Colloid solutions for fluid resuscitation (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

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Status: *Commented*

This record should be cited as:
Bunn F, Alderson P, Hawkins V. Colloid solutions for fluid resuscitation. *Cochrane Database of Systematic Reviews* 2003, Issue 1. Art. No.: CD001319. DOI: 10.1002/14651858.CD001319.

This version first published online: 20 January 2003 in Issue 1, 2003.
Date of most recent substantive amendment: 17 September 2002

ABSTRACT

Background
Colloids are widely used in the replacement of fluid volume. However doubts remain as to which colloid is best. Different colloids vary in their molecular weight and therefore in the length of time they remain in the circulatory system. Because of this and their other characteristics, they may differ in their safety and efficacy.

Objectives
To compare the effects of different colloid solutions in patients thought to need volume replacement.

Search strategy
We searched the Cochrane Injuries Group specialised register, the Cochrane Controlled Trials Register (2002 Issue 3), MEDLINE (1994-2002/07), EMBASE (1974-2002 August week 1), and the National Research Register (2002 issue 3). Bibliographies of trials retrieved were searched, and drug companies manufacturing colloids were contacted for information. The search was last updated in September 2002.

Selection criteria
Randomised and quasi-randomised trials comparing colloid solutions in critically ill and surgical patients thought to need volume replacement. The main outcomes measured were death, amount of whole blood transfused, and incidence of adverse reactions.

Data collection and analysis
Two authors independently extracted the data and assessed the quality of the trials.

Main results
Fifty-seven trials met the inclusion criteria, with a total of 3659 participants. Quality of allocation concealment was judged to be adequate in 20 trials and poor or uncertain in 37.

Deaths were obtained from 36 trials. For albumin or PPF versus hydroxyethyl starch (HES) 20 trials (n=1029) reported mortality. The pooled relative risk (RR) was 1.17 (95% CI 0.91, 1.50). For albumin or PPF versus gelatin four trials (n=542) reported mortality. The RR was 0.99 (0.69, 1.42). For gelatin vs HES 11 trials (n=945) reported mortality, RR was 1.00 (0.78,1.28). RR was not estimable in the albumin vs dextran, gelatin vs dextran, and HES vs dextran groups.

Thirty-six trials recorded the amount of blood transfused, however quantitative analysis was not possible due to skewness and variable reporting. Fifteen trials recorded adverse reactions, but none occurred.

Authors' conclusions
From this review, there is no evidence that one colloid solution is more effective or safe than any other, although the confidence intervals are wide and do not exclude clinically significant differences between colloids. Larger trials of fluid therapy are needed if clinically significant differences in mortality are to be detected or excluded.

PLAIN LANGUAGE SUMMARY

No strong evidence to be certain of the safety of any particular type of colloid solution for replacing blood fluids

When a person is bleeding heavily, the loss of fluid volume in their veins can lead to shock, so they need fluid resuscitation. Colloids and crystalloids are two types of solutions used to replace lost blood fluid (plasma). They include blood and synthetic products. Both types appear to be similarly effective at resuscitation, but one type of colloid (human albumin) was found by another Cochrane review to increase deaths. Different colloids may have different effects. However, the review of trials found there is not enough evidence to be sure that any particular colloid is safer than any other

BACKGROUND

Colloids are used as plasma substitutes for short-term replacement of fluid volume, while the cause of the problem is being addressed (e.g. stopping bleeding). These solutions can be blood products (human albumin solution, plasma protein fraction [PPF]) or synthetic (modified gelatins, dextrans, etherified starches). Colloid solutions are widely used in fluid resuscitation (Yim 1995) and they have been recommended in a number of resuscitation guidelines and intensive care management algorithms (Armstrong 1994; Vermeulen 1995). Previous systematic reviews have suggested that colloids are no more effective than crystalloids in reducing mortality (Schierhout 2000), and that albumin administration may increase mortality compared to crystalloids or no fluid in a range of uses (CIGAR 2000). Despite this, colloid solutions are still widely used as they are thought to remain in the intravascular space for longer than crystalloids and, therefore, be more effective in maintaining osmotic pressure.

It is plausible that colloids may vary in their safety and effectiveness. Different colloids vary in the length of time they remain in the circulatory system. It may be that some low to medium molecular weight colloids (e.g. gelatins and albumin) are more likely to leak into the interstitial space (Traylor 1996), whereas some larger molecular weight hydroxyethyl starches are retained for longer (Boldt 1996). In addition it is thought that some colloids may effect coagulation or cause other adverse effects.

The previous review of colloids against crystalloids only allows indirect comparison of the different colloids. This review examines direct comparisons of the different colloid solutions in randomised trials to complement the earlier reviews on colloids compared to crystalloids (Schierhout 2000) and human albumin (CIGAR 2000).

OBJECTIVES

To quantify the relative effects on mortality of different colloid solutions in critically ill and surgical patients requiring volume replacement, by examining direct comparisons of colloid solutions.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised and quasi-randomised (e.g. allocation by hospital number or alternation) controlled trials.

Types of participants

Patients clinically assessed as requiring volume replacement or maintenance of colloid osmotic pressure. Administration of fluid for preoperative haemodilution or volume loading, during plasma exchange, for priming extracorporeal circuits or following paracentesis are excluded.

Types of intervention

The colloid solutions considered are human albumin solutions, plasma protein fraction, modified gelatins, dextran 70, or etherified starch solutions.

Trials of other blood products not used primarily for volume replacement (e.g. fresh frozen plasma, pooled serum) were excluded.

The review compares the administration of any regimens of different classes of colloids with each other.

Types of outcome measures

The primary outcome measure is mortality from any cause at the end of the study period. We also attempted to find data on incidence of adverse reactions, allergies or anaphylactic shock, and the amount of blood (whole blood or red blood cells) transfused in each group. Some of the synthetic colloids may have anticoagulant properties and, therefore, we felt that some measure of blood loss or haemorrhage was important. However, as blood loss is too vulnerable to measurement error, we decided to use the amount of blood products transfused as an outcome measure.

Intermediate physiological outcomes were not used for several reasons. These were that they are subject to intra- and inter-observer variation, they have no face value to patients and relatives, and the ones seen as appropriate are not stable over time. Also there would need to exist a strong predictive relationship between the variable and mortality.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Injuries Group methods used in reviews.

We searched the Cochrane Injuries Group trials register, the Cochrane Controlled Trials Register (2002 Issue 3), MEDLINE (1966-2002/07), and EMBASE (1974-2002 August week 1). Bibliographies of trials retrieved were searched, and drug companies manufacturing colloids were contacted for information. The search was last updated in September 2002. Search strategies for each database are given below.

Cochrane Injuries Group Trials Register:
#1 albumin* or hypoalbumin* or plasma* or volume* or starch* or dextran* or gelofus* or haemacc* or hemacc* or colloid*.

Cochrane Controlled Trials Register (CD, 2002 issue 3):
#1 explode "Albumins" / all SUBHEADINGS
#2 explode "Plasma" / all SUBHEADINGS
#3 explode "Plasma-Substitutes" / all SUBHEADINGS
#4 (volume next replac*) or (human next albumin*)
#5 (frozen next plasma) or (fresh next plasma)
#6 plasma next protein*
#7 (low next albumin*) or hypoalbumin*
#8 starch or dextran* or gelofus* or haemacc* or hemacc*
#9 colloid or colloids
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9.

MEDLINE (Silverplatter, 1966-2002/07):
#1 explode "Albumins" / all SUBHEADINGS
#2 explode "Plasma" / all SUBHEADINGS
#3 explode "Plasma-Substitutes" / all SUBHEADINGS
#4 (volume next replac*) or (human next albumin*)
#5 (frozen next plasma) or (fresh next plasma)
#6 plasma next protein*
#7 (low next albumin*) or hypoalbumin*
#8 starch or dextran* or gelofus* or haemacc* or hemacc*
#9 colloid or colloids
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
#11 #10 and (optimally sensitive MEDLINE search strategy for identifying randomised controlled trials) (Clarke 2001).

EMBASE (Ovid, 1974-2002 Aug week 1):
#1 exp ALBUMIN/
#2 exp PLASMA/
#3 exp Plasma Substitute/
#4 volume adj replac$
#5 human adj albumin$
#6 (frozen adj plasma) or (fresh adj plasma)
#7 plasma adj protein$
#8 hypoalbumin$ or (low adj albumin)
#9 starch or dextran$ or gelofus$ or haemacc$ or hemacc$
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
#11 Randomized Controlled Trial/ (25290)
#12 randomi$ or double blind$ or single blind$
#13 #11 or #12
#14 #10 and #13.

National Research Register (CD, 2002 issue 3):
As MEDLINE.

Trials were also identified using searches done for an earlier review of colloids vs crystalloids (Schierhout 2000), which included BIDS Index to Scientific and Technical Proceedings, drawing on the handsearching of 29 international journals and the proceedings of several international meetings on fluid resuscitation, and checking the reference lists of the trials found.

To identify unpublished trials we searched the UK National Research Register, the register of the Medical Editors' Trial Amnesty, on the Cochrane Library, and we contacted the UK Medicines Control Agency. We also contacted the medical directors of the following companies who all manufacture colloids: Alpha Therapeutic UK Limited (Albutein), American Critical Care McGraw (Hespan), Bayer (Plasbumin), Baxter (Gentran), Bio Products Laboratory (Zenalb), Cambridge Laboratories (Rheomacrodex), Centeon Limited (Albuminar), CIS UK Ltd , CP (Lomodex), Common Services Agency, Consolidated (Gelofusine), DuPont (Hespan) Fresenius (eloHAES and HAES-Steril), Geistlich Sons Ltd (Hespan and Pentaspan), Hoechst (Haemaccel), Mallinckrodt Medical GMBH (Infoson), Nycomed, Oxford Nutrition (Elohes), Pharmacia and Upjohn Ltd (Rheomacrodex), and Sorin Biomedica Diagnostics Spa.

