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, 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 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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REFERENCES

References to studies included in this review

Boldt 1986 *{published data only}*

Boldt J, von Bormann B, Kling D, Borner U, Mulch J, Hempelmann G. Volume replacement with a new hydroxyethyl starch preparation (3 percent HES 200/0.5) in heart surgery [Volumenersatz mit einem neuen hydroxyathylstarke - praparat (3% HAS 200/0.5) in der herzchirurgie]. *Infusionsther Klin Ernahr* 1986;**13**(3):145–51.

Boldt 1993 *{published data only}*

Boldt J, Knothe C, Zickmann B, Andres P, Dapper F, Hempelmann G. Influence of different intravascular volume therapies on platelet function in patients undergoing cardiopulmonary bypass. *Anesthesia and Analgesia* 1993;**76**(6):1185–90.

Boldt 2001 *{published data only}*

Boldt J, Suttner S, Huttner I, Kumle B, Piper S, Krumholz W. Are costs of a crystalloid-based volume replacement regimen lower than of a colloid-based volume replacement stategy. *Infusion Therapy and Transfusion Medicine* 2001;**28**:144–9.

Boutros 1979 *{published data only}*

Boutros AR, Ruess R, Olson L, Hoyt JL, Baker WH. Comparison of hemodynamic, pulmonary, and renal effects of use of three types of fluids after major surgical procedures on the abdominal aorta. *Critical Care Medicine* 1979;**7**(1):9–13.

Bowser-Wallace 1986 *{published data only}*

Bowser-Wallace BH, Caldwell FT Jr. A prospective analysis of hypertonic lactated saline v. Ringer's lactate-colloid for the resuscitation of severely burned children. *Burns* 1986;**12**(6):402–9.

Chavez-Negrete 1991 *{published data only}*

Chavez-Negrete A, Lajluf Cruz S, Frati Munari A, Perches A, Argulero R. Treatment of hemorrhagic shock with intraosseus or intravenous infusion of hypertonic saline eextran solution. *European Surgical Research* 1991;**23**(2):123–9.

Dawidson 1991 *{published data only}*

Dawidson IJ, Willms CD, Sandor ZF, Coorpender LL, Reisch JS, Fry WJ. Ringer's lactate with or without 3% dextran-60 as volume expanders during abdominal aortic surgery. *Critical Care Medicine* 1991;**19**(1):36–42.

Dehne 2001 *{published data only}*

Dehne MG, Muhling J, Sablotzki A, Dehn K-L, Sucke N, Hempelmann G. Hydroxyethyl starch (HES) does not directly affect renal function in patients with no prior renal impairment. *Journal of Clinical Anaesthesia* 2001;**13**(2):103–11.

Eleftheriadis 1995 *{published data only}*

Eleftheriadis S, Sedemund-Adib B, Klotz K-F, Hubner N, Kuppe H. Volume Replacement After Cardiac Surgery: Comparison Of Ringer, HES 6% And Gelatine 3.5%. *Intensive Care Medicine* 1995;**21**(suppl 1):S216.

Ernest 1999 *{published data only}*

Ernest D, Belzberg A, Dodek P. Distribution of normal saline and 5% albumin infusions in septic patients. *Critical Care Medicine* 1999;**27**(1):46–50.

Evans 1996 *{published and unpublished data}*

Evans PA, Garnett M, Boffard K, Kirkman E, Jacobson BF. Evaluation of the effect of colloid (Haemaccel) on the bleeding time in the trauma patient. *Journal of the Royal Society of Medicine* 1996;**89**(2):101–4.

Gallagher 1985 *{published data only}*

Gallagher JD, Moore RA, Kerns D, Jose AB, Botros SB, Flicker S, Naidech H, Clark DL. Effects of colloid or crystalloid administration on pulmonary extravascular water in the postoperative period after coronary artery bypass grafting. *Anesthesia and Analgesia* 1985;**64**(8):753–8.

Goodwin 1983 *{published data only}*

Goodwin CW, Dorethy J, Lam V, Pruitt BA Jr. Randomized trial of efficacy of crystalloid and colloid resuscitation on hemodynamic response and lung water following thermal injury. *Annals of Surgery* 1983;**197**(5):520–31.

Grundmann 1982 *{published data only}*

Grundmann R, Heistermann S. Postoperative albumin infusion therapy based on colloid osmotic pressure. A prospectively randomized trial. *Archives of Surgery* 1985;**120**(8):911–5.

Grundmann R, Meyer H. The significance of colloid osmotic pressure measurement after crystalloid and colloid infusions. *Intensive Care Medicine* 1982;**8**(4):179–86.

Hall 1978 *{published data only}*

Hall K, Sorensen B. The treatment of burn shock. *Scandinavian Journal of Plastic and Reconstructive Surgery* 1973;**7**:67–73.

Hall K, Sorensen B. The treatment of burns shock. In: VrabecR, KonickovaL, MoserovaJ editor(s). *Basic problems in burns*. Berlin: Springer-Verlag, 1975.

Hall KV, Sorensen B. The treatment of burn shock: results of a 5-year randomized, controlled clinical trial of Dextran 70 v Ringer lactate solution. *Burns* 1978;**5**(1):107–12.

