

# Do Colloids Improve Mortality Compared With Crystalloids for Resuscitation of Critical Patients?



## TAKE-HOME MESSAGE

When used as an intravenous resuscitation fluid in critically ill adult and pediatric patients, colloids, including starches, dextrans, albumin, fresh frozen plasma, and gelatins, do not improve mortality compared with crystalloids.

## METHODS

### DATA SOURCES

Authors searched the Cochrane Central Register of Controlled Trials, MEDLINE Ovid, EMBASE Ovid, PubMed, Web of Science, the National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov), the World Health Organization International Clinical Trials Registry Platform, OpenGrey, and reference lists of relevant systematic reviews identified during their search on February 23, 2018, for randomized controlled trials and quasi-randomized trials including critically ill patients and comparing crystalloids with colloids.

### STUDY SELECTION

Studies had to compare crystalloids with starches, dextrans, either albumin or fresh frozen plasma, or gelatins individually. Crystalloids could be either isotonic or hypertonic. Subjects in the studies had to be described as critically ill and requiring fluid volume replacement for burns, trauma, or severe medical conditions such as sepsis. Exclusion criteria included elective surgical procedures, neonates, women experiencing cesarean section, colloids

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Lewis SR, Pritchard MW, Evans DJW, et al. Colloids versus crystalloids for fluid resuscitation in critically ill people. *Cochrane Database Syst Rev.* 2018;8:CD000567.**

## Results

Select outcome measures for starches versus crystalloids.

Outcome	Subjects (No. of Studies)	RR (95% CI)	I <sup>2</sup> , %
Mortality within 30 days	10,135 (11)	0.99 (0.90-1.09)	12
Blood transfusion	1,917 (8)	1.19 (1.02-1.39)	14
RRT	8,527 (9)	1.30 (1.14-1.48)	0
Allergic reactions	7,757 (3)	2.59 (0.27-24.91)	0
Itching	6,946 (2)	1.38 (1.05-1.82)	0
Rashes	7,007 (2)	1.61 (0.90-2.89)	0

*RRT, Renal replacement therapy.*

The authors screened 7,920 titles and abstracts and reviewed 251 full-text articles. They included 69 studies according to eligibility criteria, with a total of 30,020 subjects. Twenty-eight studies evaluated starch solutions, 20 dextrans, 22 albumin or fresh frozen plasma, and 7 gelatins.

There was no mortality benefit for any colloid over crystalloids at any of the mortality endpoints, end of follow-up, within 30 days, or within 90 days. Subjects who received starches had a higher incidence of blood transfusion (RR 1.19; 95% confidence interval [CI] 1.02 to 1.39), renal replacement therapy (RR 1.30; 95% CI 1.14 to

administered for a known nutritional deficiency, preoperative hydration, and fluids administered specifically for intracranial pressure control after head injury. Primary outcomes measured were all-cause mortality at the end of follow-up, within 30 days, and within 90 days. Secondary outcomes were transfusion of blood products, renal replacement therapy, and adverse events, including allergic reactions, itching, and rashes.

## DATA EXTRACTION AND SYNTHESIS

Three authors screened the titles independently in pairs, using Covidence software (Melbourne, Victoria, Australia) and standard data extraction forms to select relevant references from the search results. A fourth author was consulted to resolve disagreements between paired reviewers. Full texts were reviewed for inclusion and exclusion criteria. Dichotomous data were collected for each outcome measure (ie, number of subjects who died in each group at the end of follow-up). Review Manager (version 5; Nordic Cochrane Centre, Copenhagen, Denmark) was used to calculate risk ratios (RRs) with the Mantel-Haenszel model, as well as a random-effects statistical model for variation among subject groups. Risk of bias was assessed for each study with the Cochrane Risk of Bias Tool, including the following domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and baseline characteristics. Selective reporting and publication bias were assessed with clinical trial registers and prospectively published protocols. Heterogeneity was calculated with the  $I^2$  statistic and  $\chi^2$  test.

1.48), and itching (1.38; 95% CI 1.05 to 1.82) (Table).

## Commentary

Colloids have previously been shown to confer no mortality benefit over crystalloids for fluid resuscitation of critically ill patients; however, the need remains for a rapid and reliable intravascular volume expander.<sup>1</sup> This review found no mortality benefit for colloids over crystalloids for critically ill patients. In addition, starches may even carry a risk of harm and adverse effects, including itching and a greater need for blood transfusions and renal replacement therapy.<sup>2</sup>

However, fluid resuscitation is rarely the definitive therapy for critically ill patients. It is a temporizing measure to bridge patients to either definitive therapy or resolution of their critical illness. Therefore, although this review did not find a mortality benefit with colloids over crystalloids when used in critically ill patients overall, unique cohorts of patients may benefit from colloids. For instance, the Prehospital Air Medical Plasma (PAMPer) trial, a randomized controlled trial of 501 injured patients at risk for hemorrhagic shock, found a mortality benefit at 30 days with out-of-hospital administration of thawed plasma.<sup>3</sup> Intravenous albumin has been shown to reduce mortality and renal impairment among patients with cirrhosis and spontaneous bacterial peritonitis.<sup>4</sup> Although a mortality benefit was

not found, the Albumin Italian Outcome Sepsis (ALBIOS) trial found a reduced time to stopping vasopressors with administration of albumin to patients in severe sepsis or septic shock.<sup>5</sup> Last, the type of crystalloid, balanced versus nonbalanced, may affect outcomes in critically ill patients.<sup>6</sup>

Although this was a rigorous search and analysis of the literature, a few limitations to the results exist. First, none of the results had high certainty of evidence. Second, although some studies evaluated emergency department (ED) patients, the analysis did not examine the effect in critically ill ED patients being acutely resuscitated. Third, all critically ill patients and their mixed conditions were pooled; therefore, specific conditions, such as trauma or sepsis, were not specifically examined.

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3. Sperry JL, Guyette FX, Brown JB, et al. Prehospital plasma during air medical transport in trauma patients at risk for hemorrhagic shock. *N Engl J Med*. 2018;379:315-326.
4. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med*. 1999;341:403-409.
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