There were no language restrictions in any of the searches.

METHODS OF THE REVIEW

Trial identification

One reviewer examined the electronic search results for reports of possibly relevant trials and these reports were then retrieved in full. Two reviewers (PA and FB) applied the selection criteria independently to the trial reports, resolving disagreements by discussion.

Quality assessment
Since there is evidence that the quality of allocation concealment particularly affects the results of studies (Schulz 1995), two reviewers scored this quality on the scale used by Schulz (Schulz 1995) as shown below, assigning C to poorest quality and A to best quality:

A=trials deemed to have taken adequate measures to conceal allocation (i.e. central randomisation; numbered or coded bottles or containers; drugs prepared by the pharmacy; serially numbered, opaque, sealed envelopes; or other description that contained elements convincing of concealment).

B=trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories.

C=trials in which concealment was inadequate (such as alternation or reference to case record numbers or to dates of birth)

Where the method used to conceal allocation was not clearly reported, the author was contacted, if possible, for clarification. We then compared the scores allocated and resolved differences by discussion.

Data extraction

Two reviewers independently extracted information on the following: method of allocation concealment, number of randomised patients, type of participants and the interventions. The outcome data sought were numbers of deaths, volume of blood transfused, and incidence of adverse or allergic reactions. The reviewers were not blinded to the authors or journal when doing this, as the value of this has not been established (Berlin 1997). Results were compared and any differences resolved by discussion.
Where there was insufficient information in the published report, we attempted to contact the authors for clarification.

Analysis

The following comparisons were made:
- albumin or PPF vs etherified starch
- albumin or PPF vs modified gelatin
- albumin or PPF vs dextran 70
- modified gelatin vs etherified starch
- modified gelatin vs dextran 70
- etherified starch vs dextran 70.

For each trial the relative risk of death and 95% confidence interval was calculated, such that a relative risk of more than 1 indicates a higher risk of death in the first group named. Relative risk was chosen as a measure, as it is more readily applied to the clinical situation.

The groups of trials were examined for statistical evidence of heterogeneity using a chi-square test. If there was no obvious heterogeneity on visual inspection or statistical testing, pooled relative risks and 95% confidence intervals were calculated using a fixed-effects model.

We assessed the skewness of continuous data by checking the mean and standard deviation (if available). If the standard deviation is more than twice the mean for data with a finite end point (such as 0 in the case of bleeding), the data are likely to be skewed and it is inappropriate to apply parametric tests (Altman 1996). This is because the mean is unlikely to be a good measure of central tendency. If parametric tests could not be applied, we tabulated the data.

The effect of excluding trials judged to have inadequate (scoring C) allocation concealment were examined in a sensitivity analysis.

DESCRIPTION OF STUDIES

For more detailed descriptions of individual studies, please see the table of included studies.

A total of 57 trials met the inclusion criteria, with a total of 3659 participants. The earliest trial was from 1980 and the most recent from 2001. From the drug companies we contacted, we were sent information by Hoechst, Baxter Health Care Ltd, Fresenius Ltd, CIS UK Ltd, and Rhemoacrodex. No new trials were identified from the information sent to us.

The trials included the following comparisons:
Albumin or PPF vs starch (n=35 trials with 1482 participants in these groups)
Boldt 1986, Boldt 1996A, Boldt 1996B, Boldt 1996C, Boldt 1993, Boldt 1995, Boldt 1998, Brock 1995, Brutocao 1996, Claes 1992, Diehl 1982, Falk 1988, Fulachier 1994, Gahr 1981, Gallagher 1985, Gold 1990, Hausdorfer 1986, Hippala 1995, Huskisson 1993, Kirklin 1984, London 1989, Munsch 1988, Munoz 1980, Moggio 1983, Mastroianni 1994, Prien 1990, Rosencher 1992, Rackow 1983, Rackow 1989, Shatney 1983, Vogt 1994, Vogt 1996, Vogt 1999, Von Sommoggy 1990, Woittiez 1997.

Albumin or PPF vs dextran (n=5 trials with 390 participants in these groups):
Hedstrand 1987, Hippala 1995, Karanko 1987, Lisander 1996, Tollosfrud 1995

Albumin or PPF vs gelatin (n=13 trials with 997 participants in these groups):
Boldt 1986, Du Gres 1989, Huskisson 1993, Karanko 1987, Stockwell 1992, Stoddart 1996, Tollosfrud 1995, Wahba 1996.

Starch vs gelatin (n=15 trials with 848 participants in these groups):
Allison 1999, Asfar 2000, Beards 1994, Berard 1995, Beyer 1997, Boldt 1986, Boldt 2000, Boldt 2001, Carli 2000, Dytkowska, Haisch 2001a, Haisch 2001b, Huskisson 1993, Huttner 2000, Schortgen 2001.

Starch vs dextran (n=1 trial with 30 participants in these groups): Hippala 1995.

Dextran vs gelatin (n=2 trial with 42 participants in these groups): Karanko 1987, Tollosfrud 1995.

The trials included patients with hypovolaemia, sepsis, trauma, and patients who had undergone surgery.

The trials tended to report surrogate outcomes such as hemodynamic variables. Data on death were obtainable from only 31 of

the trials. Information on the amount of blood transfused was available in 31 of the trials. However this was reported in a variety of different ways that made combining the data in a meta-analysis unfeasible.

Inclusion and exclusion criteria varied, but many of the studies excluded patients with previous adverse reactions to colloids, clotting problems, or renal disease.

METHODOLOGICAL QUALITY

Using predefined criteria (Schulz 1995) the quality of allocation concealment was judged to be adequate in 20 trials, unclear in 29 trials and inadequate in eight trials. Where the method of allocation concealment was unclear, we attempted to contact all of the trialists and we obtained information from 11 of them. However, due to the lack of reported information on the process of randomisation and allocation concealment, we were unable to properly assess the quality of the majority of the trials. Ten trials mentioned blinding. In four of these those giving the treatment were blinded, in four those giving post-operative care and were blinded and in the other two trials the outcome assessors were blinded.

RESULTS

Of the 57 trials identified 24 reported mortality data. Information on death was obtained from a further 12 trials by contact with the authors. We therefore had data on death from 36 trials.

Albumin or PPF vs starch:
Twenty trials (1029 participants) reported mortality data. The pooled relative risk was 1.17 (95% CI 0.91-1.50).

Albumin or PPF vs gelatin:
Four trials (542 participants) reported mortality but only one of those trials had any deaths. The relative risk was 0.99 (95% CI 0.69-1.42).

Albumin or PPF vs dextran:
Three trials reported mortality and were included in the meta-analysis. There were no deaths so relative risk was not estimable.

Gelatin vs starch:
Eleven trials (945 participants) reported mortality and the pooled relative risk was 1.00 (95% CI 0.78-1.28).

Gelatin vs dextran 70
There were two trials which reported mortality. There were no deaths so the relative risk was not estimable.

Hydroxyethyl starch vs dextran 70:
No trials reported mortality.

Thirty-five trials recorded the amount of blood transfused. As the data was reported in various ways, often lacking a measure of variation, and was also skewed we did not attempt a quantitative synthesis. This data can be seen in the "other data" table. Fifteen trials reported the incidence of adverse or allergic reactions or anaphylactic shock: all reported that there were no such incidents.

The effect of excluding trials judged to have inadequate (scoring C) allocation concealment was examined in a sub-group analysis. This made no significant difference to the results.

DISCUSSION

Despite finding 57 trials we cannot make any conclusions about the relative effectiveness of different colloid solutions. A previous review suggested that albumin may increase mortality in critically ill patients (CIGAR 2000), but there are too few data available to show in direct comparisons whether the synthetic alternatives are safer. The confidence intervals are wide and do not exclude clinically significant differences between colloids.

Mortality was selected as the main outcome measure in this systematic review for several reasons. In the context of critical illness, death or survival is a clinically relevant outcome that is of immediate importance to patients, and data on death are reported in many of the studies. Furthermore, one might expect that mortality data would be less prone to measurement error or biased reporting than would data on pathophysiological outcomes. The use of a pathophysiological end point as a surrogate for an adverse outcome assumes a direct relationship between the two, an assumption that may sometimes be inappropriate. Finally, when trials collect data on a number of physiological end-points, there is the potential for bias due to the selective publication of end-points showing striking treatment effects.

There was wide variation in the participants, intervention regimens, and the length of follow-up. The length of follow-up is not reported in many of the studies. Where it is reported it ranges from a matter of hours to months, which may explain a lot of the heterogeneity in overall event rates. The effect of these factors was not examined in a sensitivity analysis, as there was felt to be insufficient data to justify examining subgroups.

Many of the trials were small, and some had been done some time ago. Although older trials will not necessarily be of poorer quality, it may be that treatment protocols have subsequently altered making these trials less relevant to current clinical practice.

AUTHORS' CONCLUSIONS

Implications for practice

Previous reviews have failed to show any benefit of colloids over crystalloids for volume replacement (Schierhout 2000) and suggested that albumin solution may increase mortality in critically ill patients (CIGAR 2000).

This review does not provide any evidence that one colloid is safer than another, but does not rule out clinically significant differences.

Implications for research

Trials of fluid therapy need to be larger in order to exclude clinically significant differences between colloids in patient relevant outcomes. However, trials should probably first address the question of whether colloids are any more effective than crystalloid solutions.