Hartmann 1993 *{published data only}*

Hartmann M, Jonsson K, Zederfeldt B. Effects of dextran and crystalloids on subcutaneous oxygen tension and collagen accumulation. A randomized study in surgical patients. *European Surgical Research* 1993;**25**:270–7.

Jelenko 1978 *{published data only}*

Jelenko C 3rd. Fluid therapy and the HALFD method. *Journal of Trauma* 1979;**19**(11 Suppl):866–7.

Jelenko C 3rd, Solenberger RI, Wheeler ML, Callaway BD. Shock and resuscitation. III. Accurate refractometric COP determinations in hypovolemia treated with HALFD. *JACEP* 1979;**8**(7):253–6.

Jelenko C 3rd, Wheeler ML, Callaway BD, Divilio LT, Bucklen KR, Holdredge TD. Shock and resuscitation. II: Volume repletion with minimal edema using the "HALFD"(Hypertonic Albuminated Fluid Demand) regimen. *JACEP* 1978;**7**(9):326–33.

Jelenko C 3rd, Williams JB, Wheeler ML, et al.Studies in shock and resuscitation, I: use of a hypertonic, albumin-containing, fluid demand regimen (HALFD) in resuscitation. *Crit Care Med* 1979;**7**(4):157–67.

Karanko 1987 *{published data only}*

Karanko M, Klossner J, Laksonen V. Restoration of volume by crystalloid versus colloid after coronary artery bypass: haemodynamics,

lung water, oxygenation and outcome. *Critical Care Medicine* 1987; **15**:559–66.

Lang 2001 *{published data only}*

Lang K, Boldt J, Suttner S, Haisch G. Colloids versus crystalloids and tissue oxygen tension in patients undergoing major abdominal surgery. *Anesthesia and Analgesia* 2001;**93**(2):405–9.

Ley 1990 *{published data only}*

Ley SJ, Miller K, Skov P. Crystalloid versus colloid fluid therapy after cardiac surgery. *Clinical Studies in Cardiac Care* 1990;**19**(1):31–40.

Lowe 1977 *{published data only}*

Lowe RJ, Moss GS, Jilek J, Levine HD. Crystalloid versus colloid in the etiology of pulmonary failure after trauma - a randomized trial in man. *Critical Care Medicine* 1979;**7**(3):107–12.

Lowe RJ, Moss GS, Jilek J, Levine HD. Crystalloid vs colloid in the etiology of pulmonary failure after trauma: a randomized trial in man. *Surgery* 1977;**1**(6):676–83.

Moss GS, Lowe RJ, Jilek J, Levine HD. Colloid or crystalloid in the resuscitation of hemorrhagic shock: a controlled clinical trial. *Surgery* 1981;**89**(4):434–8.

Lucas 1978 *{published data only}*

Clift DR, Lucas CE, Ledgerwood AM, Sardesai V, Kithier K, Grabow D. The effect of albumin resuscitation for shock on the immune response to tetanus toxoid. *Journal of Surgical Research* 1982;**32**:449–52.

Johnson SD, Lucas CE, Gerrick SJ, Ledgerwood AM, Higgins. Altered coagulation after albumin supplements for treatment of oligaemic shock. *Archives of Surgery* 1979;**114**:379–83.

Lucas CE, Bouwman DL, Ledgerwood AM, Higgins R. Differential serum protein changes following supplemental albumin resuscitation for hypovolemic shock. *Journal of Trauma* 1980;**20**(1):47–51.

Lucas CE, Weaver D, Higgins RF, Ledgerwood AM, Johnson SD, Bouwman DL. Effects of albumin versus non-albumin resuscitation on plasma volume and renal excretory function. *Journal of Trauma* 1978;**18**:565–70.

Weaver DW, Ledgerwood AM, Lucas CE, Higgins R, Bouwman DL, Johnson SD. Pulmonary effects of albumin resuscitation for severe hypovolaemic shock. *Archives of Surgery* 1978;**113**:387–92.

Mattox 1991 *{published data only}*

Maningas PA, Mattox KL, Pepe PE, Jones RL, Feliciano DV, Burch JM. Hypertonic saline-dextran solutions for the prehospital management of traumatic hypotension. *American Journal of Surgery* 1989; **157**(5):528–33.

Mattox KL, Maningas PA, Moore EE, et al.Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The U.S.A. Multicenter Trial. *Annals of Surgery* 1991;**213**(5):482–91.

Mazher 1998 *{published data only}*

Mazher R, Samenesco A, Royston D, Rees A. Cardiopulmonary effects of 7.2% saline solution compared with gelatin infusion in the early postoperative period after coronary artery bypass grafting. *Journal of Thoracic and Cardiovascular Surgery* 1998;**115**(1):178–87.

McNulty 1993 *{published data only}*

McNulty SE, Sharkey SJ, Asam B, Lee JH. Evaluation of STAT-CRIT Hematocrit Determination in comparison to Coulter and Centrifuge: the effects of isotonic hemodilution and albumin administration. *Anesthesia and Analgesia* 1993;**76**:830–4.

Metildi 1984 *{published data only}*

Metildi LA, Shackford SR, Virgilio RW, Peters RM. Crystalloid versus colloid in fluid resuscitation of patients with severe pulmonary insufficiency. *Surgery, Gynecology and Obstetrics* 1984;**158**(3):207–12.

