 200/0.5 (n = 62)

**Outcomes**
- Requirement for supplemental intervention with rescue colloid
- Time taken to achieve initial cardiovascular stability
- Time taken to achieve sustained cardiovascular stability
- Volume required
- Change in haematocrit
- Days in hospital
- 1 death reported but not specified in which group

**Notes**
- Length of follow-up not clear

### Risk of bias

<table>
<thead>
<tr>
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</tr>
</tbody>
</table>

### Woittiez 1997

**Methods**
- RCT, allocation concealment by sealed opaque envelopes
- No information on blinding or loss to follow-up

**Participants**
- 60 patients who had developed hypoalbuminaemia (< 20 g/L) after major surgery
- 2 patients died after randomisation and before treatment started. They were excluded from the analysis

**Interventions**
- 1. Saline (500 mL/24 hours) (n = 16)
- 2. 20% Albumin (300 mL/24 hours) (n = 15)
- 3. 10% HES (500 mL/24 hours) for 3 days (n = 27)
- Aim was to restore COP

**Outcomes**
- Changes in fluid balance, serum albumin, COP and clinical signs of oedema were followed daily
- Death rates supplied by the author
Woittiez 1997  (Continued)

Notes  
Length of follow-up unspecified

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
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</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear</td>
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</tbody>
</table>

Wu 2001

Methods  
RCT. No details given of randomisation method

Participants  
41 adolescent or adult patients in emergency department suffering from shock

Interventions  
1. 4% Modified fluid gelatin: succinated gelatin 40 g/L, sodium chloride 7 g/L, sodium hydroxide 1.36 g/L (n = 18)  
2. Ringer’s lactate (n = 16)

Outcomes  
Death  
Haemodynamic variables

Notes  
Not intention-to-treat: 5 patients who received blood transfusion and 2 who had surgery within the first hour of resuscitation were dropped from the analysis  
Length of follow-up not clear

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>Unclear</td>
</tr>
</tbody>
</table>

Younes 1992

Methods  
Randomised “in a double blind fashion”  
Blinding by use of similar bottles  
No loss to follow-up

Participants  
Participants were emergency department admissions, SBP < 80 mmHg, ≥ 19 years  
Exclusion criteria: pregnant, pre-existing cardiac or metabolic disease

Interventions  
1. 6% Dextran 70 in 7.5% saline (n = 35)  
2. 7.5% Saline (n = 35)  
3. 0.9% Saline (n = 35)  
Allocated fluid was for initial bolus of 250 mL, followed by isotonic crystalloids as needed
### Younes 1992 (Continued)

| Outcomes          | Deaths reported  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fluid balance</td>
</tr>
<tr>
<td>Notes</td>
<td>Follow-up to discharge from hospital</td>
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</table>

**Risk of bias**

<table>
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<tr>
<th>Bias</th>
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<td>Unclear risk</td>
<td>Unclear</td>
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</tbody>
</table>

### Younes 1994

**Methods**

Trial conducted in a “double blind randomised fashion”
Blinding by use of coded, identical containers

**Participants**

Participants were trauma admissions to the emergency department requiring treatment for haemorrhagic hypovolaemia; all were over 15 years old
Exclusion criteria: pregnant, cardiac or renal failure, cardiac arrest on arrival

**Interventions**

1. 6% Dextran 70 in 7.5% saline (n = 101)
2. 0.9% Saline (n = 111)
Allocated fluid was for the first IV infusion only

**Outcomes**

Deaths reported
Complications

**Notes**

Follow-up period was 30 days

**Risk of bias**

<table>
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<th>Bias</th>
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<tbody>
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<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

### Younes 1998

**Methods**

RCT, allocation by sealed envelope
Blinding not mentioned
No apparent loss to follow-up

**Participants**

Trauma patients SBP < 90 mmHg admitted to the emergency department, with no previous treatment

**Interventions**

1. 10% Pentastarch (n = 12)
2. 0.9% Saline (n = 11)
Fluid given in 250 mL boluses until systolic blood pressure > 100 mmHg
### Outcomes
- Deaths reported
- No complications reported in either group

### Notes
- Follow-up to 24 hours

### Risk of bias

<table>
<thead>
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<th>Bias</th>
<th>Authors' judgement</th>
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<td>Unclear risk</td>
<td>Unclear</td>
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</tbody>
</table>