Use of surrogate outcomes, such as physiological measurements should be discouraged unless there is a strong relationship with outcomes of interest to patients and relatives.

FEEDBACK

Colloid solutions for fluid resuscitation

Summary

1. Please explain, in the 'what's new' section, in what respects this update differs from the previous version.
2. The drug companies listed in the acknowledgments are not in alphabetic order: please do so or explain the reason for the order shown (e.g. in order of helpfulness).
3. Fresenius is misspelt
4. In the references to included trials, please use an asterisk to identify those trials which are the main publication where there are more than one article referring to a trial.

Author's reply

1. The review has been marked as an update by mistake. As of September 1999 no substantial updates have been made.
2. The drug companies have been re-ordered alphabetically.
3. The spelling of Fresenius is corrected.
4. The primary reference has been marked with an asterisk.

Contributors

Comment by Andrew Herxheimer
Response by Frances Bunn

POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

We wish to acknowledge the help of Ralph Bloch, Olivier Duperrex, Andrew Smith, Peter Smith and Reinhard Wentz, who assisted with translating articles. Also many thanks to the authors who provided us with details of their studies.
We are grateful to the drug companies, Baxter Healthcare Ltd, CIS Ltd, Fresenius, Hoechst, and Pharmalink who responded to our request for information.

SOURCES OF SUPPORT

External sources of support

- NHS Research and Development Programme UK

Internal sources of support

- University of Hertfordshire UK

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Allison 1999
Methods	Randomised controlled trial. Randomisation was based on date of admission (on even dates patients received HES) Analysis not intention to treat
Participants	45 patients with blunt trauma who required colloid infusion. Patients were excluded if they were less than 12yrs old, did not require admission to the ITU, died within 24 hours, were pregnant or in renal failure. 8 gelatine and 6 HES patients excluded after randomisation.
Interventions	1) HES (200/0.45 Pentaspan) n=24. 2) Gelatine (gelofusine) n=21 After 24 hours, colloid administration was at the discretion of the clinician.
Outcomes	Glasgow coma score, volumes of blood and platelets infused, haematological parameters.

Characteristics of included studies (*Continued*)

Notes	Data were collected until the patient left the ITU or for a maximun of 5 days. Main outcome of interest was capillary leak.
Allocation concealment	C – Inadequate

Study	**Asfar 2000**
Methods	Randomised unblinded controlled trial. Allocation using sequentially numbered sealed opaque envelopes (information obtained on contact with the author).
Participants	34 septic, hypovolaemic, ventilated and hemodynamically controlled patients. Inclusion criteria: patients aged over 16yr, systolic arterial pressure higher than 90mmHg and hypovolemia defined by PAOP of 12mmHg or less. Patients with an overt hemodynamic, ventilatory or acid base status instability were excluded. Sepsis was identified by either positive bacterial blood cultures, bronchoalveolar lavage or clinical evidence of infection.
Interventions	1) 6% HES (n=16). 2) 4% Modified fluid gelatin (MFG) (n=18).
Outcomes	Haemodynamic and tonometric parameters. Death.
Notes	Follow-up was for one hour. Two patients in the HES grp were excluded because they experienced haemodynamic instability. The final analysis was made on remaining 16 patients.
Allocation concealment	A – Adequate

Study	**Beards 1994**
Methods	Randomised controlled trial (allocation by alternation). Information on allocation concealment was obtained on contact with the author.
Participants	28 patients with hypovolaemia, mechanically ventilated for concurrent acute respiratory failure. Patients fulfilled the following inclusion criteria: age >16 yrs, body weight between 50 and 85kg, mean arterial pressure <80mmHg (or 30mmHg less than previously recorded); pulmonary artery occlusion pressure <10mmHg with oliguria (i.e urine output <15 ml/hr).
Interventions	1) Rapid infusion of 500ml modified fluid gelatin (n=15). 2) Rapid infusion of 500ml hetastarch (n=13).
Outcomes	Haemodynamic variables were measured for 30 minutes. Oxygen variables were measured for 30 minutes. Deaths in hospital reported.
Notes	Patients were followed up to discharge from hospital.
Allocation concealment	C – Inadequate

Study	**Berard 1995**
Methods	Randomised controlled trial. A set of 200 tickets (type 1) and another set of 200 tickets (type 2) were mixed in a box. One ticket was drawn at random for each patient. Information on method of randomisation was obtained on contact with the author. Blinding not mentioned.
Participants	319 patients in a resuscitation service receiving medical (gastrointestinal haemorrhage) and surgical cases. Patients were excluded if they had had a prior allergic reaction.
Interventions	1) Gelatin (n=153). 2) HES (n=146) The prescribers chose the quantity of colloid, guided by normal practice.
Outcomes	Death. Amount of colloid and red blood cells given.

	Cost.
Notes	20 patients lost to follow up, no explanation given. Follow up to discharge.
Allocation concealment	C – Inadequate

Study	**Beyer 1997**
Methods	Randomised controlled trial. Allocation was by a list of random numbers read by someone not entering patients into the trial (closed list). Information on method of allocation concealment was obtained by contact with the author. No blinding.
Participants	48 patients undergoing major elective hip surgery with an expected blood loss of >1000 ml. Exclusion criteria were haemoglobin concentration < or equal to 11g/dl, heart failure and coronary artery disease, myocardial infarction within the past 6 months, hypertension (>180mmHg systolic), impaired renal function, pregnancy, known hypersensitivity to HES or gelatin, patient taking drugs that may specifically affect blood viscosity, diuresis or clotting.
Interventions	1) 3% modified fluid gelatin (n=22). 2) 6% HES (n=19) Both groups also given Ringer's lactate. Fluids administered according to haemodynamic and clinical parameters.
Outcomes	Haemodynamic variables. Packed cell volume, haemoglobin, clotting times. Incidence of allergic reactions. Information on death was obtained by contact with the author.
Notes	Seven patients were lost to follow up but only 5 were accounted for.
Allocation concealment	A – Adequate

Study	**Boldt 1986**
Methods	Randomised controlled trial, using sealed opaque envelopes. Information on allocation concealment was obtained on contact with the authors. Blinding not mentioned. 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) 500ml 20% human albumin solution (n=15) 2) 500ml 3% HES (n=13) 3) 500ml 3.5% gelatine (n= 14) 4) no colloid (n=13)
Outcomes	Haemodynamic variables were measured. Incidence of anaphalactic shock measured. Blood transfused.
Notes	Follow-up until discharge from intensive care.
Allocation concealment	B – Unclear

Study	**Boldt 1993 A**
Methods	Randomised controlled trial. Method of allocation concealment not described in published report. Authors were contacted and confirmed the use of sequentially numbered sealed opaque envelopes.
Participants	75 men undergoing elective aortocoronary bypass grafting, who had a pulmonary capillary wedge pressure of less than 5mmHg after induction of anaesthesia.
Interventions	1) Albumin 5%. (n=15)

	2) 6% HES, HMW (n=15) 3) 6% HES, LMW (n=15) 4) Gelatin 3.5% (n=15) 5) No additional volume.
Outcomes	Deaths not reported. Authors were contacted and confirmed that there were no deaths in the albumin nor the control group.
Notes	Follow-up 1 day.
Allocation concealment	A – Adequate

Study	**Boldt 1995**
Methods	Randomised controlled trial. Randomisation was by the use of sequentially numbered sealed opaque envelopes. Information on allocation concealment was obtained on contact with the author. Blinding of outcome assessors not mentioned.
Participants	30 consecutive trauma patients (injury severity score >15) and 30 consecutive septic patients who underwent major surgery. Exclusions: patients suffering from renal failure requiring haemofiltration, severe liver dysfunction or coagulation abnormalaties in their history were excluded as were patients who were receiving aspirin or other cyclooxygenase inhibitors.
Interventions	1) 10% HES, LMW (n=15 trauma pts and 15 sepsis patients) 2) 20% human albumin (n=15 trauma pts and 15 sepsis pts). Fluid was given to maintain CVP and PCWP between 12 and 16mmHg.
Outcomes	Haemodynamic parameters. Deaths
Notes	Length of follow-up was 5 days. Deaths were reported within the study period and later (time not specified).
Allocation concealment	A – Adequate

Study	**Boldt 1996 A**
Methods	Randomised controlled trial, allocation by sequentially numbered sealed opaque envelopes. Outcome assessors blinded to treatment.
Participants	30 trauma patients and 30 patients suffering from sepsis secondary to major general surgery. Exclusions were patients with renal impairment, liver insufficinecy, disseminated intravascular coagulation or septic shock.
Interventions	1) 10% HES (n=30) 2) 20% human albumin solution (n=30) All patients also received Ringer's lactate solution. Volume therapy was given to maintain PCWP between 12 and 18mm Hg.
Outcomes	Haemodynamic variables. Death at 5 days and discharge from intensive care.
Notes	
Allocation concealment	A – Adequate

Study	**Boldt 1996 B**
Methods	Randomised controlled trial. Randomisation was by the use of sequentially numbered sealed opaque envelopes. Information on allocation concealment was obtained on contact with the author. The doctors giving the fluid were blinded to the solution but blinding of outcome assessors not mentioned. Loss to follow up not mentioned.
Participants	45 consecutive trauma patients transferred to the surgical intensive care unit. Inclusion criteria were an injury severity score of >15 points.