Modig 1983 *{published data only}*

Modig J. Advantages of dextran 70 over Ringer acetate solution in shock treatment and in prevention of adult respiratory distress syndrome. A randomized study in man after traumatic-haemorrhagic shock. *Resuscitation* 1983;**10**(4):219–26.

Modig J. Effectiveness of dextran 70 versus Ringer's acetate in traumatic shock and adult respiratory distress syndrome. *Critical Care Medicine* 1986;**14**(5):454–7.

Nagy 1993 *{published data only}*

Nagy KK, Davis J, Duda J, Fildes J, Roberts R, Barrett J. A comparison of pentastarch and lactated Ringer's solution in the resuscitation of patients with hemorrhagic shock. *Circulatory Shock* 1993;**40**(4): 289–94.

Ngo 2001 *{published data only}*

Ngo NT, Cao XT, Kneen R, Wills B, Nguyen VM, Nguyen TQ, Chu VT, Nguyen TT, Simpson JA, Solomon T, White NJ, Farrar J. Acute management of dengue shock syndrome: a randomised double-blind comparison of 4 intravenous fluid regimes in the first hour. *Clinical Infectious Diseases* 2001;**32**(2):204–13.

Nielsen 1985 *{published data only}*

Nielsen OM, Engell HC. Extracellular fluid volume and distribution in relation to changes in plasma colloid osmotic pressure after major surgery. A Randomised Study. *Acta Chir Scand* 1985;**151**:221–5.

Pockaj 1994 *{published data only}*

Pockaj BA, Yang JC, Lotze MT, et al.A prospective randomized trial evaluating colloid versus crystalloid resuscitation in the treatment of the vascular leak syndrome associated with interleukin-2 therapy. *Journal of Immunotherapy* 1994;**15**(1):22–8.

Prien 1990 *{published data only}*

Prein T, Backhaus N, Pelster F, et al.Effect of intraoperative fluid adminstration and colloid osmotic pressure on the formation of intestinal edema during gastrointestinal surgery. *Journal of Clinical Anesthesia* 1990;**2**:317–23.

Rackow 1983 *{published data only}*

Haupt, MT, Rackow, EC. Colloid osmotic pressure and fluid resuscitation with hetastarch, albumin, and saline solutions. *Critical Care Medicine* 1982;**10**(3):159–62.

Kaufman BS, Rackow EC, Falk JL. Fluid resuscitation in circulatory shock. Colloids versus crystalloids. *Current Studies in Hematology and Blood Transfusion* 1986;**53**:186–98.

Rackow EC, Falk JL, Fein IA, et al.Fluid resuscitation in circulatory shock: a comparison of the cardiorespiratory effects of albumin, hetastarch, and saline solutions in patients with hypovolemic and septic shock. *Crit Care Medicine* 1983;**11**(11):839–50.

Rocha e Silva 1994

Rocha e Silva M, Poli de Figueiredo LF. Hypertonic-hyperoncotic saline solution for the treatment of post-traumatic hypotension in

the emergency room. The Brazilian multi-center trial. SALT 6. International Conference on Hypertonic Resuscitation, Teton Village. June 2-3 1994.

SAFE 2004 *{published data only}*
The SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *New England Journal of Medicine* 2004;**350**(22):2247–56.

Shah 1977 *{published data only}*
Shah DM, Broner BD, Dutton RE, Newell JC, Powers SR. Cardiac output and pulmonary wedge pressure. Use for evaluation of fluid replacement in trauma patients. *Archives of Surgery* 1977;**112**:1161–8.

Shires 1983 *{published data only}*
Shires G, Peitzman A, Albert S, Illner H, Silane M, Perry M, et al.Response of extravascular lung water to intraoperative fluids. *Annals of Surgery* 1983;**197**:515–8.

Sirieix 1999 *{published data only}*
*Sirieix D, Hongnat J-M, Delayance S, D'Attellis N, Vicaut E, Berribi A, et al.Comparison of the acute haemodynamic effects of hypertonic or colloid infusions immediately after mitral valve repair. *Critical Care Medicine* 1999;**27**:2159–65.

Skillman 1975 *{published data only}*
Skillman JJ, Restall DS, Salzman EW. Randomized trial of albumin vs. electrolyte solutions during abdominal aortic operations. *Surgery* 1975;**78**(3):291–303.

Tollofsrud 1995 *{published data only}*
Tollofsrud S, Svennevig JL, Breivik H, et al.Fluid balance and pulmonary functions during and after coronary artery bypass surgery: Ringer's acetate compared with dextran, polygeline, or albumin. *Acta Anaesthesiologica Scandinavica* 1995;**39**:671–7.

Tollofsrud 1998 *{published data only}*
Tollofsrud S, Noddeland H. Hypertonic saline and dextran after coronary artery surgery mobilises fluid excess and improves cardiorespiratory functions. *Acta Anaesthesiologica Scandinavica* 1998;**42**:154–61.

Vassar 1990 *{published data only}*
Vassar MJ, Perry CA, Holcroft JW. Analysis of potential risks associated with 7.5% sodium chloride resuscitation of traumatic shock. *Archives of Surgery* 1990;**125**(10):1309–15.

