

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

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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 on mortality of colloids compared to crystalloids for fluid resuscitation in critically ill patients.

### Search strategy

We searched the Injuries Group specialised register, Cochrane Controlled Trials Register, MEDLINE, EMBASE and BIDS Index to Scientific and Technical Proceedings, and checked reference lists of trials and review articles.

### Selection criteria

All randomised and quasi-randomised trials of colloids compared to crystalloids, in patients requiring volume replacement. Cross-over trials and trials in pregnant women and neonates were excluded.

### Data collection and analysis

Two reviewers independently extracted data and rated quality of allocation concealment. Trials with a 'double-intervention', such as those comparing colloid in hypertonic crystalloid to isotonic crystalloid, were analysed separately. The analysis was stratified according to colloid type and quality of allocation concealment.

### Main results

#### *Colloids compared to crystalloids*

Albumin or plasma protein fraction. Nineteen trials reported data on mortality, including a total of 7576 patients. The pooled relative risk (RR) from these trials was 1.02 (95% confidence interval [95% CI] 0.93 to 1.11). When the trial with poor quality allocation concealment was excluded, pooled RR was 1.01 (95% CI 0.92 to 1.10).

Hydroxyethyl starch. Ten trials compared hydroxyethyl starch with crystalloids, including a total of 374 randomised participants. The pooled RR was 1.16 (95% CI 0.68 to 1.96).

Modified gelatin. Seven trials compared modified gelatin with crystalloid, including a total of 346 randomised participants. The pooled RR was 0.54 (95% CI 0.16 to 1.85).

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

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

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

### Authors' conclusions

There is no evidence from randomised controlled trials 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 randomised controlled trials.

## PLAIN LANGUAGE SUMMARY

No evidence that colloids are more effective than crystalloids in reducing mortality in people who are critically ill or injured

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

## BACKGROUND

Fluid resuscitation for hypovolaemia is a mainstay of the medical management of critically ill patients, whether as a result of trauma, burns, major surgery or sepsis. Although recent studies (Bickell 1994) have suggested that the timing of volume replacement deserves careful consideration, when it comes to selecting the resuscitation fluid clinicians are faced with a range of options. At one level the choice is between a colloid or crystalloid solution. Colloids are widely used, having been recommended in a number of resuscitation guidelines and intensive care management algorithms (Vermeulen 1995; Armstrong 1994). The US Hospital Consortium Guidelines recommend that colloids are used in haemorrhagic shock prior to the availability of blood products, and in non-haemorrhagic shock following an initial crystalloid infusion. A 1995 survey of US academic health centres, however, found that the use of colloids far exceeded even the Hospital Consortium recommendations (Yim 1995). Surveys of burn care in the US (Fakhry 1995) and in Australia (Victorian DUAC 1991) found that the use of colloids for resuscitation varied without a set pattern. The choice of fluid has considerable cost implications. Volume replacement with colloids is considerably more expensive than with crystalloids. Clinical studies have shown that colloids and crystalloids have different effects on a range of important physiological parameters. Because of these differences, all-cause mortality is arguably the most clinically relevant outcome measure in randomised trials comparing the two fluid types. Although there have been previous meta-analyses of mortality in randomised trials comparing colloids and crystalloids (Velanovich 1989, Bissonni 1991), 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 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 determine the effects on mortality of using colloids compared to crystalloids, during fluid resuscitation in critically ill patients.

## 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 or quasi-random allocation. As the comparison between fluid type was in terms of effects on mortality, randomised cross-over trials were excluded.

### Types of participants

Critically ill patients (excluding neonates) who required volume replacement. Types of participants included were those who were critically ill as a result of trauma, burns, were undergoing surgery, or had other critical conditions such as complications of sepsis.

Preoperative elective surgical patients were excluded.

### Types of intervention

The colloids considered were 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, it was excluded. 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. Trials where both groups received blood were included.

Trials of fluids used for other purposes were excluded. For example, trials of pre-loading in preparation for elective surgery, and trials in patients undergoing fluid loading before cardiopulmonary bypass, were excluded.

### 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

See: methods used in reviews.

MEDLINE: latest search, September 2002.

- #1 colloid\*
- #2 albumin\*
- #3 ppf
- #4 dextran
- #5 gelatin\*
- #6 gentran\*
- #7 haemaccel\*
- #8 hemaccel\*
- #9 pentastarch
- #10 pentaspan
- #11 hetastarch
- #12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
- #13 crystalloid\*
- #14 ringer\*
- #15 hartman\*
- #16 sodium\*
- #17 potassium\*
- #18 salin\*
- #19 #13 or #14 or #15 or #16 or #17 or #18
- #20 fluid
- #21 therapy
- #22 fluid near2 therapy
- #23 volume
- #24 restor\*
- #25 volume near2 restor\*
- #26 fluid
- #27 resuscit\*
- #28 restor\*
- #29 therap\*
- #30 fluid near2 (resuscit\* or restor\* or therap\*)

- #31 plasma
- #32 substit\*
- #33 fluid
- #34 volume
- #35 substit\*
- #36 replace\*
- #37 (plasma near2 substit\*) or ((fluid or volume) near2 (substit\* or replace\*))
- #38 #22 or #25 or #30 or #37
- #39 #12 and #19 and #38
- #40 controlled
- #41 clinical
- #42 trial\*
- #43 controlled clinical trial\*
- #44 randomi\*
- #45 controlled
- #46 trial\*
- #47 randomi\* controlled trial\*
- #48 explode research design/ all subheadings
- #49 double
- #50 blind
- #51 double blind
- #52 meta
- #53 analysis
- #54 metaanalysis
- #55 meta analysis or metaanalysis
- #56 clinical trial in pt
- #57 #43 or #47 or #48 or #51 or #55 or #56
- #58 #39 and #57

The reference lists of all identified trials and review articles were checked, and we contacted the trialists, to ask if any studies had been missed.

The update of the Injuries Group review on Human albumin (Albumin 2004) also found new papers that were relevant for this review. The major SAFE trial (SAFE 2004) was published after the search was done but, the reviewers being aware of its publication, it was also considered and was found to meet the inclusion criteria.

Full details of the search strategies used can be obtained from the Injuries Group Trials Search Co-ordinator.

## METHODS OF THE REVIEW

Allocation concealment was scored as described by Schulz (Schulz 1995). In particular, the presence of solutions in identical containers was only taken to mean adequate concealment if the fluid containers were used sequentially.

Information on blinding and loss to follow-up was collected but not scored.

As a result of comments on the previous version of this review, trials were stratified by type of fluid rather than type of original injury.