### Zetterstrom 1981a

#### Methods
- The patients were randomly divided into 2 groups
- Allocation concealment was by sealed opaque envelopes (information supplied by study author)
- Blinding not mentioned
- No loss to follow-up

#### Participants
- Adults undergoing elective major abdominal surgery

#### Interventions
1. Standard volume replacement regimen (1 L dextran 70 then up to 4 units of RBC with electrolyte, then whole blood or RBC with plasma; postoperative patients were given crystalloids and whole blood) plus 20% human albumin solution 100 mL at end of operation, 200 mL to 300 mL on same day, then 200 mL on first postoperative day, then 100 mL for next 3 days (n = 15)
2. Standard volume replacement regimen (as above) (n = 15)

#### Outcomes
- Deaths reported
- Haemodynamic variables

#### Notes
- Length of follow-up unspecified

### Risk of bias

<table>
<thead>
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<tbody>
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<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>
### Zetterstrom 1981b

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

#### Risk of bias

<table>
<thead>
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</table>

### Zhu 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>135 participants with severe sepsis</td>
</tr>
</tbody>
</table>
| Interventions | 1. 7.5% Hypertonic saline plus 6% HES 130/0.4 (n = 45)  
2. Ringer's lactate plus 6% HES 130/0.4 (n = 45)  
3. Ringer's lactate (n = 45) |
| Outcomes | Biomarkers, fluid requirements, and MODS. Mortality was also reported |
| Notes | - |

#### Risk of bias

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</table>

ACE: angiotensin-converting enzyme; ARDS: adult respiratory distress syndrome; ASA: American Society of Anesthesiologists; bpm: beats per minute; COP: colloid osmotic pressure; CPR: cardiopulmonary resuscitation; GI: gastrointestinal; HES: hydroxyethyl starch; HR: heart rate; ICU: intensive care unit; IV: intravenous; LVEDP: left ventricular end diastolic pressure; LVEF: left ventricular ejection fraction; MODS: multiple organ dysfunction syndrome.
Characteristics of excluded studies  

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artru 1989</td>
<td>Intervention to control intracranial pressure not directed at fluid resuscitation</td>
</tr>
<tr>
<td>Bocanegra 1966</td>
<td>Study contained 2 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</td>
</tr>
<tr>
<td>Boldt 1996</td>
<td>All groups received some colloid</td>
</tr>
<tr>
<td>Boldt 2007</td>
<td>Comparison was not between colloids and crystalloids, rather 2 different colloid solutions</td>
</tr>
<tr>
<td>Bothner 1998</td>
<td>Participants were having minor elective surgery, therefore not considered to be critically ill</td>
</tr>
<tr>
<td>Breheme 1993</td>
<td>Intervention directed at haemodilution, not at volume replacement</td>
</tr>
<tr>
<td>Bueno R 2004</td>
<td>The participants had elective surgery</td>
</tr>
<tr>
<td>Chin 2006</td>
<td>Participants were undergoing elective surgery, therefore not considered to be critically ill</td>
</tr>
<tr>
<td>Golub 1994</td>
<td>Albumin given solely as a nutritional supplement</td>
</tr>
<tr>
<td>Goslinga 1992</td>
<td>Intervention directed at haemodilution, not volume replacement</td>
</tr>
<tr>
<td>Green 2008</td>
<td>Article is a review</td>
</tr>
<tr>
<td>Greenhalgh 1995</td>
<td>Intervention directed at the maintenance of serum albumin levels, not for volume replacement</td>
</tr>
<tr>
<td>Hauser 1980</td>
<td>Cross-over trial</td>
</tr>
<tr>
<td>Ko 2007</td>
<td>Comparison of crystalloids and colloids as pre-loading solutions</td>
</tr>
<tr>
<td>Krasheninnikov 2007</td>
<td>Not an RCT</td>
</tr>
<tr>
<td>Lagonidis 1995</td>
<td>Intervention was pre-loading for coronary artery bypass surgery</td>
</tr>
<tr>
<td>Lange 2011</td>
<td>Article was a review</td>
</tr>
<tr>
<td>Lobo 2008</td>
<td>Experiment conducted on rabbits</td>
</tr>
<tr>
<td>Marhofer 1999</td>
<td>Trial of fluid for pre-loading before spinal anaesthesia</td>
</tr>
<tr>
<td>Study</td>
<td>Summary</td>
</tr>
<tr>
<td>-------</td>
<td>---------</td>
</tr>
<tr>
<td>Mittermayr 2007</td>
<td>Patients were undergoing elective surgery</td>
</tr>
<tr>
<td>Mittermayr 2008</td>
<td>Outcome was the change in concentration of tissue-type plasminogen activator</td>
</tr>
<tr>
<td>Morrison 2011</td>
<td>Study evaluated the effect of hypertonic saline in patients with blunt head injury</td>
</tr>
<tr>
<td>Niemi 2008</td>
<td>Solutions were used for pump priming</td>
</tr>
<tr>
<td>Nilsson 1980</td>
<td>Albumin given as a nutritional supplement</td>
</tr>
<tr>
<td>Oliviera 2002</td>
<td>The participants had sepsis</td>
</tr>
<tr>
<td>Paton-Gay 2007</td>
<td>The outcome was non-relevant to comparing crystalloids and colloids</td>
</tr>
<tr>
<td>Paul 2003</td>
<td>The participants had elective surgery</td>
</tr>
<tr>
<td>Rehm 2001</td>
<td>2 colloids (albumin and hetastarch) compared</td>
</tr>
<tr>
<td>Steinberg 1989</td>
<td>Cross-over trial</td>
</tr>
<tr>
<td>Tiryakioglu 2008</td>
<td>Patients were undergoing elective surgery and not considered critically ill. Also, the solutions were used as priming solutions</td>
</tr>
<tr>
<td>Tseng 2008</td>
<td>Crystalloid and colloid treatment was not randomised</td>
</tr>
<tr>
<td>Valetova 2007</td>
<td>Patients were randomised depending upon their treatment not prior to treatment</td>
</tr>
<tr>
<td>van der Heijden 2009</td>
<td>The report did not provide separate data for the 3 arms that received colloids (gelatin 4%, hydroxyethyl starch 6% and albumin 5%)</td>
</tr>
<tr>
<td>Vercueil 2006</td>
<td>Article is a review</td>
</tr>
<tr>
<td>Wilkes 2001</td>
<td>1 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 1 of these with patients who had the other</td>
</tr>
<tr>
<td>Woods 1993</td>
<td>This quasi-randomised trial looked at albumin supplementation in postoperative 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</td>
</tr>
</tbody>
</table>
**Characteristics of ongoing studies**  
*ordered by study ID*