Vassar 1991 *{published data only}*
Holcroft JW, Vassar MJ, Turner JE, Derlet RW, Kramer GC. 3% NaCl and 7.5% NaCl/dextran 70 in the resuscitation of severely injured patients. *Annals of Surgery* 1987;**206**(3):279–88.

Vassar MJ, Perry CA, Gannaway WL, Holcroft JW. 7.5% sodium chloride/dextran for resuscitation of trauma patients undergoing helicopter transport. *Archives of Surgery* 1991;**126**(9):1065–72.

Vassar 1993a *{published data only}*
Vassar MJ, Perry CA, Holcroft JW. Prehospital resuscitation of hypotensive trauma patients with 7.5% NaCl versus 7.5% NaCl with added dextran: a controlled trial. *Journal of Trauma* 1993;**34**(5):622–32.

Vassar 1993b *{published data only}*
Vassar MJ, Fischer RP, O'Brien PE, et al.A multicenter trial for resuscitation of injured patients with 7.5% sodium chloride. The effect of added dextran 70. The Multicenter Group for the Study of Hypertonic Saline in Trauma Patients. *Archives of Surgery* 1993;**128**(9):1003–11.

Virgilio 1979 *{published data only}*
Virgilio RW, Rice CL, Smith DE, et al.Crystalloid vs. colloid resuscitation: is one better? A randomized clinical study. *Surgery* 1979;**85**(2):129–39.

Wahba 1996 *{published data only}*
Wahba A, Sendtner E, Strotzer M, Wild K, Birnbaum DE. Fluid therapy with Ringer's solution versus Haemaccel following coronary artery bypass surgery. *Acta Anaesthesiologica Scandinavica* 1996;**40**:1227–33.

Woittiez 1997 *{published and unpublished data}*
Hondebrink Y, Jeekel L, Oude Nijhuis J, Woittiez AJJ. Restoration of colloid osmotic pressure in hypoalbuminaemic patients. *Intensive Care Medicine* 1997;**23**(supp 1):S184.

Wu 2001 *{published data only}*
Wu J, Huang M, Tang G, Kao W, Shih H, Su C, Lee C. Hemodynamic response of modified fluid gelatin compared with lactated ringer's solution for volume expansion in emergency resuscitation of hypovolemic shock patients: preliminary report of a prospective, randomized trial. *World Journal of Surgery* 2001;**25**(5):598–602.

Younes 1992 *{published data only}*
Younes RN, Aun F, Accioly CQ, Casale LP, Szajnbok I, Birolini D. Hypertonic solutions in the treatment of hypovolemic shock: a prospective, randomized study in patients admitted to the emergency room. *Surgery* 1992;**111**(4):380–5.

Younes 1994 *{published data only}*
Younes R, Aun F, Ching C, Goldenberg D, Franco M, Miura F, et al.Prognostic factors to predict outcome following the administration of hypertonic/hyperoncotic solution in hypovolaemic patients. *Shock* 1997;**7**:79–83.

Younes RN, Aun F, Ching C, et al.Prognosis following the administration of hypertonic/hyperoncotic solutions in hypovolemic patients. SALT 6. International Conference on Hypertonic Resuscitation. Teton Village. June 2-3 1994.

Younes 1998 *{published data only}*
Younes R, Yin K, Amino C, Itinoshe M, Rocha e Silva M, Birolini D. Use of pentastarch solution in the treatment of patients with hemorrhagic hypovolemia: randomized phase II study in the emergency room. *World Journal of Surgery* 1998;**22**:2–5..

Zetterstrom 1981a *{published data only}*
Zetterstrom H, Hedstrand U. Albumin treatment following major surgery. I. Effects on plasma oncotic pressure, renal function and peripheral oedema. *Acta Anaesthesiologica Scandinavica* 1981;**25**:125–32.

Zetterstrom 1981b *{published data only}*
Zetterstrom H. Albumin treatment following major surgery. II. Effects on postoperative lung function and circulatory adaptation. *Acta Anaesthesiologica Scandinavica* 1981;**25**:133–41.

References to studies excluded from this review

Artru 1989
Artru F, Philippon B, Flachaire E, et al.A controlled study of Dextran 40: effect on cerebral blood flow and metabolic rates in acute head trauma. *Intensive Care Medicine* 1989;**15**(8):499–504.

Bocanegra 1966

Bocanegra M, Hinostroza F, Kefalides NA, Markley K, Rosenthal SM. A long-term study of early fluid therapy in severely burned adults. 3. Simultaneous comparison of saline solution alone or combined with plasma. *Journal of the American Medical Association* 1966; **195**(4):268–74.

Boldt 1996

Boldt J, Heesen M, Padberg W, Martin K, Hempelmann G. The influence of volume therapy and pentoxifylline infusion on circulating adhesion molecules in trauma patients. *Anaesthesia* 1996;**51**:529–35.

Bothner 1998

Bothner U, Georgieff M, Vogt N. Assessment of the safety and tolerance of 6% hydroxyethyl starch (200/0.5) solution: a randomized, controlled epidemiology study. *Anesthesia and analgesia* 1998; **86**:850–5.

Breheme 1993

Brehme S, Keysser G, Turowski A, Schmidt HH. Hemorheologic effects of hydroxyethyl starch 200/0.5, dextran 40, oxypolygelatine and full electrolyte solution over 48 hours [Hamorheologische Wirkungen von Hydroxyathylstarke 200/0,5, Dextran 40, Oxypolygelatine und Vollelektrolytlosung uber 48 Stunden]. *Z-Gesamte-Inn-Med* 1993;**48**(10):506–10.