Relative risk (RRs) and 95% confidence interval (95% CI) were calculated for each study using a fixed effects model. Each comparison was then inspected visually for evidence of heterogeneity and a chi-squared test performed. 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.

Trials with allocation concealment judged as inadequate were then excluded and the calculations repeated.

## DESCRIPTION OF STUDIES

There were 53 trials meeting the inclusion criteria for study design, participants and interventions. We were able to obtain data on deaths for 46 of these. Details of the remaining trials are also reported in the Table of Included Studies for completeness.

Reasons for exclusion of trials were: the use of a cross-over design, testing a resuscitation algorithm, giving the control group oral fluids, the intervention being directed to the maintenance of serum albumin levels, for haemodilution, for fluid loading and for the reduction of intracranial pressure (see Table of Excluded Studies).

Of the 46 randomised controlled trials with data on deaths, the quality of allocation concealment was adequate in six trials and unclear in most of the others.

There were 42 comparisons of colloids and crystalloids (add-on colloid), nine comparisons of colloid in hypertonic crystalloid with isotonic crystalloid, and three comparisons of colloid with hypertonic crystalloid (see Table of Included Studies).

## METHODOLOGICAL QUALITY

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 Table of Included studies.

## RESULTS

### Colloids compared to crystalloids

#### *Albumin or plasma protein fraction*

Twenty trials reported data on mortality, including a total of 7576 patients. The pooled RR from these trials was 1.02 (95% CI 0.93

to 1.11). When the one trial with poor quality allocation concealment (Lucas 1978) was excluded, the pooled RR was 1.01 (95% CI 0.92 to 1.01).

#### *Hydroxyethyl starch*

Ten trials compared hydroxyethyl starch with crystalloids, including a total of 374 randomised participants. The pooled RR was 1.16 (95% CI 0.68 to 1.96).

#### *Modified gelatin*

Seven trials compared modified gelatin with crystalloid, including a total of 346 randomised participants. The pooled RR was 0.54 (95% CI 0.16 to 1.85).

#### *Dextran*

Nine trials compared dextran with a crystalloid, including a total of 834 randomised participants. 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. Its relative risk of death was 0.50 (0.06 to 4.33).

Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised participants. The pooled RR was 0.88 (0.74 to 1.05).

### Colloids in isotonic crystalloid compared to hypertonic crystalloid

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

## DISCUSSION

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

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

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

As regards the effects of albumin versus crystalloid, most of the information (as indicated by the weighting in the meta-analysis) was provided by the SAFE trial. 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 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 relative risk for death with albumin in this updated meta-analysis is now 1.02 (0.93 to 1.11). It is important to note that the effect estimate from the SAFE trial is entirely consistent with the results of previous trials of albumin in hypovolaemia and there is no significant heterogeneity ( $I^2 = 0\%$ ,  $p = 0.46$ ).

The results of this updated meta-analysis have important policy implications. There is still no evidence that colloids are superior to crystalloids as a treatment for intravascular volume resuscitation in critically ill patients. Importantly, the SAFE trial also provided no evidence of any other clinical advantages from using albumin. It also debunked the belief, from pathophysiological inference, that very large volumes of crystalloid must be administered to reach the same resuscitation end-points as can be achieved using much

smaller volumes of colloid. In the SAFE trial, the ratio of albumin administered to saline administered was approximately 1:1.4. Colloids, in particular albumin, are considerably more expensive than crystalloids, and albumin is a blood product and so carries at least a theoretical infectious disease risk. The economic opportunity cost of on-going colloid use, particularly albumin use, is likely to be considerable and for this reason its on-going use in this context is unjustified.

## AUTHORS' CONCLUSIONS

### Implications for practice

There is no evidence from randomised controlled trials 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 randomised controlled trials in subsets of patients of particular concern, can be justified.

### Implications for research

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

## POTENTIAL CONFLICT OF INTEREST

None known.

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- \* Indicates the major publication for the study*

## TABLES

### Characteristics of included studies

Study	Boldt 1986
Methods	Randomised controlled trial, 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 aorto-coronary bypass surgery. Exclusion criteria were ejection fraction < 50% and LVEDP > 15 mmHg.
Interventions	1) 300ml 20% human albumin solution (n=15). 2) 500ml 3% hydroxyethylstarch (n=13). 3) 500ml 3.5% gelatine (n= 14). 4) No colloid (n=13).
Outcomes	Haemodynamic variables were measured. Deaths not reported.
Notes	Follow-up until discharge from intensive care.
Allocation concealment	B – Unclear
Study	Boldt 1993
Methods	Randomised controlled trial. Allocation concealment by sealed opaque envelopes (information from author).

**Characteristics of included studies (Continued)**

	Blinding and loss to follow-up not mentioned.
Participants	75 men undergoing elective aortocoronary bypass grafting, who had a pulmonary capillary wedge pressure of less than 5 mmHg after induction of anaesthesia.
Interventions	1) 5% albumin (n=15). 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 post-op.
Outcomes	Deaths not reported, author confirmed there were no deaths.
Notes	Follow-up to 1 day.
Allocation concealment	B – Unclear

**Study Boldt 2001**

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

**Study Boutros 1979**

Methods	Randomised controlled trial ("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.
Notes	Follow-up to discharge from hospital.
Allocation concealment	B – Unclear

**Study Bowser-Wallace 1986**

Methods	Quasi-randomised controlled trial (allocation by alternation). Blinding not mentioned.
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**Characteristics of included studies (Continued)**

	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) 2ml/kg/%burn Ringer's lactate over 24 hrs, then 0.5ml plasmanate/kg/%burn over 24 hrs plus 5% dextrose (n=19). 2) 2ml/kg/%burn hypertonic lactated saline over 24 hrs, then 0.6ml/kg/%burn hypertonic lactated saline over 24 hrs plus oral Haldane's solution. (n=19) IV fluids stopped at 48 hrs (n=19).
Outcomes	Deaths reported. Fluid and electrolytes given, weight, haematocrit.
Notes	Follow-up to 5 days.
Allocation concealment	C – Inadequate

**Study Chavez-Negrete 1991**

Methods	Randomised controlled trial (allocation by "random" numbers). Blinding not mentioned. No loss to follow-up.
Participants	Adults admitted to an emergency room with acute gastrointestinal haemorrhage, systolic blood pressure 90 mmHg or less for up to 1 hr and normal electrocardiograph. Excluded if pregnant or had renal, cardiac or neurological disease.
Interventions	1) Initial infusion of 250ml 7.5% saline/6% Dextran 60 given IV (16 patients) or intraosseous (n=10). 2) Initial IV infusion of 250ml 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.
Allocation concealment	B – Unclear

