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

Schierhout G, Roberts I, Alderson P, Bunn F.

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[Intervention Review]

Colloids versus crystalloids for fluid resuscitation in critically ill patients

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ABSTRACT

Objectives

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

Search methods

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

Selection criteria

All randomised and quasi-random 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, which compared 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: Thirty-four trials reported data on mortality, including a total of 1537 patients. Eighteen trials examined the effect on mortality of resuscitation with albumin or plasma protein fraction compared with crystalloid. The pooled relative risk from these trials was 1.52 (95% confidence interval 1.08 to 2.13). The risk of death in the albumin treated group was 6% higher than in the crystalloid treated group (1% to 11%). When trials with poor quality allocation concealment were excluded the pooled relative risk was 1.34 (0.95 to 1.89).

Hydroxyethylstarch: Five trials compared hydroxyethylstarch with crystalloids including a total of 158 randomised participants. The pooled relative risk was 1.28 (0.73 to 2.24).

Modified gelatin: Three trials compared modified gelatin with crystalloids including a total of 70 randomised participants. The pooled relative risk was 0.33 (0.02 to 7.32).

Dextran: Eight trials compared dextran with a crystalloid including a total of 668 randomised participants. The pooled relative risk was 1.24 (0.94 to 1.65).

Colloids in hypertonic crystalloid compared to isotonic crystalloid:

One trial compared albumin in hypertonic saline with isotonic crystalloid. The pooled relative risk was 0.50 (0.06 to 4.33).

Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised participants. The pooled relative risk was 0.88 (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 crystalloids in patients with trauma, burns and 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 patient types can be justified outside the context of randomised controlled trials.

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 Drug Usage Advisory Committee 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; Bisonni 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 was 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.

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 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 interventions

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

MEDLINE, latest search, March 1999

#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.

Searches were performed in November 1998, using variations on the above strategy, covering the following databases and time periods:

EMBASE 1998
PubMed 8/1998 - 12/1998
Science Citation Index 1990-1998
Cochrane Controlled Trials Register all years

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

Data collection and analysis

For the first version of this review, searching and decisions about the inclusion of studies were 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.

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.

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 risks and 95% confidence intervals 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.

RESULTS

Description of studies

There were 44 trials meeting the inclusion criteria for study design, participants and interventions. We were able to obtain data on deaths for 35 of these. Details of the remaining nine 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 35 randomised controlled trials with data on deaths, the quality of allocation concealment was adequate in four trials, unclear in 24 trials, and inadequate in the remaining seven trials.

There were 27 comparisons of colloids and crystalloids (add-on colloid), nine comparisons of colloid in hypertonic crystalloid with isotonic crystalloid, and one trial compared colloid in isotonic crystalloid to hypertonic crystalloid (see Table of Included Studies).

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 Table of Included Studies.

Effects of interventions

Colloids compared to crystalloids:

Albumin or plasma protein fraction: Thirty-four trials reported data on mortality, including a total of 1537 patients. Eighteen trials examined the effect on mortality of resuscitation with albumin or plasma protein fraction compared with crystalloid. The pooled relative risk from these trials was 1.52 (95% confidence interval 1.08 to 2.13). The risk of death in the albumin treated group was 6% higher than in the crystalloid treated group (1% to 11%). When trials with poor quality allocation concealment were excluded the pooled relative risk was 1.34 (0.95 to 1.89).

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Colloids in hypertonic crystalloid compared to isotonic crystalloid:

One trial compared albumin and hypertonic saline with isotonic crystalloid. The pooled relative risk was 0.50 (0.06 to 4.33).

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

Colloids in isotonic crystalloid compared to hypertonic crystalloid:

Only one trial compared colloids in isotonic crystalloid with hypertonic crystalloid. There were no deaths in either 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.

A systematic review recently published in a paper journal addressed a similar question to this review (Choi 1999). As would be expected there are differences in the studies included in the two reviews. The results were not presented stratified by fluid type, so direct comparison of the results of these reviews is difficult. Nevertheless, the overall result of the Choi review was that there was no clear benefit of colloids over crystalloids.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from randomised controlled trials that resuscitation with colloids reduces the risk of death in patients with trauma, burns and 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 subgroups of patients to identify people who may benefit from colloids rather than crystalloids.

ACKNOWLEDGEMENTS

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CHARACTERISTICS OF STUDIES

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

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.

Risk of bias

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

Boldt 1993

Methods	Randomised controlled trial. Allocation concealment by sealed opaque envelopes (information from author). 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 mm Hg 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.

Risk of bias

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

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.

Risk of bias

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

Bowser-Wallace 1986

Methods	Quasi-randomised controlled trial (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) 2ml/kg/%burn Ringer's lactate over 24 hrs, then 0.5ml/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.
Outcomes	Deaths reported. Fluid and electrolytes given, weight, haematocrit.
Notes	Follow up to 5 days.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

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 (10 patients). 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.

Risk of bias

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

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) IV 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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

Eleftheriadis 1995

Methods	Patients "randomizedly distributed".

Eleftheriadis 1995 *(Continued)*

	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.

Risk of bias

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

Evans 1996

Methods	Randomised controlled trial (method of allocation unclear). Blinding not mentioned. No loss to follow up.
Participants	Aged 16 or more, admitted with trauma to an emergency centre within 2 hours after injury, only crystalloid as a pre-hospital infusion. 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	Death not reported. Clotting variables.
Notes	Follow up period unspecified.

Risk of bias

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

Gallagher 1985

Methods	Randomised controlled trial. Method of allocation concealment not described. Author contacted - allocation concealment by computerised system - patient details were entered before treatment assignment was revealed. Blinding not mentioned.

Gallagher 1985 *(Continued)*

	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 Ringers.
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

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

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.