Golub 1994

Golub R, Sorrento JJ Jr, Cantu R Jr, Nierman DM, Moideen A, Stein HD. Efficacy of albumin supplementation in the surgical intensive care unit: a prospective, randomized study. *Critical Care Medicine* 1994;**22**(4):613–9.

Goslinga 1992

Goslinga H, Eijzenbach V, Heuvelmans JH, van de Nes JC, Kurk RM, Bezemer PD. [Individualized hemodilution in acute brain infarct using a 20% albumin solution and physiological saline solution]. *Ned Tijdschr Geneeskd* 1992;**136**(49):2422–8.

Goslinga H, Eijzenbach V, Heuvelmans JH, et al.Custom-tailored hemodilution with albumin and crystalloids in acute ischemic stroke. *Stroke* 1992;**23**(2):181–8.

Goslinga H, Heuvelmans JH, Schmid Schonbein H. Hemodilution and rehydration in acute ischemic stroke. A preliminary report on the Amsterdam Stroke Study. *Acta Med Austriaca* 1991;**18**(Suppl 1): 41–4.

Greenhalgh 1995

Greenhalgh DG, Housinger TA, Kagan RJ, et al.Maintenance of serum albumin levels in pediatric burn patients: a prospective, randomized trial. *Journal of Trauma* 1995;**39**(1):67-73; discussion 73-4.

Hauser 1980

Hauser CJ, Shoemaker WC Turpin I, Goldberg SJ. Oxygen transport response to colloids and crystalloids in critically ill surgical patients. *Surgery* 1980;**150**(6):811–16.

Lagonidis 1995

Lagonidis D, Magder S. Acute volume loading with colloid vs. crystalloid after coronary artery bypass. *Intensive Care Medicine* 1992;**18:** (suppl 2):S225.

Marhofer 1999

Marhofer P, Faryniak B, Oismuller C, Koinig H, Kapral S, Mayer N. Cardiovascular efffects of 6% hetastarch and lactated Ringer's solution during spinal anaesthesia. *Regional Anesthesia and Pain Medicine* 1999;**24**:399–404.

Nilsson 1980

Nilsson E, Lamke O, Liljedahl SO, Elfstrom K. Is albumin therapy worthwhile in surgery for colorectal cancer?. *Acta Chir Scand* 1980; **146**:619–22.

Rehm 2001

Rehm M, Haller M, Orth V, Kreimeier U, Jacob M, Dressel H, Mayer S, Brechtelsbauer H, Finsterer U. Changes in blood volume and hematocrit during acute preoperative volume loading with 5% albumin or 6% hetastarch solutions in patients before radical hysterectomy. *Anesthesiology* 2001;**95**(4):849–56.

Steinberg 1989

Steinberg B, Kochs E, Bause H, Schulte am Esch J. Effects of low molecular weight hydroxyethyl starch (HES 40) in comparison with Ringer solution on oxygen tension in skeletal muscles of infected patients. *Anasth Intensivther Notfallmed* 1989;**24**(6):377–81.

Wilkes 2001

Wilkes N, Woolf R, Mutch M, Mallett S, Peache T, Stephens R, Mythen M. The effects of balanced versus saline-based heta-starch and crystalloid solutions on acid-base and electroyte status and gastric mucosal perfusion in elderly sugical patients. *Anaesthesia and Analgesia* 2001;**93**(4):811–16.

Woods 1993

Woods MS, Kelley H. Oncotic pressure, albumin and ileus: the effect of albumin replacement on postoperative ileus. *The American Surgeon* 1993;**59**:758–63.

References to studies awaiting assessment

Bueno R 2004

Bueno R, Resende AC, Melo R, Neto VA, Stolf NA. Effects of hypertonic saline-dextran solution in cardiac valve surgery with cardiopulmonary bypass. *Annals of Thoracic Surgery* 2004;**77**(2):604–11.

Oliviera 2002

Oliviera RP, Weingartner R, Ribas EO, Moraes RS, Friedman G. Acute haemodynamic effects of a hypertonic saline/dextran solution in stable patients with severe sepsis. *Intensive Care Medicine* 2002;**28** (11):1574–81.

Paul 2003

Paul M, Dueck M, Joachim Herrman H, Holzki J. A randomized, controlled study of fluid management in infants and toddlers during surgery: hydroxyethyl starch 6% (HES 70/0.5) vs lactated Ringer's solution. *Paediatric Anaesthesia* 2003;**13**(7):603–8.

Additional references

Albumin 2004

The Albumin Reviewers (Alderson P, Bunn F, Lefebvre C, Li Wan Po A, Li L, Roberts I, Schierhout G). Human albumin solution for resuscitation and volume expansion in critically ill patients (Cochrane Review). *The Cochrane Library* 2004, Issue 3.Art. No.: CD001208. DOI: .

Armstrong 1994

Armstrong RF, Bullen C, Cohen SL, Singer M, Webb AR. *Critical Care Algorithms*. Oxford: Oxford University Press, 1994.