**Study Dawidson 1991**

Methods	Randomised controlled trial (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 hrs after operation, guided by haemodynamic variables.
Outcomes	Death. Volume transfused, weight change, haemodynamic variables.
Notes	Follow-up to discharge from hospital.
Allocation concealment	C – Inadequate

**Study Dehne 2001**

Methods	Randomised controlled trial; allocation by sealed envelope assignment.
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### Characteristics of included studies (Continued)

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

#### Study **Eleftheriadis 1995**

Methods	Patients "randomizedly distributed". Blinding not mentioned. Unable to assess loss to follow-up.
Participants	Participants were undergoing coronary artery bypass surgery.
Interventions	1) 6% hydroxyethylstarch. 2) 3.5% gelatine. 3) Ringer's lactate Allocated fluid was used in the post-operative period only guided by mean arterial pressure.
Outcomes	Deaths were not reported. Haemodynamic variables.
Notes	Follow-up period unspecified.
Allocation concealment	B – Unclear

#### Study **Ernest 1999**

Methods	Randomised controlled trial, allocation concealment not described. No blinding. No loss to follow-up mentioned.
Participants	Patients with a clinical diagnosis of sepsis.
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.
Allocation concealment	B – Unclear

#### Study **Evans 1996**

Methods	Quasi-randomised trial (allocation by day of the week). Blinding not mentioned. No loss to follow-up.
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**Characteristics of included studies (Continued)**

Participants	Aged 16 or more, 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.
Allocation concealment	C – Inadequate

**Study Gallagher 1985**

Methods	Randomised controlled trial. Method of allocation concealment not described. Author contacted - allocation concealment by computerised system - patient details were entered before treatment assignment was revealed. Blinding not mentioned. No loss to follow-up.
Participants	Patients after coronary artery bypass graft surgery. Exclusions: 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% hydroxyethylstarch (n=5) 3) IV Ringer's lactate (n=5). Fluid used from admission to intensive care post op, guided by PAWP. RBC given if needed. Five patients received 5% albumin. Five patients received lactated Ringer's.
Outcomes	Deaths were not reported. Author contacted and confirmed that there were no deaths in any group. Haemodynamic data.
Notes	Follow-up to 1 day.
Allocation concealment	A – Adequate

**Study Goodwin 1983**

Methods	Randomised controlled trial - 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 0.3-0.5ml/kg/%burn, then 5% dextrose.
Outcomes	Deaths reported. Lung water in some. Infections.
Notes	Follow-up to discharge from hospital.
Allocation concealment	B – Unclear



**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Grundmann 1982</b>
Methods	Randomised controlled trial. 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 19-84). 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Hall 1978</b>
Methods	Quasi-randomised controlled trial (participants were stratified by age, extent of burn and aetiology, and then allocated by alternation). Blinding not mentioned. No loss to follow-up.
Participants	Burns covering more than 10% of the body surface (for children), and more than 15% of the body surface (for adults). No exclusions mentioned.
Interventions	1) 120ml/%burn IV 6% Dextran 70 in 0.9% saline over 48 hrs plus oral water or IV 5% dextrose for 'metabolic requirements' (n=86). 2) 4ml/kg/%burn IV Ringer's lactate over 24 hrs, then 10% of initial body weight of fluid over 24 hrs plus oral water (n=86).
Outcomes	Death. Fluid given, haemodynamic variables.
Notes	Follow-up to discharge from hospital.
Allocation concealment	C – Inadequate

<b>Study</b>	<b>Hartmann 1993</b>
Methods	Randomised controlled trial (method of allocation unclear). Blinding not mentioned. No loss to Follow-up.
Participants	Adults undergoing major abdominal surgery. Exclusions: cardiorespiratory dysfunction, uraemia, diabetes, taking steroids, anticoagulants or diuretics.
Interventions	1) IV Dextran 70 in saline (concentration not given) with 2.5% dextrose. (n=15). 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. Post-operative fluids according to the trial group guided by tissue oxygen tension to the end of resuscitation.
Outcomes	Death not reported. Fluid given, haemodynamic variables.

### Characteristics of included studies (Continued)

Notes	Follow-up to 7 days.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Jelenko 1978</b>
Methods	Randomised controlled trial, 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 (240MeQ Na+, 120 MeQ chloride, 120 MeQ lactate), (n=7). 2) Hypertonic saline (240MeQ Na+, 120 MeQ chloride, 120 MeQ 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Karanko 1987</b>
Methods	Randomised controlled trial. Description of allocation procedure unclear. Blinding not mentioned. No loss to follow-up.
Participants	32 adult men scheduled for coronary artery bypass surgery. Exclusions: left ventricular ejection fraction under 40%, abnormal lung function.
Interventions	1) Colloid group received 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. Lung water.
Notes	Follow-up 2 weeks.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Lang 2001</b>
Methods	Randomised controlled trial, using a closed-envelope system.
Participants	42 patients scheduled for elective major abdominal surgery.
Interventions	1) Lactated Ringer's (n=21). 2) 6% HES, molecular weight 139kD, degree of substitution 0.4 (n=21).
Outcomes	Deaths. Haemodynamics and laboratory data. Tissue oxygenation. Volume input and output.
Notes	Follow-up period unclear.
Allocation concealment	A – Adequate

<b>Study</b>	<b>Ley 1990</b>
Methods	Randomised controlled trial.

**Characteristics of included studies (Continued)**

	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 1.5L then 5% plasma protein fraction (n=11). 2) 0.9% saline (n=10). Allocated fluid was used for post-operative fluid resuscitation.
Outcomes	Deaths were not reported. Pulmonary and peripheral oedema. Haemodynamic variables.
Notes	Follow-up to discharge.
Allocation concealment	B – Unclear

**Study Lowe 1977**

Methods	Randomised controlled trial, 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 intra-operative period.
Outcomes	Deaths reported.
Notes	Follow-up to 5 days post-operatively. Data on the 30 participants with chest injuries who were left out of the Lowe 1977 report, but included in Moss 1981, have been included in the meta-analysis.
Allocation concealment	B – Unclear

**Study Lucas 1978**

Methods	Randomised controlled trial. Randomisation was based on the last digit of each patient's case number.
Participants	52 seriously injured patients.
Interventions	1) Standard resuscitation regimen ('balanced electrolyte', blood, fresh frozen plasma) plus salt poor albumin, maximum 150g during surgery and 150g per day for the next 5 days (n=27). 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.
Allocation concealment	C – Inadequate

**Study 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 an hour of injury, who had systolic blood pressure of 90mmHg or less and were 16 years or older. 72% of participants had sustained penetrating trauma.