Characteristics of included studies (*Continued*)

	All patients were haemodynamically stable before being admitted to the study.
Interventions	1) 10% HES (n=15). 2) 20% human albumin (n=15). 3) unspecified volume therapy regime (n=15). The allocated solution was given to maintain CVP and or PAWP between 12 and 18mmHg.
Outcomes	Death. Haemodynamic variables. Circulating adhesion molecules.
Notes	Deaths were reported within the study period and later (left ITU).
Allocation concealment	A – Adequate

Study	**Boldt 1996 C**
Methods	Randomised controlled study. Randomisation was by the use of sequentially numbered sealed opaque envelopes. Outcome variables were collected by an investigator who was blinded to the treatment. Loss to follow up not mentioned.
Participants	56 patients from the surgical intensive care unit. 28 patients with an injury severity score >15 and 28 patients with sepsis secondary to major surgery. Patients with renal insufficiency, urine output <20ml h, severe liver dysfunction or disseminated intravascular coagulation were excluded.
Interventions	1) 10% HES, LMW (trauma n=14, sepsis n=14) 2) 20% human albumin. (trauma n=14, sepsis n=14) Fluid was infused to maintain PCWP at 10-15mmHg.
Outcomes	Haemodynamic variables. Death.
Notes	Length of follow up was 5 days. Deaths were reported within the study period and later (time not specified).
Allocation concealment	A – Adequate

Study	**Boldt 1998**
Methods	Randomised controlled trial. Sequentially numbered sealed opaque envelopes were used. Information on allocation concealment was obtained on contact with the authors. Blinding of outcome assessors not mentioned. Loss to follow up not mentioned.
Participants	150 traumatised patients (injury severity score >15) and 150 postoperative patients with sepsis. Patients suffering from renal failure, severe liver insufficiency, or with major coagulation abnormalaties were not included.
Interventions	1) 10% HES, LMW (n=150). 2) 20% human albumin (n=150). Both for 5 days to maintain the pulmonary wedge pressure between 12 and 15 TORR
Outcomes	Death. Haemodynamic variables. Organ function. Coagulation.
Notes	Deaths were reported within the study period and after the study period (time not specified).
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Boldt 2000**
Methods	Randomised controlled trial. Allocation by sequentially numbered sealed opaque envelopes (information obtained by contacting the author)
Participants	150 patients undergoing major abdominal surgery
Interventions	1) 6% HES, LMW (n=50). 2) 6% HES, MMW (n=50). 3) 3% modified fluid gelatin (n=50) To keep MAP more than 70 mm Hg and CVP between 10 and 14 mm Hg. Volume was given perioperatively until the morning of the first post-op day. For each hour of surgery 500-800ml of crsytalloids was routinely infused.
Outcomes	Death. Haemodynamic variables, blood loss, blood transfused, cost.
Notes	Deaths were reported for the study period (when there were no deaths) and after the study period (when there was 1 death in the HES 70 grp, 2 deaths in the HES 200 grp and 1 death in the gelatin grp). The study period lasted until the first day post-op.
Allocation concealment	A – Adequate

Study	**Boldt 2001**
Methods	Randomised controlled trial. Allocation by a "closed envelope system". Volume therapy was done by doctors who did not know the aim of the study.
Participants	75 patients undergoing major abdominal surgery. Volume was administered to keep the CVP between 8 and 12mmHg.
Interventions	1) 6% HES (n=25). 2) 6% HES (n=25). 3) 4% modified fluid gelatin (n=25) All groups also received 500ml of ringers lactate for each hour of surgery.
Outcomes	Death. Haemodynamic variables, blood loss, blood transfused.
Notes	There were no deaths in the study period (until first postoperative day) but afterwards there was one death in the colloids group and no deaths in the gelatin group.
Allocation concealment	A – Adequate

Study	**Brock 1995**
Methods	Randomised controlled trial with list of random numbers read by someone entering patients into the trial (open list). Data on allocation concealment was obtained on contact with the authors.
Participants	21 patients who had undergone cardiac surgery.
Interventions	1) 10% HES. 200/0.5 in 7.2% saline (n=7) 2) 5% human albumin (n=7). 3) 6% hydroxyethylstarch in 0.9% saline (n=7).
Outcomes	Hemodynamic variables were collected. Data on death was obtained on contact with the authors.
Notes	

Characteristics of included studies (*Continued*)

Allocation concealment	C – Inadequate

Study	**Brutocao 1996**
Methods	Randomised double-blind controlled trial with pharmacy controlled randomisation. Information on allocation concealment was obtained on contact with the authors.
Participants	Children aged 1 year or more who were undergoing surgical repair of a congenital heart disease. Exclusion criteria included amrinone therapy, renal disease, coagulopathy or a known bleeding diathesis.
Interventions	1) 5% albumin (n=18). 2) 6% HES (n=20). Volume expansion was administered as clinically indicated to maintain adequate central venous pressure, perfusion and urine output. The total amount of colloid therapy was determined by care providers blinded to the randomisation.
Outcomes	Haemodynamic variables. Coagulation variables. Information on death was obtained on contact with the authors.
Notes	Follow-up was until discharge from hospital. 9 children excluded post randomisation because they did not require colloid.
Allocation concealment	A – Adequate

Study	**Carli 2000**
Methods	Randomised controlled trial. Each centre had a list and the patients were randomised by the regulatory Dr of the Institute.
Participants	164 trauma patients. Patients were included if their SBP was less than 100mmHg, associated with signs of hypoperfusion.
Interventions	1) HES (Hesteril 6%) (n= 85). 2) Gelatin (Plasmion) (n=79)
Outcomes	Glasgow coma score. Haemodynamic variables Units of blood transfused Adverse reaction
Notes	There were 13 deaths from heart failure but these patients were excluded from the final analysis.
Allocation concealment	B – Unclear

Study	**Claes 1992**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	20 patients undergoing brain tumor surgery and 20 patients undergoing transabdominal hysterectomy. Exclusion criteria were preexisting coagulopathies; abnormal preoperative coagulation screening tests; intake of drugs affecting haemostasis within 2 wk preoperatively as well as liver or kidney dysfunction.
Interventions	1000ml of fluid for volume replacement, either as 1) 6% HES (n=19). 2) 5% human albumin solution in 0.9% NaCl (n=21).
Outcomes	Haemodynamic variables. Coagulation variables.
Notes	Follow up 48 hrs post-op.

Allocation concealment	B – Unclear

Study	**Diehl 1982**
Methods	Randomised controlled trial. Patients were allocated to groups according to their hospital identification number. Blinding not mentioned. No loss to follow up.
Participants	60 Patients undergoing coronary artery bypass.
Interventions	1) 6% HES (n=27) 2) 5% albumin (n=33) for volume expansion during the first 24 hours postoperatively. Neither hetastarch or albumin was used intraoperatively or in the pump prime.
Outcomes	Death. Coagulation data. Haemodynamic variables.
Notes	Followup 7 days post-op.
Allocation concealment	C – Inadequate

Study	**Du Gres 1989**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	30 patients post cardiac surgery. Patients were included if they were haemodynamically stable, were without serious 'rhythm' problems, had a mean arterial pressure less than 90mmHg, a mean pulmonary artery pressure less than 20mmHg and a central venous pressure less than 10mmHg. Patients excluded if they needed blood transfusion, had a hematocrit less than 28% or haemoglobin less than 9g/100ml.
Interventions	1) 4% human albumin (n=15). 2) Haemaccel (n=15).
Outcomes	Haemodynamic parameters.
Notes	Follow up 4 hours.
Allocation concealment	B – Unclear

Study	**Dytkowska 1998**
Methods	Randomised controlled trial. No information given on method of allocation concealment
Participants	40 patients post cardiac surgery. Patients were excluded if they had co-existing cardiogenic shock, renal failure with creatine level over 3.0mg or severe clotting disorders.
Interventions	1) 200/0 HAES 6% (n=20). 2) Gelafundin (n=20) Colloids were administered to patients with diagnosed symptoms of hypovolaemia, during the first 24 hours post-op. Infusion rate was adjusted to patients needs but it did not exceed 1000ml/h
Outcomes	Haemodynamic parameters. Biochemical parameters. Adverse reactions.
Notes	Follow up 2 hours.
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Falk 1988**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	12 patients with septic shock. Patients were excluded from the study if the pretreatment PAWP was greater than 10mmHg.
Interventions	1) 250ml of 5% albumin (n=6). 2) 250ml of 6% HES (n=6). every 15 minutes until the PAWP was increased to 15mmHg. The test infusion was then continued at 100 mL/hour to maintain PAWP at 15 mm Hg for the next 24 hours.
Outcomes	Haemodynamic variables. Clotting variables.
Notes	Follow up 24 hours.
Allocation concealment	B – Unclear

Study	**Fulachier 1994**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	16 patients undergoing cardiac surgery (8 were undergoing valve replacement and 8 coronary bypass) Patients were excluded if they were over 80, under 18 yrs of age, had been included in other studies, had received colloids in the month preceding surgery, had coagulation abnormalaties or who were undergoing inotropic treatment.
Interventions	1) 500ml of a 4% solution of human albumin in Ringer's lactate (n=8) 2) 500ml of hydroxyethylstarch (n=8) until starting cardiopulmonary bypass.
Outcomes	Haemodynamic variables.
Notes	Follow up 30 minutes.
Allocation concealment	B – Unclear

Study	**Gahr 1981**
Methods	Randomised controlled trial. No information given on method of randomisation. No loss to follow up
Participants	20 patients with hypovolaemia following abdominal surgery for malignoma.
Interventions	1) 500ml HES 450/0.7 (n=10). 2) 500ml human albumin 5% (n=10) during the first 24 hrs after the operation
Outcomes	Haemodynamic parameters Coagulation data.
Notes	Follow up 6 hrs.
Allocation concealment	B – Unclear