Bickell 1994
Bickell WH, Wall MJ, Pepe PE, Martin R, Ginger VF, Allen MK, Mattox KL. Immediate Versus Delayed Resuscitation For Hypotensive Patients With Penetrating Torso Injuries. *New England Journal of Medicine* 1994;**331**:1105–9.

Bisonni 1991
Bisonni RS, Holtgrave DR, Lawler F, Marley DS. Colloids versus crystalloids in fluid resuscitation: an analysis of randomized controlled trials. *Journal of Family Practice* 1991;**32**(4):387–90.

Fakhry 1995
Fakhry SM, Alexander J, Smith D, Meyer AA, Peterson HD. Regional and institutional variation in burn care. *Journal of Burn Care and Rehabilitation* 1995;**16**(1):86–90.

Gosling 1998
Gosling P. Newer synthetic colloids should not be abandoned. *BMJ* 1998;**317**:277.

Oxman 1994
Oxman AD, Cook DJ, Guyatt GH. User's guide to the medical literature. VI. How to use an overview. *Journal of the American Medical Association* 1994;**272**:1367–71.

Schulz 1995
Schulz KF, Chalmers I, Hayes RJ, Altman DG. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of the American Medical Association* 1995; **273**(5):408–12.

Velanovich 1989
Velanovich V. Crystalloid versus colloid fluid resuscitation: a meta-analysis of mortality. *Surgery* 1989;**105**(1):65–71.

Vermeulen 1995
Vermeulen LC, Ratko TA, Erstad BL, Brecher ME, Matuszewski K A. A paradigm for consensus. The University Hospital Consortium guidelines for the use of albumin, nonprotein colloid, and crystalloid solutions. *Archives of Internal Medicine* 1995;**155**(4):373–9.

Victorian DUAC 1991
Subcommittee of the Victorian Drug Usage Advisory Committee. Human albumin solutions: an audit of use in three major metropolitan hospitals. *Medical Journal of Australia* 1991;**154**(10):657–60.

Yim 1995
Yim JM, Vermeulen LC, Erstad BL, Matuszewski KA, Burnett DA, Vlasses PH. Albumin and nonprotein colloid solution use in US academic health centers. *Archives of Internal Medicine* 1995;**155**(22): 2450–5.

References to other published versions of this review

Schierhout 1998
Schierhout G, Roberts I. Fluid resuscitation with colloids or crystalloid solutions in critically ill patients: a systematic review of randomised controlled trials. *BMJ* 1998;**316**:961–4.

* *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.

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.

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 substitiution 0.5 (n=15). 3) 6% HES: molecular weight 200kD, degree of substitiution 0.60-0.66 (n=15). 4) 6% HES: molecular weight 450kD, degree of substitiution 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.

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*)

Study	**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.
Allocation concealment	B – Unclear

Study	**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.
Allocation concealment	C – Inadequate

Study	**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.

Characteristics of included studies (*Continued*)

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

Study	**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.
Allocation concealment	B – Unclear

Study	**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.
Allocation concealment	B – Unclear

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

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

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

	Haemodynamic variables.
Notes	Follow-up to discharge.
Allocation concealment	B – Unclear

Study	**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.
Outcomes	Deaths reported. Development of respiratory distress syndrome.
Notes	Follow-up to definitive reconstructive surgery.
Allocation concealment	C – Inadequate

Study	**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 Ringer's lactate was given.
Outcomes	Deaths were not reported. Haemodynamic variables.
Notes	Follow-up to discharge.
Allocation concealment	C – Inadequate

Study	**Ngo 2001**
Methods	Randomised controlled trial, opaque envelopes containing only treatment pack number.
Participants	230 children with dengue shock syndrome.
Interventions	1) Dextran 70 (n=55). 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.

	And noted that there were no deaths in any group
Notes	Follow-up period unclear.
Allocation concealment	A – Adequate

Study	**Nielsen 1985**
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

Study	**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	
Allocation concealment	B – Unclear

Study	**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.

Allocation concealment	B – Unclear

Study	**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.
Allocation concealment	B – Unclear

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

Study	**SAFE 2004**
Methods	Randomised controlled trial. Randomisation by minisation 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 over19-month period
Interventions	1) 4% albumin (Albumex, CSL) (n=3499). 2) Normal saline (n=3501).
Outcomes	Death. Pateints 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

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

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	**Sirieix 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, I 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.

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

Study	**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.
Allocation concealment	B – Unclear

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

Study	**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) 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 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) 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*)

Study	**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.
Allocation concealment	A – Adequate

Study	**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
Allocation concealment	B – Unclear

Study	**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.

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 randmisation 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*)

Study	**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.
Allocation concealment	B – Unclear

Study	**Younes 1998**
Methods	Randomised controlled trial, allocation by sealed envelope. Blinding not mentioned, no apparent loss to follow-up.
Participants	Trauma patients with systolic blood pressure <90mmHg admitted to the emergency room, with no previous treatment.
Interventions	1) 10% pentastarch (n=12). 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

Study	**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.
Allocation concealment	B – Unclear

Study	**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.
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 sugery.
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 receveived saline plus hetastarch; the other received 'balanced' fluid plus hetatstarch. 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

Title	Colloids versus crystalloids for fluid resuscitation in critically ill patients
Authors	Roberts I, Alderson P, Bunn F, Chinnock P, Ker K, Schierhout G
Contribution of author(s)	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. 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.
Issue protocol first published	1997/4
Review first published	1997/4
Date of most recent amendment	24 August 2005
Date of most recent SUBSTANTIVE amendment	24 August 2004
What's New	August 2004 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.