### CHEST Trial

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Crystalloid Versus Hydroxyethyl Starch Trials (CHEST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Multicentre phase 3 RCT of fluid resuscitation</td>
</tr>
<tr>
<td>Participants</td>
<td>7000 patients in ICU requiring fluid resuscitation</td>
</tr>
</tbody>
</table>
| Interventions       | 1. 6% HES (130/0.4)  
2. Saline             |
| Outcomes            | 90 days all-cause mortality                          |
| Starting date       | December 2009                                        |
| Contact information | John A Myburgh, The George Institute, Sydney, New South Wales, Australia |
| Notes               | NCT00935168                                          |

### RASP trial

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Lactated Ringer Versus Albumin in Early Sepsis Therapy (RASP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>RCT</td>
</tr>
<tr>
<td>Participants</td>
<td>360 patients with severe sepsis or septic shock</td>
</tr>
</tbody>
</table>
| Interventions       | 1. Ringer's lactate  
2. 4% Albumin          |
| Outcomes            | 28 days all-cause mortality                                    |
| Starting date       | May 2012                                                       |
| Contact information | Juliano P Almeida, Cancer Institute of Sao Paulo, School of Medicine, University of Sao Paulo |
| Notes               | NCT01337934                                                    |

### The 6S trial

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Scandinavian Starch for Severe Sepsis/Septic Shock Trial (6S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Multicentre, randomised, double-blinded trial with concealed allocation</td>
</tr>
<tr>
<td>Participants</td>
<td>800 patients with severe sepsis in 30 Scandinavian ICUs</td>
</tr>
</tbody>
</table>
### The 6S trial *(Continued)*

| Interventions | 1. 6% HES 130/0.4 in Ringer’s acetate  
|               | 2. Ringer’s acetate |

| Outcomes | The composite end point of 90-day mortality or end-stage kidney failure is the primary outcome measure |

| Starting date | December 2009 |

| Contact information | Anders Perner, ICU, Rigshospitalet, University of Copenhagen |

| Notes | NCT00962156 |

HES: hydroxyethyl starch; ICU: intensive care unit; RCT: randomised controlled trial.