Study	**Gallagher 1985**
Methods	Randomised controlled trial. Author contacted - allocation concealment by computerised system - patient details were entered before treatment assignment was revealed.
Participants	10 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) 5% albumin (n=5). 2) 6% HES (n=5).
Outcomes	Data on deaths from author. Haemodynamic data.
Notes	Follow up 1 day.
Allocation concealment	A – Adequate

Study	**Gold 1990**
Methods	Randomised controlled trial. Randomisation was done by alternation. Colloid solution was blinded by covering with foil. Information on allocation concealment was obtained by contact with the author. No loss to follow up.
Participants	40 Surgical patients undergoing abdominal aortic aneurysm surgery.
Interventions	1) 1g/kg of albumin 5% solution (n=20). 2) 1g/kg or hetastarch 6% solution (n=20).
Outcomes	Haemodynamic and coagulation variables were measured. Data on death was obtained on contact with the author.
Notes	Length of follow up not specified.
Allocation concealment	C – Inadequate

Study	**Haisch 2001a**
Methods	Randomised controlled trial. No information given on method of allocation concealment. Patient management by doctors who were blided to the grouping.
Participants	42 patients undergoing cardiac surgery. Patients were excluded if they had: an MI within previous 3 months, renal insufficiency, liver insufficiency, non controlled diabetes mellitus, preoperative coagulation abnormalities or patients treated with heparin or cyclooxygenase inhibitors within last 7 days.
Interventions	1) Gelatin (n=21). 2) HES (n=21).
Outcomes	Deaths. Use of blood products.
Notes	Follow up until first postoperative day.
Allocation concealment	B – Unclear

Study	**Haisch 2001b**
Methods	Randomised controlled trial using computer generated random numbers. No information given on allocation concealment.
Participants	42 patients undergoing major abdominal surgery for malignancies. Patients were excluded if they had cardiac insufficiency, renal insufficiency, altered liver function, pre-operative anemia, pre-operative coagulation abnormalities or if they had had cycloxygenase inhibitors.
Interventions	1) HES (n=21). 2) Gelatin (n=21) until the morning of the first post-operative day.
Outcomes	Death. Use of allogenic blood products.

Characteristics of included studies (*Continued*)

	Coagulation variables.
Notes	Follow up until first postoperative day.
Allocation concealment	B – Unclear

Study	**Hausdorfer 1986**
Methods	Randomised controlled trial. No information given on method of randomisation.
Participants	30 children undergoing major surgery. During about 3 hours of surgery, the patients lost up to 15% of blood volume.
Interventions	1) Human albumin 5% (n=15). 2) HES 6% (n=15) with 14ml/kg body weight each, respectively.
Outcomes	Haemodynamic variables.
Notes	Follow up 24 hours post-op.
Allocation concealment	B – Unclear

Study	**Hedstrand 1987**
Methods	Randomised controlled trial. no information given on method of randomisation. Post-op care staff were blinded. No loss to follow up.
Participants	275 patients underdoing major surgery. Patients were excluded if they if they were known to have decreased serum albumin levels or expected to sustain plasma loss, or had pronounced cardiovascular disease.
Interventions	1) PPF (n=142). 2) Dextran (n=133.
Outcomes	Volume transfused. Complication rates. Serum albumin Deaths
Notes	Follow up one month.
Allocation concealment	B – Unclear

Study	**Hiippala 1995**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. 3 patients lost to follow up (explanation given).
Participants	60 patients undergoing major abdominal or urological surgery. Patients who had used platelet inhibiting drugs or had a diagnosed haemostatic defect were excluded.
Interventions	1) 3% dextrose (n=15). 2) 4% HES (n=15). 3) 6% HES (n=15). 4) 5% albumin (n=15).
Outcomes	Haemodynamic variables. Clotting variables. Blood loss.
Notes	Follow up 3 days post-op.
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Huskisson 1993**
Methods	Randomised controlled trial. No information given on method of randomisation.
Participants	27 children returning to the intensive care unit following hypothermic open heart surgery.
Interventions	1) Albumin. 2) Gelatin. 3) Hetastarch.
Outcomes	Haemodynamic variables.
Notes	
Allocation concealment	B – Unclear

Study	**Huttner 2000**
Methods	Randomised controlled trial. Allocation concealment using 'blind envelopes'. Anaesthetists responsible for patients management were blinded to the grouping.
Participants	60 patients undergoing major abdominal surgery. Patients were excluded if they had any of the following: cardiac insufficiency, renal insufficiency, liver dysfunction, pre-operative anaemia or coagulation abnormalities, or were on cyclooxygenase inhibitors or non steroidal therapy.
Interventions	1) 4% Gelatin (n=20). 2) 6% LMW HES (n=20). 3) 6% MMW HES (n=20).
Outcomes	Haemodynamic variables. Clotting. variables. Death
Notes	Follow up until first postoperative day.
Allocation concealment	A – Adequate

Study	**Karanko 1987**
Methods	Randomised controlled trial. Patients were randomised in blocks of four. Paper was put into a hat and taken out by an independant person. Information on method of randomisation was obtained on contact with the author. Blinding not mentioned. No loss to follow up.
Participants	48 patients who had undergone coronary bypass surgery 20 hrs earlier.
Interventions	1) 4% PPF (n=15). 2) 6% dextran-70 (n=10). 3) 5.5% Oxypolygelatin (n=12), 4) Control group (n=11). This group were not selected randomly.
Outcomes	Hemodynamic variables. Data on death was obtained on contact with the author.
Notes	Follow up 28 hrs. No deaths within the study period.
Allocation concealment	C – Inadequate

Study	**Kirklin 1984**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.

Characteristics of included studies (*Continued*)

Participants	30 patients undergoing coronary artery operations. Patients were excluded if they had undergone previous cardiac operations, if they had severe coagulopathies, anemia or chronic renal failure.
Interventions	1) 6% HES (n=15). 2) 5% albumin (n=15). Both fluids infused over 24 hours to maintain left artial pressure between 6 and 12mmHg and cardiac index greater than 2.0L/min/m2
Outcomes	Haemodynamic and coagulation variables and data on death and adverse reactions were collected.
Notes	Follow up until discharge from Intensive care. 34 patients were originally included in the trial but data from 4 of them was not included in the final analysis.
Allocation concealment	B – Unclear

Study	**Lisander 1996**
Methods	Randomised controlled trial. Randomisation using sequentially numbered sealed opaque envelopes. Information on allocation concealment was obtained on contact with the author. No loss to follow up. Blinding not mentioned.
Participants	40 patients undergoing revision hip arthroplasty.
Interventions	1) albumin 40g/L (n=20). 2) dextran 70 60g/L (n=20). Patients all received enoxaparin 40mg daily.
Outcomes	External blood loss. Red cell balance. Packed cell volume.
Notes	Follow up until discharge from hospital. Data on death was obtained on contact with the author.
Allocation concealment	A – Adequate

Study	**London 1989**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	93 male cardiac surgical patients. Patients were excluded from the study if they had a significant coagulopathy or were anaemic (haematocrit value <30%).
Interventions	1) 10%. pentastarch in 0.9% saline (n=50). 2) 5% human albumin in 0.9% saline (n=44) to provide volume expansion during the first 24 hours after cardiac operations.
Outcomes	Haemodynamic variables. Coagulation variables. Death. Length of stay.
Notes	One patient was treated twice with an 8-month interval. Follow up until discharge from hospital.
Allocation concealment	B – Unclear

Study	**Mastroianni 1994**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned.
Participants	34 patients undergoing open heart surgery were enrolled.

Characteristics of included studies (*Continued*)

Interventions	1) 10% pentastarch. (n=12). 2) 5% albumin (n=17).
Outcomes	Haemodynamics variables. Clotting variables. Pulmonary oedema. Death.
Notes	Follow up 7 days. Four patients in the pentastarch group, and one patient in the albumin group were excluded after randomisation.
Allocation concealment	B – Unclear

Study	**Moggio 1983**
Methods	Patients were randomised according to the last digit of their hospital identification numbers. No loss to follow up. Blinding not mentioned.
Participants	47 postoperative open heart surgery patients. Operations performed included coronary revascularisation, valve operations, and combined coronary and valve procedures. Patients with pre existing hepatic or renal disease were not eligible for the study.
Interventions	1) 5% albumin in 0.9% NaCl (n=23). 2) 6% HES in 0.9% NaCl (n=24).
Outcomes	Haemodynamic variables. Clotting variables.
Notes	Follow up not specified.
Allocation concealment	C – Inadequate

Study	**Munoz 1980**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No mention of loss to follow up.
Participants	14 patients with shock due to haemorrhage or sepsis.
Interventions	Patients received either 1) HES (hespan) 2) 5% albumin Number in each group not reported.
Outcomes	Haemodynamic variables.
Notes	Follow up 4 hrs post infusion.
Allocation concealment	B – Unclear

Study	**Munsch 1988**
Methods	Randomised controlled trial. No information given on method of randomisation. Blinding not mentioned. No loss to follow up.
Participants	40 consecutive patients undergoing elective coronary artery bypass graft surgery.
Interventions	1) HES 6% (n=20) or 2) PPF (n=20) as their postoperative volume expander.