**Characteristics of included studies (Continued)**

Interventions	1) 250 mL Dextran-70 in 7.5% NaCl (n=211). 2) 250 mL Ringer's lactate, saline or plasmalyte. (n=211) Allocated fluid was for initial pre-hospital resuscitation only.
Outcomes	Deaths reported.
Notes	Follow-up to hospital discharge or transfer.
Allocation concealment	C – Inadequate

**Study Mazher 1998**

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

**Study McNulty 1993**

Methods	Randomised controlled trial. 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.
Allocation concealment	B – Unclear

**Study Metildi 1984**

Methods	Randomised controlled trial. Blinding not mentioned. No loss to follow-up.
Participants	Participants were admissions to an intensive care and a trauma unit with adult respiratory distress syndrome and established pulmonary failure. Included both trauma and non-trauma patients.
Interventions	1) 5% salt-poor albumin (n=20). 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.

**Characteristics of included studies (Continued)**

	Haemodynamic variables.
Notes	Follow-up to discharge.
Allocation concealment	B – Unclear
<b>Study</b>	<b>Modig 1983</b>
Methods	Quasi-randomised controlled trial, allocation by admission date. Blinding not mentioned. No loss to follow-up.
Participants	Participants were trauma admissions to an emergency department with a systolic blood pressure of less than 70mmHg. Age range was 20-58 years.
Interventions	1) Dextran-70 in Ringer's lactate (n=12). 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 respiratory distress syndrome.
Notes	Follow-up to definitive reconstructive surgery.
Allocation concealment	C – Inadequate
<b>Study</b>	<b>Nagy 1993</b>
Methods	Randomised controlled trial, contact with author showed it was an open label study. Blinding not mentioned. No loss to follow-up.
Participants	Participants were adult admissions to a trauma unit, with measurable systolic blood pressure less than 90 mmHg.
Interventions	1) Pentastarch in 0.9% NaCl (n=21). 2) Ringer's lactate (n=20). Allocated fluid was used throughout resuscitation with the exception that colloid patients received a maximum 4L of pentastarch, after which Ringer's lactate was given.
Outcomes	Deaths were not reported. Haemodynamic variables.
Notes	Follow-up to discharge.
Allocation concealment	C – Inadequate
<b>Study</b>	<b>Ngo 2001</b>
Methods	Randomised controlled trial, opaque envelopes containing only treatment pack number.
Participants	230 children with dengue shock syndrome.
Interventions	1) Dextran 70 (n=55). 2) 3% gelatine (n=56). 3) Lactated Ringer's (n=55). 4) 'Normal' saline (n=56).
Outcomes	Initial pulse recovery time. Occurrence of timing and subsequent episodes of shock. Fall in haematocrit. Volume of fluid administered till recovery. Complications.

**Characteristics of included studies (Continued)**

	And noted that there were no deaths in any group
Notes	Follow-up period unclear.
Allocation concealment	A – Adequate
<b>Study</b>	<b>Nielsen 1985</b>
Methods	Randomised controlled trial. 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 80g albumin on the day of the operation, and 20g per day for the next 3 days. Albumin given as 100mL 20% human albumin solution. (n=13) 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.
Allocation concealment	B – Unclear
<b>Study</b>	<b>Pockaj 1994</b>
Methods	Randomised controlled trial, 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 boluses of 5% albumin in saline (n=36 reported). 2) 250 mL boluses of 0.9% normal saline. (n=40 reported) Boluses guided by haemodynamic variables. Both groups also received 0.45% saline with 10mmol/L KCl.
Outcomes	Deaths. Toxic effects of chemotherapy. Haemodynamic variables.
Notes	
Allocation concealment	B – Unclear
<b>Study</b>	<b>Prien 1990</b>
Methods	Randomised controlled trial. Blinding not mentioned. No loss to Follow-up.
Participants	Participants were undergoing modified Whipple's operation.
Interventions	1) 10% hydroxyethyl starch in 0.9% saline plus plasma protein fraction if requirements > 20mL/kg. (n=6) 2) 20% human albumin solution. (n=6) 3) Ringer's lactate. Allocated fluid was administered intra-operatively only.
Outcomes	Deaths. Intestinal oedema formation.
Notes	Follow-up period was unspecified.

## Characteristics of included studies (Continued)

Allocation concealment B – Unclear

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<b>Study</b>	<b>Rackow 1983</b>
Methods	Randomised controlled trial, allocation concealment unclear. Blinding not mentioned. No loss to follow-up.
Participants	Participants were aged 54 to 97, and had any one of the following pre-determined indicators of shock: systolic blood pressure of 90 mmHg or less, a cardiac index of less than 2.2 L./min.m <sup>2</sup> , a serum arterial lactate greater than 18mg/dl and WP less than 15mmHg.
Interventions	1) 6% hydroxoethyl starch (n=9). 2) 5% albumin (n=9). 3) 0.9% saline. (n=8). Allocated fluid was given as needed until the end of resuscitation.
Outcomes	Deaths reported. Fluid balance.
Notes	Follow-up to discharge from hospital.
Allocation concealment	B – Unclear

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

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<b>Study</b>	<b>SAFE 2004</b>
Methods	Randomised controlled trial. Randomisation by minimisation algorithm accessed through secure website
Participants	Patients aged 18 years and above admitted to closed multidisciplinary intensive care units in 16 tertiary hospitals in Australia over 19-month period
Interventions	1) 4% albumin (Albumex, CSL) (n=3499). 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.
Allocation concealment	A – Adequate

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<b>Study</b>	<b>Shah 1977</b>
Methods	Randomised controlled trial. Allocation by sealed envelope. Blinding not mentioned. No loss to follow-up.

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**Characteristics of included studies (Continued)**

Participants	Patients with severe, multiple trauma and a systolic blood pressure of less than 90mmHg. All patients were adults and both sexes were included.
Interventions	1) 5% salt-poor albumin in Ringer's lactate (n=9). 2) Ringer's lactate (n=11). Volume infused guided by physiological parameters.
Outcomes	Death reported. Haemodynamic variables.
Notes	Length of follow-up not stated.
Allocation concealment	B – Unclear

**Study Shires 1983**

Methods	Patients 'assigned randomly'. Blinding not mentioned. No loss to follow-up.
Participants	People undergoing aortic reconstruction surgery. No exclusion criteria mentioned.
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	Lung water. Haemodynamic variables. Death.
Notes	Follow-up to two days post-op.
Allocation concealment	B – Unclear

**Study Siriex 1999**

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

**Study Skillman 1975**

Methods	Randomised controlled trial, allocation concealment unclear. Blinding not mentioned.
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**Characteristics of included studies (Continued)**