Risk of bias

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

Grundmann 1982

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.

Risk of bias

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

Hall 1978

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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

Hartmann 1993

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.
Notes	Follow up to 7 days.

Risk of bias

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

Jelenko 1978

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.

Risk of bias

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

Karanko 1987

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.

Risk of bias

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

Ley 1990

Methods	Randomised controlled trial. 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.

Risk of bias

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

Lowe 1977

Methods	Randomised controlled trial, allocation by sealed envelopes.

Lowe 1977 *(Continued)*

	Blinding not mentioned. No loss to follow up.
Participants	Participants with serious trauma.
Interventions	1) 25% albumin in Ringers lactate. 2) Ringers lactate. Allocated fluid was used throughout the pre- and intra-operative period.
Outcomes	Deaths reported.
Notes	Follow up to 5 days post-operatively. Data on the 30 participants with chest injuries who were left out of the Lowe 1977 report, but included in Moss 1981, have been included in the meta-analysis.

Risk of bias

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

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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

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 90m mmHg or less and were 16 years or older. 72% of participants had sustained penetrating trauma.

Mattox 1991 *(Continued)*

Interventions	1) 250 mL Dextran-70 in 7.5% NaCl. (n=211) 2) 250 mL Ringers 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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

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.

Risk of bias

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

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.

McNulty 1993 *(Continued)*

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

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

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) Ringers 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

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

Modig 1983

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.

Modig 1983 *(Continued)*

Outcomes	Deaths reported. Development of respiratory distress syndrome.
Notes	Follow up to definitive reconstructive surgery.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

Nagy 1993

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 recieved a maximum 4L of pentastarch, after which Ringers lactate was given.
Outcomes	Deaths were not reported. Haemodynamic variables.
Notes	Follow up to discharge.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

Nielsen 1985

Methods	Randomized 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.

Nielsen 1985 *(Continued)*

Notes	Length of follow up 4 days.

Risk of bias

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

Pockaj 1994

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	

Risk of bias

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

Prien 1990

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 unspecifed.

Prien 1990 *(Continued)*

Risk of bias

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

Rackow 1983

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.m2, 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.

Risk of bias

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

Rocha e Silva 1994

Methods	Randomised controlled trial.
Participants	[Trauma]. 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 Ringers lactate. Allocated fluid was used for the first intravenous infusion only.
Outcomes	Death was the main outcome measure, but the data are unpublished.
Notes	Follow up to 30 days. By April 1994, 125 patients had been entered into the study.

Risk of bias

Bias	Authors' judgement	Support for judgement

Rocha e Silva 1994 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	B - Unclear

Shah 1977

Methods	Randomised controlled trial. Allocation by sealed envelope. Blinding not mentioned. No loss to follow up.
Participants	Patients with severe, multiple trauma and a systolic blood pressure of less than 90mmHg. All patients were adults and both sexes were included.
Interventions	1) 5% salt-poor albumin in Ringers 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.

Risk of bias

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

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.

Risk of bias

Bias	Authors' judgement	Support for judgement

Shires 1983 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	B - Unclear

Skillman 1975

Methods	Randomised controlled trial, 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 1g/kg and 5% albumin 1L. (n=7) 2) Ringers lactate. Allocated fluid was given intra-operatively. All patients received crystalloids only for pre-loading before surgery.
Outcomes	Deaths were not reported.
Notes	

Risk of bias

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

Tollofsrud 1995

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

Risk of bias

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

Vassar 1990

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. 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) Ringers 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

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

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 helicoptor 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 eurological disease. Peripheral oedema.
Interventions	1) 4.2% dextran 70 in 7.5% saline or 6% dextran 70 in 7.5% saline. (n=83) 2) Ringers 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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Vassar 1993b

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 helicoptor 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.

Vassar 1993b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

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 maintenence of pre-defined physiological parameters, and the resuscitation was continued with the allocated fluid until the day following the operation. This was followed by 5% dextrose in half-normal saline, with potassium chloride as needed.
Outcomes	Deaths reported.
Notes	Follow up two and a half weeks

Risk of bias

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

Wahba 1996

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) Haemaccell. (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.
Notes	Follow up to discharge.

Risk of bias

Wahba 1996 *(Continued)*

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

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.

Risk of bias

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

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 80mm Hg 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.

Risk of bias

Younes 1992 *(Continued)*

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

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 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.

Risk of bias

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

Zetterstrom 1981a

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.

Risk of bias

Bias	Authors' judgement	Support for judgement

Zetterstrom 1981a *(Continued)*

Allocation concealment (selection bias)	Unclear risk	B - Unclear

Zetterstrom 1981b

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.

Risk of bias

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

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

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

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

Study	Reason for exclusion
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 sugery.
Nilsson 1980	Albumin given as a nutritional supplement.
Steinberg 1989	Cross-over trial.
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.

WHAT'S NEW

Date	Event	Description
10 May 2017	Amended	Converted to new review format.

HISTORY

Review first published: Issue 4, 1997

Date	Event	Description
14 April 1999	New citation required and conclusions have changed	Substantive amendment

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Institute of Child Health, University of London, UK.

External sources

- NHS R&D Programme: Mother and Child Health, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Albumins [therapeutic use]; Blood Proteins [therapeutic use]; Colloids [*therapeutic use]; Critical Illness [mortality] [*therapy]; Dextrans [therapeutic use]; Fluid Therapy [methods]; Gelatin [therapeutic use]; Hydroxyethyl Starch Derivatives [adverse effects] [therapeutic use]; Isotonic Solutions [*therapeutic use]; Plasma Substitutes [adverse effects] [therapeutic use]; Randomized Controlled Trials as Topic; Rehydration Solutions [therapeutic use]; Resuscitation [*methods]

MeSH check words

Humans