Characteristics of included studies (*Continued*)

Outcomes	Haemodynamic variables. Clotting variables. Death. Adverse reactions.
Notes	Follow up 7 days post -op.
Allocation concealment	B – Unclear

Study	**Prien 1990**
Methods	Randomised controlled trial. Method of allocation concealment unknown. Blinding not mentioned. Loss to follow up not mentioned.
Participants	18 patients undergoing modified Whipple's operation (hemipancreato-duodenectomy). Patients were eligible for the study if there was an absence of major organ dysfunction and serum protein, sodium, glucose, blood urea nitrogen, haematocrit, aPTT and PT times, and platelet times were within normal limits. Specific exclusion criteria included compensated myocardial insufficiency, chronic hypertension, chronic obstructive airways disease and insulin-dependent diabetes mellitus.
Interventions	1) 10% HES (n=6). 2) 20% human albumin (n=6). 3) Ringer's lactate (n=6) All given as a volume replacement solution, which was given to maintain central venous pressure at the pre-operative level.
Outcomes	Haemodynamic variables. Clotting variables. Data on death was obtained on contact with the author.
Notes	Follow up not specified. Study was intra-operative.
Allocation concealment	B – Unclear

Study	**Rackow 1983**
Methods	Randomised controlled trial, method of allocation concealment not mentioned. Blinding not mentioned.
Participants	18 patients with hypovolemic and septic shock. Patients were excluded if they were less than 18 yrs of age, considered to be in a terminal state, or had a significant coagulopathy.
Interventions	1) albumin (n=9). 2) HES (n=9). Patients received 250ml of the treatment fluid every 15 min as a fluid challenge. The fluid challenge ended when the WP equalled 15 mmHg. Thereafter the treatment fluid was given in sufficient quantities to maintain the WP at 15mmHg for the next 24h, at which point the study was completed.
Outcomes	Death. Haemodynamic variables. Respiratory variables.
Notes	Deaths given for study period and for length of hospital stay. Survival until discharge was used for the mortality data for this review.
Allocation concealment	B – Unclear

Study	**Rackow 1989**
Methods	Randomised controlled trial. Method of allocation concealment was not recorded.

Characteristics of included studies (*Continued*)

	No loss to follow up. Blinding not mentioned.
Participants	20 patients with severe sepsis and systemic hypoperfusion. Patients were excluded from the study if they were <21 yrs of age, pregnant, considered to be terminal, or they manifested spontaneous bleeding.
Interventions	1) 5% albumin (n=10) 2) 10% hydroxyethyl starch (pentastarch) (n=10) Each group received 250ml of the treatment fluid every 15 mins until either the WP was > or equal to 15mm Hg or a maximum volume of 2000ml of study colloid was infused.
Outcomes	Haemodynamic variables Clotting variables Deaths Allergic reactions.
Notes	Length of follow up unspecified.
Allocation concealment	B – Unclear

Study	**Rosencher 1992**
Methods	Randomised controlled trial. Randomisation was done using sequentially numbered, sealed, opaque envelopes. Information on allocation concealment was obtained on contact with the author. No mention of blinding. Loss to follow up not mentioned.
Participants	16 patients undergoing total hip replacement.
Interventions	1) 4% albumin 2) elohes (LMW hydroxyethyl starch). Numbers in each group not reported.
Outcomes	Bleeding. Clotting variables.
Notes	Data on death was obtained on contact with the author. Follow up for 5 days post op.
Allocation concealment	A – Adequate

Study	**Schortgen 2001**
Methods	Randomised controlled trial. Allocation was by sealed opaque envelopes serially numbered and used in sequence.
Participants	129 patients with severe sepsis or septic shock over 18 years of age. Patients were excluded if they were pregnant, had a history of allergy to HES or gelatin, had severe acute or chronic renal dysfunction or previous administration of HES or mannitol.
Interventions	1) 6% hydroxyethylstarch (n=65). 2) 3% fluid-modified gelatin (n= 64).
Outcomes	Death. Length of stay in ITU. Acute renal failure.
Notes	Follow up while in ITU. Data on death. was obtained on contact with the author.
Allocation concealment	A – Adequate

Study	**Shatney 1983**
Methods	Controlled clinical trial. Patients were assigned to groups in an alternating fashion.

	No loss to follow up. No mention of blinding.
Participants	32 patients with multisystem trauma and/or haemorrhagic shock. Patients with cardiac arrest on hospital admission or during the first half hour after admission were excluded from the study.
Interventions	1) Plasma protein fraction (PPF) 5% solution (n=16), 2) Hetastarch 6% (n=16). Study patients continued to receive the assigned colloid solution for the first 8 days whenever colloid was thought necessary.
Outcomes	Hepatic, pulmonary and renal function. Clotting variables Volume of fluids infused. Deaths
Notes	Follow up 8 days.
Allocation concealment	C – Inadequate

Study	**Stockwell 1992**
Methods	Randomised controlled trial. No information given on method of randomisation. No loss to follow up. Blinding not mentioned.
Participants	475 patients admitted to the intensive care unit. Patients were excluded from the study if they were under 18 yrs or if admitted for cardiac monitoring or cardiac thrombolytic therapy.
Interventions	1) 4.5% albumin (n=226). 2) A synthetic colloid polygeline (Haemaccel) (n=249) for intravenous volume replacement.
Outcomes	Death. Length of stay in ITU. Incidence of renal failure. Pulmonary oedema.
Notes	Follow up until discharge from ITU.
Allocation concealment	B – Unclear

Study	**Stoddart 1996**
Methods	Randomised blinded trial. Sequentially numbered sealed opaque envelopes were used. Information on allocation concealment was obtained on contact with the author. Anaesthetist unaware of intervention. No loss to follow up.
Participants	30 neonates undergoing major surgery. They were excluded if the body weight was less than 2kg or more than 5kg, the preoperative haemoglobin was less than 14g/d1, they had previously received blood or colloid, or they had suspected major cardiac, renal, metabolic or chromosomal abnormalities. Neonates were withdrawn from the study if either blood or more than 40ml/kg of colloid was required either during or within the first 24hr after surgery.
Interventions	1) Human albumin solution 4.5% (n=15). 2) Haemaccel (n=15).
Outcomes	Haemodynamic variables. Plasma albumin. Haemoglobin.
Notes	Follow up 24 hrs post op.

	Data on deaths not collected.
Allocation concealment	A – Adequate

Study	**Tollofsrud 1995**
Methods	Randomised controlled trial. Allocation concealment was by the use of sequentially numbered sealed opaque envelopes. Information on allocation concealment was obtained on contact with the authors. No loss to follow up. Blinding not mentioned.
Participants	40 Patients undergoing elective coronary artery bypass surgery. Patients with left ventricular ejection fraction less than 40%, valvular heart disease, ventricular aneurysm, arrhythmia, diabetes mellitus, renal failure or lung disease were excluded.
Interventions	1) Polygeline (Haemaccel) (n=10) 2) Dextran 70 (n=10) 3) Albumin 40 (n=10) 4) Ringers Lactate (n=10).
Outcomes	Death. Haemodynamic variables. Respiratory data. Cost of fluid regimens.
Notes	Length of follow up 48 hours during and after surgery.
Allocation concealment	A – Adequate

Study	**Vogt 1994**
Methods	Randomised controlled trial. No information given on method of randomisation.
Participants	40 patients undergoing major surgery. Exclusion criteria included anaemia, renal, liver and coagulation disorders.
Interventions	1) 5% human albumin (n=20). 2) 6% hydroxyethyl starch (n=20).
Outcomes	Haemodynamic variables. Coagulation. Haematological parameters. Blood loss and blood intake.
Notes	
Allocation concealment	B – Unclear

Study	**Vogt 1996**
Methods	The patients were divided into two groups using random numbers. Blinding not mentioned. No loss to follow up.
Participants	41 patients undergoing total hip arthroplasty during the perioperative period. Exclusion criteria were weight <60 kg, age <18 yrs, ASA grade>III, haematocrit <34% or >44%, history of coagulopathies or a Quick's prothrombin test of < 75%, partial thromboplastin time (PTT) > 45s, platelet count < 100,000/mm3, impaired liver function and renal failure.
Interventions	1) 6% HES (n=20). 2) 5% human albumin (n=21).
Outcomes	Haemodynamic.

	Clotting variables.
Notes	Length of follow up was 6 hrs post-op.
Allocation concealment	B – Unclear

Study	**Vogt 1999**
Methods	Randomised controlled trial. No information given on method of randomisation.
Participants	50 patients undergoing radical prostatectomy or cystectomy with bladder replacement. Exclusion criteria were: weight less than 60kg, age less than 21 yrs, ASA 1 or 2, haemoglobin less than 12g/dl, history of clotting disorders, liver function disorders, advanced renal insufficiency or hypoproteinaemnia.
Interventions	1) 5% human albumin. 2) 6% HES 200/0.5.
Outcomes	Haemodynamic parameters. Blood loss.
Notes	Follow up was for 3 days.
Allocation concealment	B – Unclear

Study	**Wahba 1996**
Methods	Randomised controlled trial. Computerised system was used for randomisation. Data on method of allocation concealment was obtained on contact with the author. Blinding not mentioned. Loss to follow up not mentioned.
Participants	20 patients who had had coronary artery bypass grafting. Patients with abnormal left-ventricular function as judged from cine-angiography were excluded as were patients on anticoagulants less than 10 days before the operation.
Interventions	1) 5% albumin (n=10) 2) Haemaccel (n=10) Number of patients in each group not specified.
Outcomes	Haemodynamic variables. Data on death was obtained on contact with the author.
Notes	Length of follow up was 2 weeks.
Allocation concealment	A – Adequate

Study	**Watkins 1990**
Methods	Randomised controlled trial. No information given on method of randomisation.
Participants	12 patients undergoing major surgery.
Interventions	1) LMW polystarch or 2) Polygelatine (Haemaccel) for postoperative volume replacement.
Outcomes	Death and incidence of adverse reactions are reported. Detailed complement assay done.
Notes	Follow up was for 24 hours after the infusion.
Allocation concealment	B – Unclear