	No loss to Follow-up.
Participants	Participants were undergoing elective abdominal reconstructive surgery.
Interventions	1) 25% salt-poor albumin 1g/kg and 5% albumin 1L. (n=7) 2) Ringer's lactate. Allocated fluid was given intra-operatively. All patients received crystalloids only for pre-loading before surgery.
Outcomes	Deaths were not reported.
Notes	
Allocation concealment	B – Unclear

<b>Study</b>	<b>Tollofsrud 1995</b>
Methods	Randomised controlled trial, allocation by sealed envelopes. Blinding not mentioned. No loss to follow-up.
Participants	Participants were adult patients in need of volume replacement during and after coronary artery bypass surgery.
Interventions	1) Haemaccel (n=10). 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Tollofsrud 1998</b>
Methods	Randomised controlled trial, allocation by sealed envelope. Described as double blind, no loss to follow-up mentioned.
Participants	Patients with three vessel coronary artery disease undergoing elective coronary artery surgery. Exclusions: LVEF<0.4, ventricular aneurysm, significant arrhythmia, diabetes, renal failure, lung disease.
Interventions	1) 4mL/kg of 75mg/mL hypertonic saline in dextran 70 60mg/mL over 30 mins (n=10). 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Vassar 1990</b>
Methods	Randomised controlled trial, 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 a systolic blood pressure below 80mmHg and were 18 years or older.

**Characteristics of included studies (Continued)**

	Pregnant women and people with preexisting cardiac, hepatic or renal disease were excluded.
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.
Allocation concealment	B – Unclear

**Study Vassar 1991**

Methods	Randomised controlled trial, 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 a systolic blood pressure of 100mmHg or less and were 18 years or older. Exclusions: preexisting cardiac renal, hepatic or neurological disease. Peripheral oedema.
Interventions	1) 4.2% dextran 70 in 7.5% saline or 6% dextran 70 in 7.5% saline. (n=83) 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 two dextran groups are combined.
Allocation concealment	A – Adequate

**Study Vassar 1993a**

Methods	Randomised controlled blind trial, 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, had systolic blood pressure 90 mmHg or less, and were 18 years or older. Exclusions: asystolic, undergoing CPR, lack sinus complex on ECG, more than 2 hours after trauma, pregnant, preexisting seizures, bleeding disorder, hepatic, cardiac or renal disease.
Interventions	1) 6% dextran 70 in 7.5% saline. (n=89) 2) 7.5% saline. (n=85) 3) 0.9% saline (n=84) Participants received 250mL 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.
Allocation concealment	A – Adequate

**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Vassar 1993b</b>
Methods	Randomised controlled trial, 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, had a systolic blood pressure of 100mmHg or less and were 18 years or older. Exclusions: asystolic, undergoing CPR, lack sinus complex on ECG, more than 2 hours after trauma, pregnant, preexisting seizures, bleeding disorder, hepatic, cardiac or renal disease.
Interventions	1) 12% dextran70 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 250mL 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.
Allocation concealment	A – Adequate

<b>Study</b>	<b>Virgilio 1979</b>
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 two and a half weeks
Allocation concealment	B – Unclear

<b>Study</b>	<b>Wahba 1996</b>
Methods	Patients 'randomly allocated'. Blinding not mentioned. Two patients excluded as they required reoperation for bleeding.
Participants	22 adult patients in need of volume replacement following coronary artery bypass surgery. Exclusions: abnormal left ventricular function, platelet active medication or heparin.
Interventions	1) Haemacell (n=10). 2) Ringer's lactate (n=10). Allocated fluid was used from the time of admission to intensive care following operation, to the end of resuscitation.
Outcomes	Deaths reported. Pulmonary oedema.

### Characteristics of included studies (Continued)

Notes Follow-up to discharge.

Allocation concealment B – Unclear

#### Study **Woittiez 1997**

Methods Randomised controlled trial, allocation concealment by sealed opaque envelopes.  
No information on blinding or loss to follow-up.

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

Interventions 1) saline (500ml/24 hr) (n=16).  
2) albumin 20% (300 ml/24h) (n=15).  
3) HES 10% (500ml/24h) for 3 days (n=27).  
Aim was to restore colloid osmotic pressure.

Outcomes Changes in fluid balance, serum albumin, COP and clinical signs of oedema were followed daily.  
Death rates supplied by the author.

Notes Length of follow-up unspecified.

Allocation concealment B – Unclear

#### Study **Wu 2001**

Methods Randomised controlled trial. No details given of randomisation method.

Participants 41 adolescent or adult patients in emergency room suffering from shock.

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

Outcomes Death  
Haemodynamic variables.

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

Allocation concealment B – Unclear

#### Study **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, who had a systolic blood pressure of less than 80mmHg and were 19 years and older.  
Exclusions: pregnant, preexisting 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 250mL, followed by isotonic crystalloids as needed.

Outcomes Deaths reported.  
Fluid balance.

Notes Follow-up to discharge from hospital.

Allocation concealment B – Unclear

**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Younes 1994</b>
Methods	Trial conducted in a 'double blind randomised fashion'. Blinding by use of coded, identical containers.
Participants	Participants were trauma admissions to the emergency room requiring treatment for haemorrhagic hypovolaemia; all were over 15 years old. Exclusions: 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 intravenous infusion only.
Outcomes	Deaths reported. Complications.
Notes	Follow-up period was 30 days.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Younes 1998</b>
Methods	Randomised controlled trial, allocation by sealed envelope. Blinding not mentioned, no apparent loss to follow-up.
Participants	Trauma patients with systolic blood pressure <90mmHg admitted to the emergency room, with no previous treatment.
Interventions	1) 10% pentastarch (n=12). 2) 0.9% saline (n=11). Fluid given in 250mL boluses until systolic blood pressure >100mmHg
Outcomes	Deaths reported. No complications reported in either group.
Notes	Follow-up to 24 hours.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Zetterstrom 1981a</b>
Methods	The patients were randomly divided into two groups. Allocation concealment was by sealed opaque envelopes (information supplied by author). Blinding not mentioned. No loss to follow-up.
Participants	Adult patients undergoing elective major abdominal surgery.
Interventions	1) Standard volume replacement regimen (1L Dextran 70 then up to 4 units of RBC with electrolyte, then whole blood or RBC with plasma; post-op patients were given crystalloids and whole blood) plus 20% human albumin solution 100ml at end of operation, 200-300ml on same day, then 200ml on first post-op day, then 100ml for next 3 days (n=15). 2) Standard volume replacement regimen as above (n=15).
Outcomes	Deaths reported. Haemodynamic variables.
Notes	Length of follow-up unspecified.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Zetterstrom 1981b</b>
Methods	The patients were randomly divided into two groups. Allocation concealment was by sealed opaque envelopes (information supplied by 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.
Allocation concealment	B – Unclear
COP = colloid osmotic pressure	
HES = hydroxyethylstarch	
LVEDP = left ventricular end diastolic pressure	
LVEF = left ventricular ejection fraction	
RBC = red blood cells	
PAWP = pulmonary artery wedge pressure	
PAP = pulmonary artery pressure	
WP = wedge pressure	

### Characteristics of excluded studies

Study	Reason for exclusion
Artru 1989	Intervention to control intracranial pressure not directed at fluid resuscitation.
Bocanegra 1966	This study contained two quasi-randomised comparisons of colloid with glucose and plasma/saline with saline. In both studies, the control solution was only given IV if the patient was in coma or shock. It was therefore not a reasonable comparison of colloid and crystalloid.
Boldt 1996	All groups received some colloid.
Bothner 1998	Participants were having minor elective surgery, therefore not considered to be critically ill.
Breheme 1993	Intervention directed at haemodilution, not at volume replacement.
Golub 1994	Albumin given solely as a nutritional supplement.
Goslinga 1992	Intervention directed at haemodilution, not volume replacement.
Greenhalgh 1995	Intervention directed at the maintenance of serum albumin levels, not for volume replacement.
Hauser 1980	Cross-over trial.
Lagonidis 1995	Intervention was pre-loading for coronary artery bypass surgery.
Marhofer 1999	Trial of fluid for preloading before spinal anaesthesia.
Nilsson 1980	Albumin given as a nutritional supplement.
Rehm 2001	Two colloids (albumin and hetastarch) compared.
Steinberg 1989	Cross-over trial.
Wilkes 2001	One group received saline plus hetastarch; the other received 'balanced' fluid plus hetastarch. Thus, each group received both a colloid and a crystalloid. This conflicts with the purpose our review which compares patients who had one of these with patients who had the other.
Woods 1993	This quasi-randomised trial looked at albumin supplementation in post operative patients, with the aim of maintaining the serum albumin. Since the main aim of giving albumin was not to replace volume, the study was excluded.

## Characteristics of excluded studies (*Continued*)

### ANALYSES

#### Comparison 01. colloid vs crystalloid (add-on colloid)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 deaths			Relative Risk (Fixed) 95% CI	Subtotals only

#### Comparison 02. colloid and hypertonic crystalloid vs isotonic crystalloid

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 deaths			Relative Risk (Fixed) 95% CI	Subtotals only

#### Comparison 03. colloid vs hypertonic crystalloid

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 deaths			Relative Risk (Fixed) 95% CI	Subtotals only

### INDEX TERMS

#### Medical Subject Headings (MeSH)

Colloids [\*therapeutic use]; Critical Illness [\*therapy]; Fluid Therapy [\*methods]; Plasma Substitutes [\*therapeutic use]; Randomized Controlled Trials; \*Rehydration Solutions; Resuscitation [methods]

#### MeSH check words

Humans

### COVER SHEET

<b>Title</b>	Colloids versus crystalloids for fluid resuscitation in critically ill patients
<b>Authors</b>	Roberts I, Alderson P, Bunn F, Chinnock P, Ker K, Schierhout G
<b>Contribution of author(s)</b>	<p>For the first version of this review, all work was by Schierhout and Roberts. The review has been updated in the light of post-publication comments in the British Medical Journal, and the search has been updated with help from Reinhard Wentz of the Cochrane Injuries Group.</p> <p>For the updated review, Alderson and Roberts examined trials for inclusion or exclusion, reaching agreement by discussion. Alderson and Bunn rechecked all the extracted data from the original review and any new studies. Roberts and Alderson amended the text of the review.</p>
<b>Issue protocol first published</b>	1997/4
<b>Review first published</b>	1997/4
<b>Date of most recent amendment</b>	24 August 2005
<b>Date of most recent SUBSTANTIVE amendment</b>	24 August 2004
<b>What's New</b>	<p>August 2004</p> <p>Six new studies have been included (Boldt 2001; Dehne 2001; Lang 2001; Ngo 2001; SAFE 2004; Wu 2001), and the analysis, results and discussion updated accordingly.</p>

An updated search for new trials was last conducted in September 2002 (SAFE 2004 was identified separately). The electronic searches will be updated again shortly, to identify any further trials since 2002.

**Date new studies sought but none found** Information not supplied by author

**Date new studies found but not yet included/excluded** Information not supplied by author

**Date new studies found and included/excluded** 24 August 2004

**Date authors' conclusions section amended** Information not supplied by author

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## GRAPHS AND OTHER TABLES

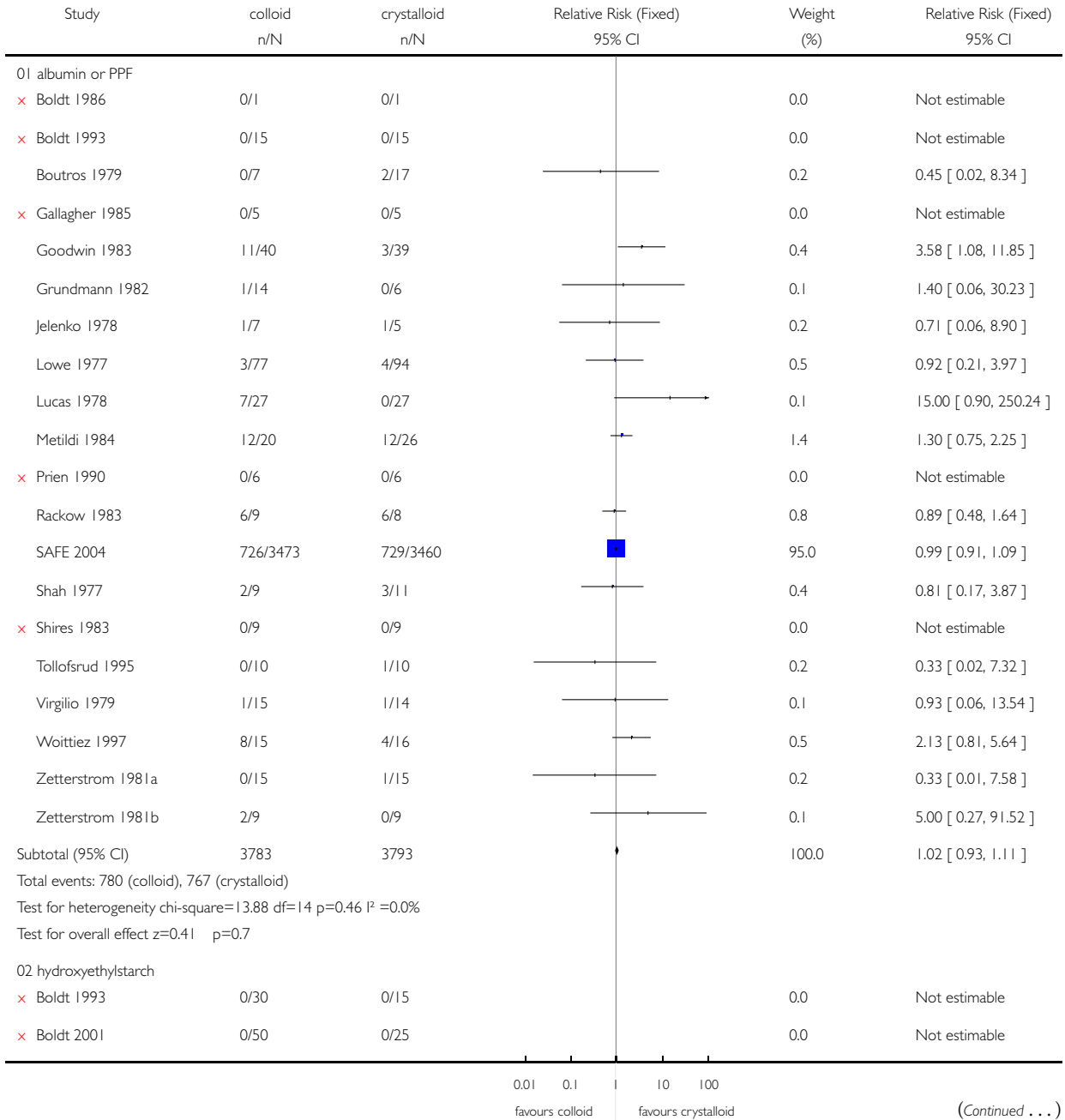


### Analysis 01.01. Comparison 01 colloid vs crystalloid (add-on colloid), Outcome 01 deaths

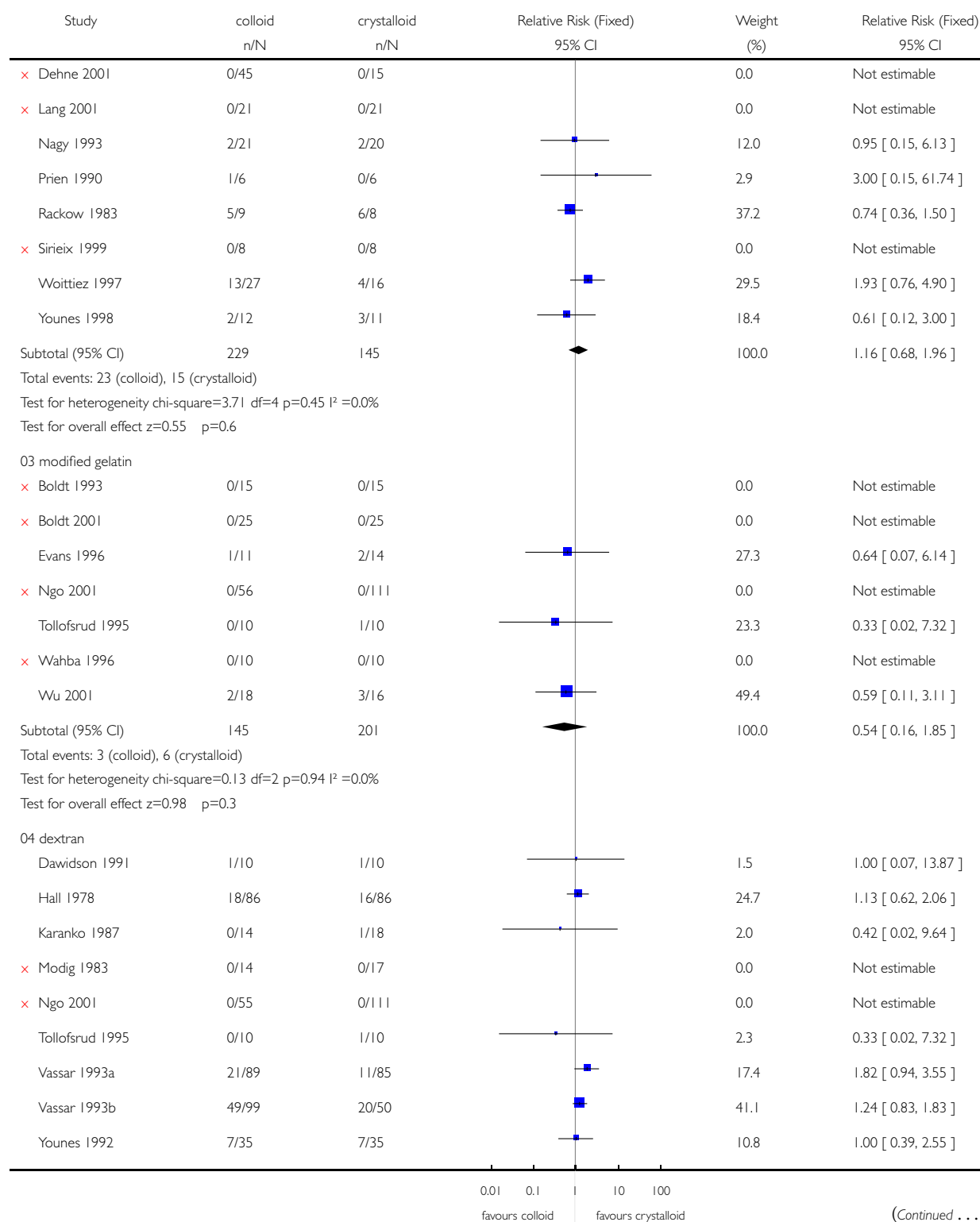
Review: Colloids versus crystalloids for fluid resuscitation in critically ill patients

Comparison: 01 colloid vs crystalloid (add-on colloid)