	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
Contact address	Mr Paul Chinnock Senior Editor PLoS Medicine 7 Portugal Place Cambridge CB5 8AF UK E-mail: pchinnock@plos.org Tel: +44 223 463344
DOI	10.1002/14651858.CD000567.pub2
Cochrane Library number	CD000567
Editorial group	Cochrane Injuries Group
Editorial group code	HM-INJ

GRAPHS AND OTHER TABLES

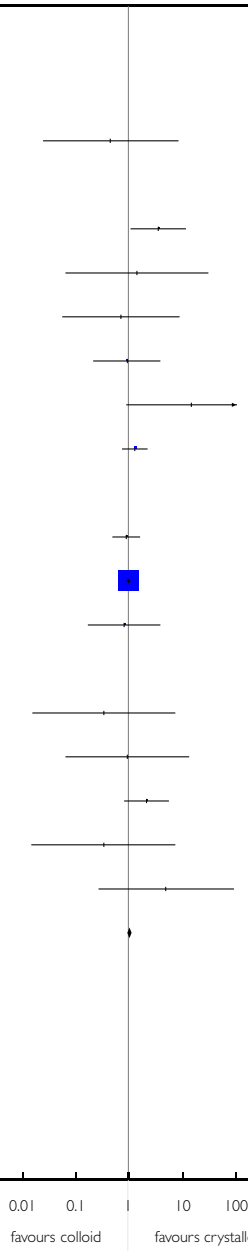
Analysis 01.01. Comparison 01 colloid vs crystalloid (add-on colloid), Outcome 01 deaths

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

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

Outcome: 01 deaths

Study	colloid n/N	crystalloid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 albumin or PPF					
× Boldt 1986	0/1	0/1		0.0	Not estimable
× Boldt 1993	0/15	0/15		0.0	Not estimable
Boutros 1979	0/7	2/17		0.2	0.45 [0.02, 8.34]
× Gallagher 1985	0/5	0/5		0.0	Not estimable
Goodwin 1983	11/40	3/39		0.4	3.58 [1.08, 11.85]
Grundmann 1982	1/14	0/6		0.1	1.40 [0.06, 30.23]
Jelenko 1978	1/7	1/5		0.2	0.71 [0.06, 8.90]
Lowe 1977	3/77	4/94		0.5	0.92 [0.21, 3.97]
Lucas 1978	7/27	0/27		0.1	15.00 [0.90, 250.24]
Metildi 1984	12/20	12/26		1.4	1.30 [0.75, 2.25]
× Prien 1990	0/6	0/6		0.0	Not estimable
Rackow 1983	6/9	6/8		0.8	0.89 [0.48, 1.64]
SAFE 2004	726/3473	729/3460		95.0	0.99 [0.91, 1.09]
Shah 1977	2/9	3/11		0.4	0.81 [0.17, 3.87]
× Shires 1983	0/9	0/9		0.0	Not estimable
Tollofsrud 1995	0/10	1/10		0.2	0.33 [0.02, 7.32]
Virgilio 1979	1/15	1/14		0.1	0.93 [0.06, 13.54]
Woittiez 1997	8/15	4/16		0.5	2.13 [0.81, 5.64]
Zetterstrom 1981a	0/15	1/15		0.2	0.33 [0.01, 7.58]
Zetterstrom 1981b	2/9	0/9		0.1	5.00 [0.27, 91.52]
Subtotal (95% CI)	3783	3793		100.0	1.02 [0.93, 1.11]
Total events: 780 (colloid), 767 (crystalloid)					
Test for heterogeneity chi-square=13.88 df=14 p=0.46 I^2 =0.0%					
Test for overall effect z=0.41 p=0.7					
02 hydroxyethylstarch					
× Boldt 1993	0/30	0/15		0.0	Not estimable
× Boldt 2001	0/50	0/25		0.0	Not estimable