Study	Woittiez 1997
Methods	Randomised controlled trial. Allocation concealment by sequentially numbered sealed opaque envelopes.
Participants	60 patients who had developed hypoalbuminaemia (<20g/l) after major surgery. 2 patients died after randomisation and before treatment started. These 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. Data on death supplied by the author.
Notes	Length of follow up unspecified.
Allocation concealment	A – Adequate

Study	von Sommoggy 1990
Methods	Randomised controlled trial. No information given on method of randomisation. No loss to follow up.
Participants	24 patients undergoing infrarenal aortofemoral bifurcation grafting.
Interventions	1) FFP and 5% human albumin (n=13). 2) Hydroxyethyl starch (HES) 200 10% and HES 450 6%. (n=11).
Outcomes	Haemodynamic variables. Clotting variables. Influence on organ function.
Notes	Follow up 6 hrs post-op.
Allocation concealment	B – Unclear

CVP = central venous pressure
HES = hydroxyethyl starch
HMW = high molecular weight
LMW = low molecular weight
LVEDP = left ventricular end diastolic pressure
MMW = medium molecular weight
MAP = mean arterial pressure
PAWP = pulmonary artery wedge pressure
PAOP = pulmonary artery occlusion pressure
PCWP = pulmonary capillary wedge pressure

Characteristics of excluded studies

Study	Reason for exclusion
Boldt 1993	Pre-bypass volume loading.
Boldt 2000b	Compares two starches with each other.
Brehme 1993	Haemodilution.
Bremerich 2000	Compares two different starches (acetyl starch with hydroxyethyl starch).
Charlet 1991	Study compared two different gelatines with each other and not with other colloids.
Christ 1997	Non-randomised trial.
Emery 1992	Trial compares 20% and 4.5% albumin with each other and not with other colloids.

Characteristics of excluded studies (*Continued*)

Gan 1999	Compares Hextend (a plasma volume expander based upon 6% hetastarch) with 6% hetastarch in saline (HES).
Hankeln 1990	Haemodilution
Harke 1976	Unable to find out if a randomised controlled trial. Methodology unclear.
Hiippala 1996	Patients were expected to have minimal blood loss
Huet 2000	Compares two starches with each other.
Jovanovic 1997	Does not mention if study was randomised. Unable to contact author for further information.
Korttila 1984	Healthy volunteers and cross over trial.
Langeron 2001	Compares two starches with each other
Puri 1983	There is no mention of a method of randomisation. Just says "Twenty-five patients studied in each group were well matched".
Rauch 2000	Compares two starches with each other.
Rehm 2000	Haemodilution.
Strauss 1985	Healthy volunteers.
Waxman 1989	Cross-over study.

ANALYSES

Comparison 01. Albumin or PPF vs Hydroxyethyl Starch

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	20	1029	Relative Risk (Fixed) 95% CI	1.17 [0.91, 1.50]
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

Comparison 02. Albumin or PPF vs Gelatin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	4	542	Relative Risk (Fixed) 95% CI	0.99 [0.69, 1.42]
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

Comparison 03. Albumin or PPF vs Dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	3	85	Relative Risk (Fixed) 95% CI	Not estimable
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

Comparison 04. Modified Gelatin vs Hydroxyethyl starch

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	11	945	Relative Risk (Fixed) 95% CI	1.00 [0.78, 1.28]
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

Comparison 05. Modified Gelatin vs Dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	2	42	Relative Risk (Fixed) 95% CI	Not estimable
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

Comparison 06. Hydroxyethyl starch vs Dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death	0	0	Relative Risk (Fixed) 95% CI	Not estimable
02 Blood/red cells transfused (skewed or inadequate data)			Other data	No numeric data

INDEX TERMS

Medical Subject Headings (MeSH)

Blood Proteins [*therapeutic use]; Colloids [therapeutic use]; Dextrans [*therapeutic use]; *Fluid Therapy; Plasma Substitutes [*therapeutic use]; Randomized Controlled Trials; Rehydration Solutions [*therapeutic use]

MeSH check words

Humans

COVER SHEET

Title	Colloid solutions for fluid resuscitation
Authors	Bunn F, Alderson P, Hawkins V
Contribution of author(s)	FB screened citations for eligibility, obtained references, contacted authors, extracted data, entered data and wrote up the review. PA screened citations for eligibility, extracted data and helped to write the review. VH obtained references, contacted authors, extracted data and helped to write the review. FB and PA updated the review.
Issue protocol first published	1998/4
Review first published	1999/2
Date of most recent amendment	18 August 2003
Date of most recent SUBSTANTIVE amendment	17 September 2002
What's New	The search for the review was updated in September 2002 and five new studies were added to the review. The five new studies all compared gelatin to starch.

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	17 September 2002
Date authors' conclusions section amended	Information not supplied by author
Contact address	Ms Frances Bunn Research Fellow Centre for Research in Primary and Community Care (CRIPACC) University of Hertfordshire College Lane Hatfield Hertfordshire AL10 9PN UK E-mail: f.bunn@herts.ac.uk Tel: 01707 286457
DOI	10.1002/14651858.CD001319
Cochrane Library number	CD001319
Editorial group	Cochrane Injuries Group
Editorial group code	HM-INJ

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Albumin or PPF vs Hydroxyethyl Starch, Outcome 01 Death

Review: Colloid solutions for fluid resuscitation

Comparison: 01 Albumin or PPF vs Hydroxyethyl Starch

Outcome: 01 Death

Study	Albumin or PPF n/N	Hydroxyethyl starch n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Boldt 1995	6/30	5/30		6.4	1.20 [0.41, 3.51]
Boldt 1996 A	9/30	7/30		8.9	1.29 [0.55, 3.00]
Boldt 1996 B	2/15	1/15		1.3	2.00 [0.20, 19.78]
Boldt 1996 C	10/28	9/28		11.4	1.11 [0.53, 2.31]
Boldt 1998	39/150	31/150		39.4	1.26 [0.83, 1.90]
× Brock 1995	0/7	0/14		0.0	Not estimable
× Brutocao 1996	0/18	0/20		0.0	Not estimable
× Diehl 1982	0/33	0/27		0.0	Not estimable
× Gallagher 1985	0/5	0/5		0.0	Not estimable
× Gold 1990	0/20	0/20		0.0	Not estimable
× Kirklin 1984	0/15	0/15		0.0	Not estimable
London 1989	1/44	2/50		2.4	0.57 [0.05, 6.05]
× Mastroianni 1994	0/18	0/16		0.0	Not estimable
× Munsch 1988	0/20	0/20		0.0	Not estimable
Prien 1990	0/6	1/6		1.9	0.33 [0.02, 6.86]
Rackow 1983	6/9	5/9		6.4	1.20 [0.57, 2.53]
Rackow 1989	5/10	5/10		6.4	1.00 [0.42, 2.40]
× Rosencher 1992	0/16	0/16		0.0	Not estimable
Shatney 1983	3/16	3/16		3.8	1.00 [0.24, 4.23]
Woittiez 1997	8/15	13/27		11.8	1.11 [0.60, 2.05]
Total (95% CI)	505	524		100.0	1.17 [0.91, 1.50]

Total events: 89 (Albumin or PPF), 82 (Hydroxyethyl starch)

Test for heterogeneity chi-square=1.62 df=10 p=1.00 I^2 =0.0%

Test for overall effect z=1.21 p=0.2

Analysis 01.02. Comparison 01 Albumin or PPF vs Hydroxyethyl Starch, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study	
Boldt 1998	Total units of red blood cells transfused given for each group (Hetastarch 356, albumin 371). No means, medians or measures of variation given.
Brock 1995	The amount of blood derivaties ('blutderivate') was given in ml as a mean and standard deviation. In the 10% starch group the mean was 379 (SD483), in the 6% starch group the mean was 243 (SD 192) and in the 5% albumin group the mean was 171 (SD236).
Brutocao 1996	Packed red cell transfusion is given in ml/kg. In the HES group the mean is 0.3, the SD 1.3 with a range of 0-6.4. In the albumin group the mean is 1.1 the SD 3.7 and the range 0-13.1
Claes 1992	Blood transfused is not recorded. Authors say "none of the patients lost an abnormally large quantity of blood or experienced a clinically perceptible coagulation disorder."
Diehl 1982	Eighteen percent (n=5) of the albumin group and 15% (n=5) of the HES group received banked blood during their stay. Blood transfused is recorded as mean number of units per person. In the albumin group this is 0.37 unit per person and in the HES group this is 0.36 unit per person.
Falk 1988	Packed red blood cells transfused at 24 hours is given in mls. The albumin group received a mean of 375 with a standard error of 244 and the HES group received a mean of 700 with a standard error of 228.
Gallagher 1985	Amount of blood products transfused post operatively was given as a mean in mls with the SEM. For the albumin group the mean was 560 mls (SEM 149.2) and for the starch group the mean was 566 mls (SEM 72.6).
Gold 1990	Packed red blood cells is given in units. The albumin group received a mean of 2.05 and the HES group received a mean of 2.50.
Hiippala 1995	Amount of red cell concentrates transfused was given as a mean and standard deviation of ml/kgBW. For albumin the mean was 20 (SD 14), for 4% HES the mean was 20 (SD 14) and for 6% HES the mean was 25 (SD 17).
Kirklin 1984	The amount of red cells given up to the first 24 hours post op is recorded. In the HES group the mean is 430 with a standard error of 90, and in the albumin group the mean is 440 with a standard error of 76
London 1989	Total post op blood transfused is given in mls. in the Albumin group the figures are given as 838 (630) and the HES group 894 (600). It does not report what the figures represent (they may be mean and SD). Intra-operatively the blood given in the albumin group was 400 (346) and in the HES group 336 (400).
Mastroianni 1994	The mean of packed red cells given was recorded in mls. For pentastarch the mean was 167 and for albumin it was 234. Another figure was given 163 for pentasarch and 148 for albumin but it was not clear what this represented.
Moggio 1983	There was no data on amount of blood transfused.
Munsch 1988	amount of whole blood transfused was given as a median volume. For the albumin group it was 830 mls (260-1800), and for the HES group it was 830 mls (50-1840).
Prien 1990	The mean and standard error for the amount of packed red cells given was recorded. For the albumin group the mean was 1.2 with a standard error of 0.7. In the HES group the mean was 1.8 with a standard error of 0.7.
Rackow 1983	Total amount of blood transfused was given in mls at the end of the maintenance period. For the albumin group the mean was 363.9 (SEM 186) and for the starch group the mean was 757.1 (SEM 201).
Rackow 1989	No data on units transfused. The authors say "there was no evidence of clinical bleeding".
Shatney 1983	The amount of red blood cells transfused was given in a graphical form not figures.
Vogt 1994	Amount of EK given was recorded as a mean and standard deviation of the mls given. For the albumin group it was 1138 (SD 763.5), and for the HES group it was 944.4 (SD 466.2).

Vogt 1996	The mean and standard deviation of packed red blood cells transfused was given for the end of surgery and at 6 hours. For the albumin group at the end of surgery the mean was 798 (SD 1147) and at 6 hrs it was 1333 (SD 1399). For the HES group at the end of surgery the mean was 763 (SD 923), and at 6 hrs the mean was 1538 (SD 1074).
Vogt 1999	During surgery the patients in the HES group Amount of packed red blood cells was given as means with standard deviations. In the HES grp the mean was 1510 ml (SD 765) and in the albumin group the mean was 1410 ml (SD 946)
von Sommoggy 1990	The trialists report 'no increased bleeding in the HES group'.

Analysis 02.01. Comparison 02 Albumin or PPF vs Gelatin, Outcome 01 Death

Review: Colloid solutions for fluid resuscitation
Comparison: 02 Albumin or PPF vs Gelatin
Outcome: 01 Death

Study	Albumin or PPF n/N	Gelatin n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Karanko 1987	0/15	0/12		0.0	Not estimable
Stockwell 1992	45/226	50/249		100.0	0.99 [0.69, 1.42]
× Tollofsrud 1995	0/10	0/10		0.0	Not estimable
× Wahba 1996	0/10	0/10		0.0	Not estimable
Total (95% CI)	261	281		100.0	0.99 [0.69, 1.42]

Total events: 45 (Albumin or PPF), 50 (Gelatin)
Test for heterogeneity: not applicable
Test for overall effect z=0.05 p=1

Analysis 02.02. Comparison 02 Albumin or PPF vs Gelatin, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study

Stockwell 1992	The volume of blood products given was recorded as a mean with the range also given. In the albumin group the mean was 1.45 1 (range 1 0-29) and in the haemacell group the mean was 1.39 1 (range 0-66).
Tollofsrud 1995	The amount of erthrocytes given was recorded as a mean and standard deviation. In the albumin group the mean was 240 (SD 310), and in the polygeline group the mean was 490 (SD 548).

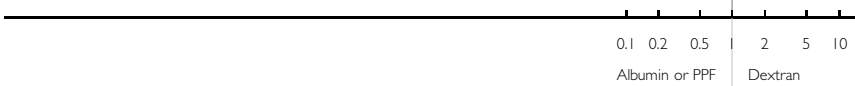
Analysis 03.01. Comparison 03 Albumin or PPF vs Dextran, Outcome 01 Death

Review: Colloid solutions for fluid resuscitation

Comparison: 03 Albumin or PPF vs Dextran

Outcome: 01 Death

Study	Albumin or PPF n/N	Dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Karanko 1987	0/15	0/10		0.0	Not estimable
× Lisander 1996	0/20	0/20		0.0	Not estimable
× Tollofsrud 1995	0/10	0/10		0.0	Not estimable
Total (95% CI)	45	40		0.0	Not estimable
Total events: 0 (Albumin or PPF), 0 (Dextran)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 03.02. Comparison 03 Albumin or PPF vs Dextran, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study

Hedstrand 1987 The perioperative and postoperative amount of red blood cells transfused was reported as a mean and standard deviation of units given. For the plasma group the mean was 5.2 (SD 4.8), and for the dextran group the mean was 5.8 (SD 4.4).

Hiippala 1995 Amount of red cell concentrates transfused was given as a mean and standard deviation of ml/kgBW. For albumin the mean was 20 (SD 14) and for dextran the mean was 19 (12).

Lisander 1996 Total red blood cells transfused is given. For the albumin group the mean is 2.3 and the standard deviation 1.6, in the Dextran group the mean is 3.8 with a standard deviation of 2.4. Red cells autotransfused is also given 312 (184) in the albumin group and 383 (259) in the dextran group.

Tollofsrud 1995 Erythrocytes given was recorded as mean and standard deviation. The mean for the albumin group was 240 (SD 310), and the mean for the dextran group was 390 (SD 417).

Analysis 04.01. Comparison 04 Modified Gelatin vs Hydroxyethyl starch, Outcome 01 Death

Review: Colloid solutions for fluid resuscitation

Comparison: 04 Modified Gelatin vs Hydroxyethyl starch

Outcome: 01 Death

Study	Gelatin n/N	Hydroxyethyl starch n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Allison 1999	0/21	1/24		1.7	0.38 [0.02, 8.83]
Asfar 2000	12/18	10/16		13.0	1.07 [0.65, 1.76]
Beards 1994	6/15	5/13		6.6	1.04 [0.41, 2.62]
Berard 1995	31/153	31/146		38.9	0.95 [0.61, 1.49]
× Beyer 1997	0/22	0/19		0.0	Not estimable
Boldt 2000	1/50	3/100		2.5	0.67 [0.07, 6.25]
Boldt 2001	0/25	1/50		1.2	0.65 [0.03, 15.50]
Haisch 2001a	1/21	1/21		1.2	1.00 [0.07, 14.95]
× Haisch 2001b	0/21	0/21		0.0	Not estimable
Huttner 2000	1/20	1/40		0.8	2.00 [0.13, 30.34]
Schortgen 2001	29/64	28/65		34.1	1.05 [0.71, 1.55]
Total (95% CI)	430	515		100.0	1.00 [0.78, 1.28]

Total events: 81 (Gelatin), 81 (Hydroxyethyl starch)

Test for heterogeneity chi-square=1.00 df=8 p=1.00 I^2 =0.0%

Test for overall effect z=0.03 p=1

Analysis 04.02. Comparison 04 Modified Gelatin vs Hydroxyethyl starch, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study

Allison 1999 The mean volume of PRBC transfused is given for each day up to and including the 5th day. For the first post-op day the HES group received a total of 3,067 ml of packed red blood cells and the Gelatine group received 2,643 ml of packed red blood cells.

Berard 1995 Blood transfused is given in units, 2.6 units for the gel group and 2.5 units for the Hydroxyethyl starch group (presumably this figure is mean).

Beyer 1997 Blood transfused is given in graphical form and not figures.

Boldt 2000 The amount of PRBC transfused is given as the total number of units for each group.
By the first post operative day the number of units of packed red blood cells transfused was:
HES 70 - 38 units
HES 200 - 40 units
Gelatin - 44 units

Boldt 2001 The amount of PRBC transfused is given as the total number of units for each group.

Blood/red cells transfused (skewed or inadequate data) (*Continued*)

Study

	By the first post operative day the number of units of packed red blood cells transfused was: HES 200 18 units HES 130 16 units Gelatin 18 units
Carli 2000	The amount of PRBC transfused is given as the total number of units for each group. 1 unit of blood was given in the gel group and no units of blood were given in the starch group.
Haisch 2001a	The amount of PRBC and FFP transfused is given as the total number of units for each group. PRBC Gelatine = 16 units Starch = 20 units FFP Gelatin = 6 Starch = 8
Haisch 2001b	The amount of PRBC and FFP transfused is given as the total number of units for each group. PRBC Gelatin = 17 Starch = 14 FFP Gelatin = 12 Starch = 12
Huttner 2000	The amount of PRBC transfused is given as the total number of units for each group. Units of PRBC were as follows: HES 51 Gelatin 29

Analysis 05.01. Comparison 05 Modified Gelatin vs Dextran, Outcome 01 Death

Review: Colloid solutions for fluid resuscitation

Comparison: 05 Modified Gelatin vs Dextran

Outcome: 01 Death

Study	Gelatin n/N	Dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Karanko 1987	0/12	0/10		0.0	Not estimable
× Tollofsrud 1995	0/10	0/10		0.0	Not estimable
Total (95% CI)	22	20		0.0	Not estimable
Total events: 0 (Gelatin), 0 (Dextran)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 05.02. Comparison 05 Modified Gelatin vs Dextran, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study

Tollofsrud 1995 Erythrocytes given was recorded as mean and standard deviation. The mean in the polygeline group was 490 (SD 548), and the mean in the dextran group was 390 (SD 417).

Analysis 06.02. Comparison 06 Hydroxyethyl starch vs Dextran, Outcome 02 Blood/red cells transfused (skewed or inadequate data)

Blood/red cells transfused (skewed or inadequate data)

Study

Hiippala 1995 Amount of red cell concentrates transfused was given as a mean and standard deviation of ml/kgBW. For dextran the mean was 19 (SD 12), for 4% starch the mean was 20 (SD 14) and for 6% starch the mean was 25 (SD 17).