Outcome: 01 deaths

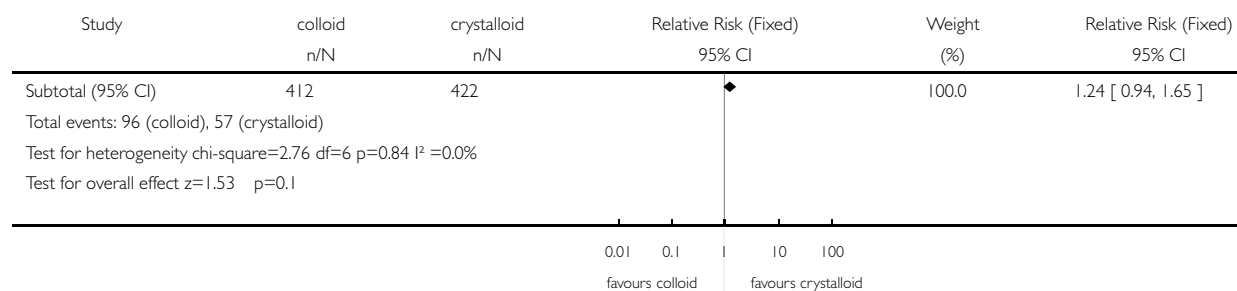


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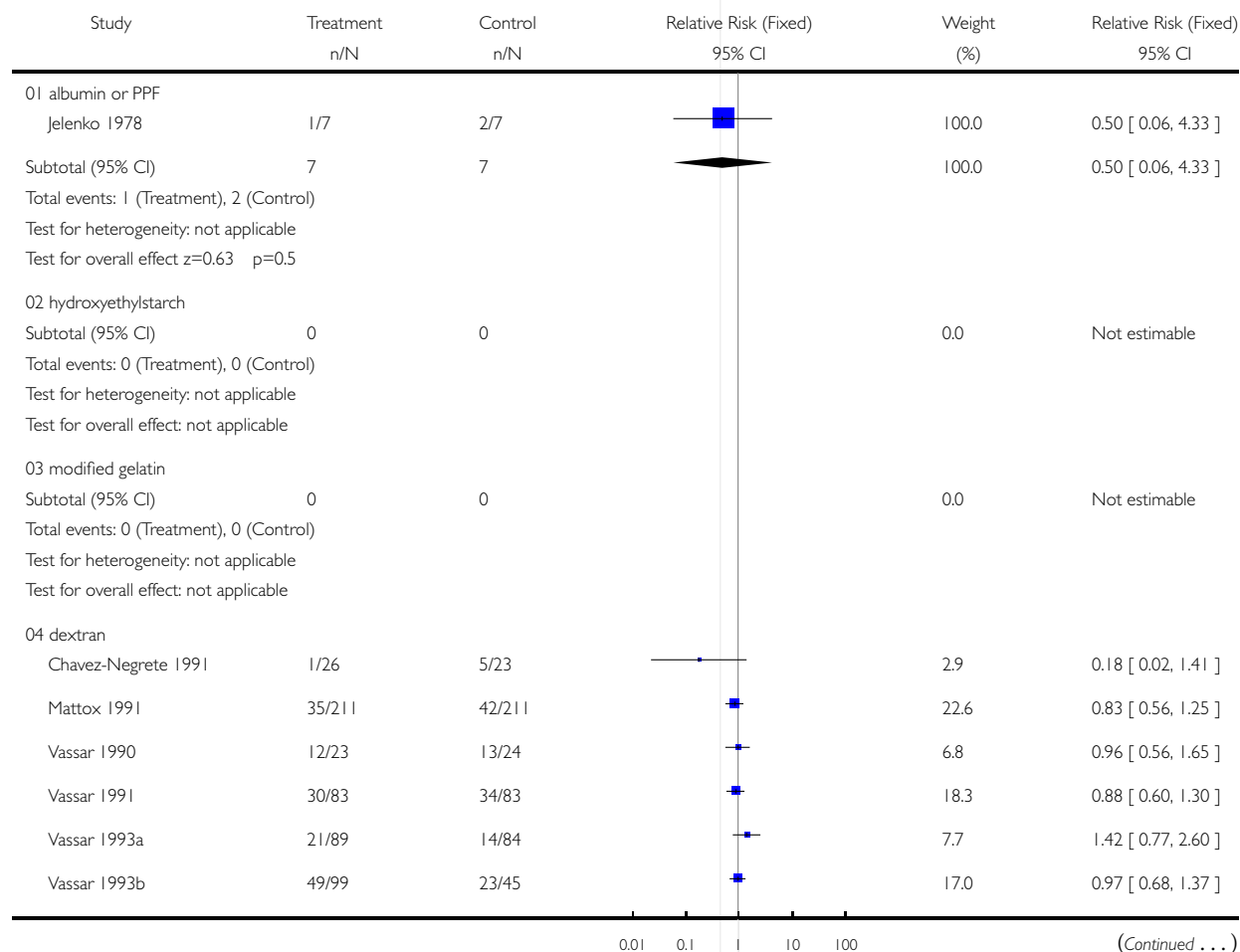


### Analysis 02.01. Comparison 02 colloid and hypertonic crystalloid vs isotonic crystalloid, Outcome 01 deaths

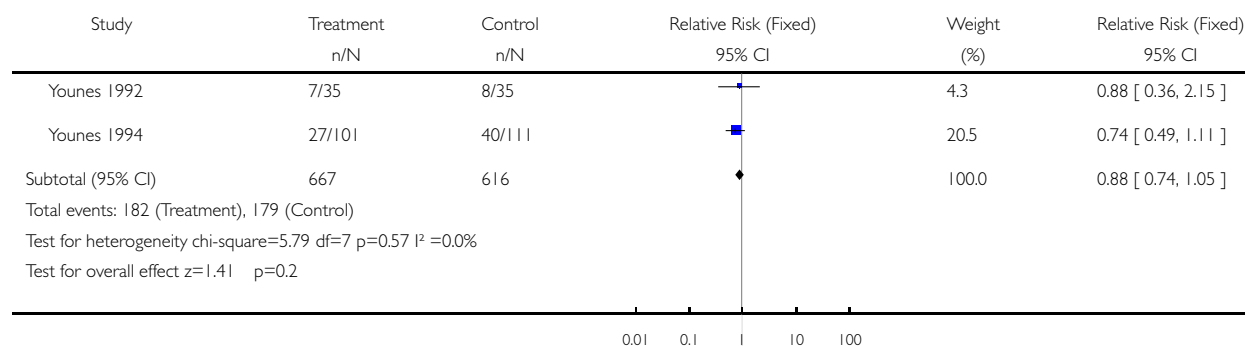
Review: Colloids versus crystalloids for fluid resuscitation in critically ill patients

Comparison: 02 colloid and hypertonic crystalloid vs isotonic crystalloid

Outcome: 01 deaths



(... Continued)



### Analysis 03.01. Comparison 03 colloid vs hypertonic crystalloid, Outcome 01 deaths

Review: Colloids versus crystalloids for fluid resuscitation in critically ill patients

Comparison: 03 colloid vs hypertonic crystalloid

Outcome: 01 deaths