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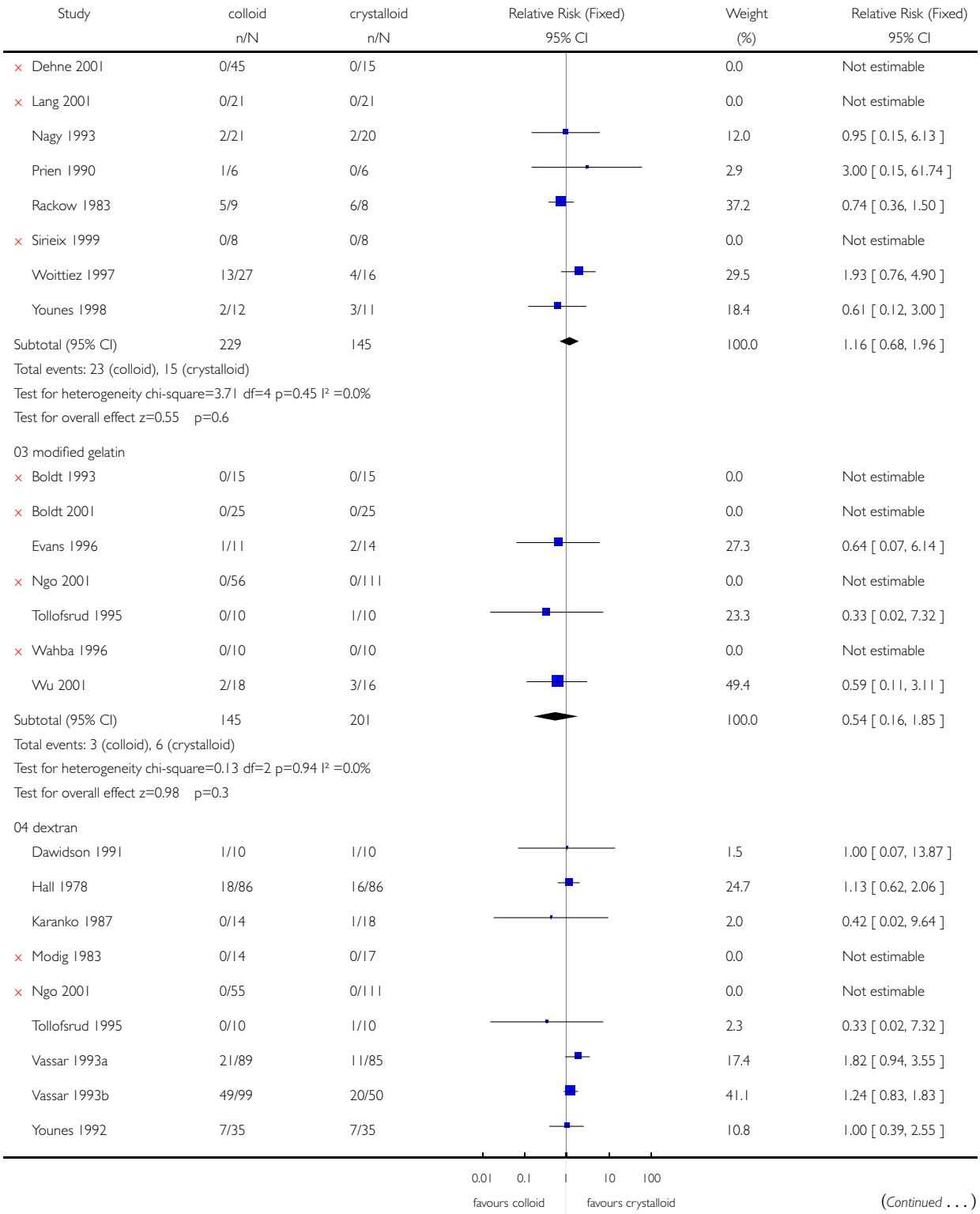

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Study	colloid n/N	crystalloid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Subtotal (95% CI)	412	422		100.0	1.24 [0.94, 1.65]
Total events: 96 (colloid), 57 (crystalloid)					
Test for heterogeneity chi-square=2.76 df=6 p=0.84 I^2 =0.0%					
Test for overall effect z=1.53 p=0.1					

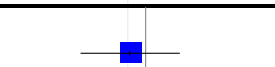
Analysis 02.01. Comparison 02 colloid and hypertonic crystalloid vs isotonic crystalloid, Outcome 01 deaths

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

Comparison: 02 colloid and hypertonic crystalloid vs isotonic crystalloid

Outcome: 01 deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 albumin or PPF					
Jelenko 1978	1/7	2/7		100.0	0.50 [0.06, 4.33]
Subtotal (95% CI)	7	7		100.0	0.50 [0.06, 4.33]
Total events: 1 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					
02 hydroxyethylstarch					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 modified gelatin					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
04 dextran					
Chavez-Negrete 1991	1/26	5/23		2.9	0.18 [0.02, 1.41]
Mattox 1991	35/211	42/211		22.6	0.83 [0.56, 1.25]
Vassar 1990	12/23	13/24		6.8	0.96 [0.56, 1.65]
Vassar 1991	30/83	34/83		18.3	0.88 [0.60, 1.30]
Vassar 1993a	21/89	14/84		7.7	1.42 [0.77, 2.60]
Vassar 1993b	49/99	23/45		17.0	0.97 [0.68, 1.37]



(*Continued* . . .)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Younes 1992	7/35	8/35		4.3	0.88 [0.36, 2.15]
Younes 1994	27/101	40/111		20.5	0.74 [0.49, 1.11]
Subtotal (95% CI)	667	616		100.0	0.88 [0.74, 1.05]
Total events: 182 (Treatment), 179 (Control)					
Test for heterogeneity chi-square=5.79 df=7 p=0.57 I^2 =0.0%					
Test for overall effect z=1.41 p=0.2					

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

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 albumin or PPF					
Bowser-Wallace 1986	3/19	0/19		100.0	7.00 [0.39, 126.92]
Subtotal (95% CI)	19	19		100.0	7.00 [0.39, 126.92]
Total events: 3 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					
02 hydroxyethylstarch					
× Sirieix 1999	0/8	0/8		0.0	Not estimable
Subtotal (95% CI)	8	8		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 modified gelatin					
× Mazher 1998	0/10	0/10		0.0	Not estimable
Subtotal (95% CI)	10	10		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
04 dextran					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable